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

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)
	Dialectical Behavioral Therapy	No Recommendation, Insufficient Evidence (I)

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	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)
	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)	

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	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	
	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	

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	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)
Allied Health Interventions	Massage	No Recommendation, Insufficient Evidence (I)
	Acupuncture	No Recommendation, Insufficient Evidence (I)

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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].

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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.

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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

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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].

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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].

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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.

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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].

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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.

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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.

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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

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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

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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

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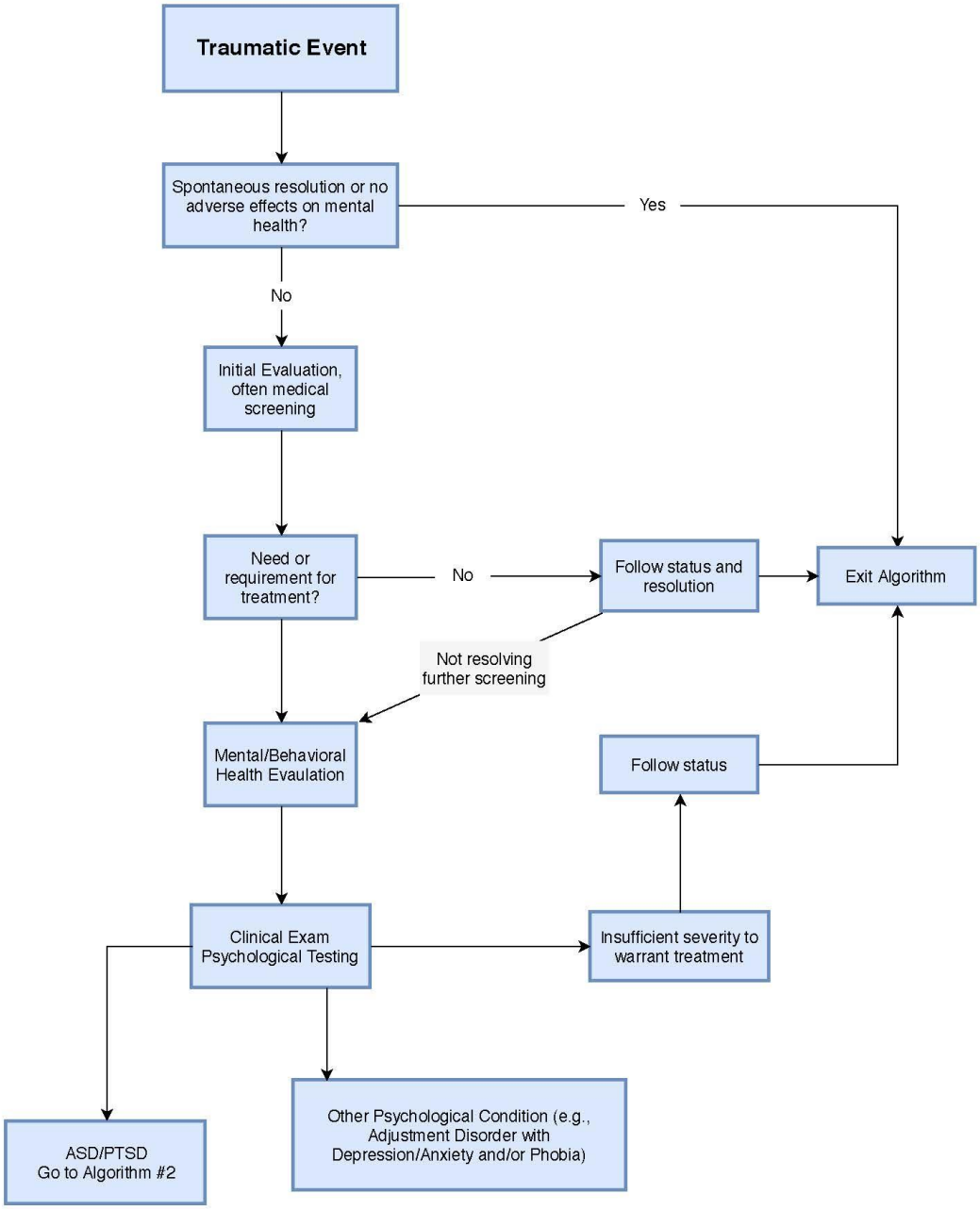
the wake of psychologically traumatic events [82, 84, 86, 87]. This final component of the discussion illustrates again the complex and multidimensional nature of PTSD.

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].

Algorithm

PTSD Algorithm 1



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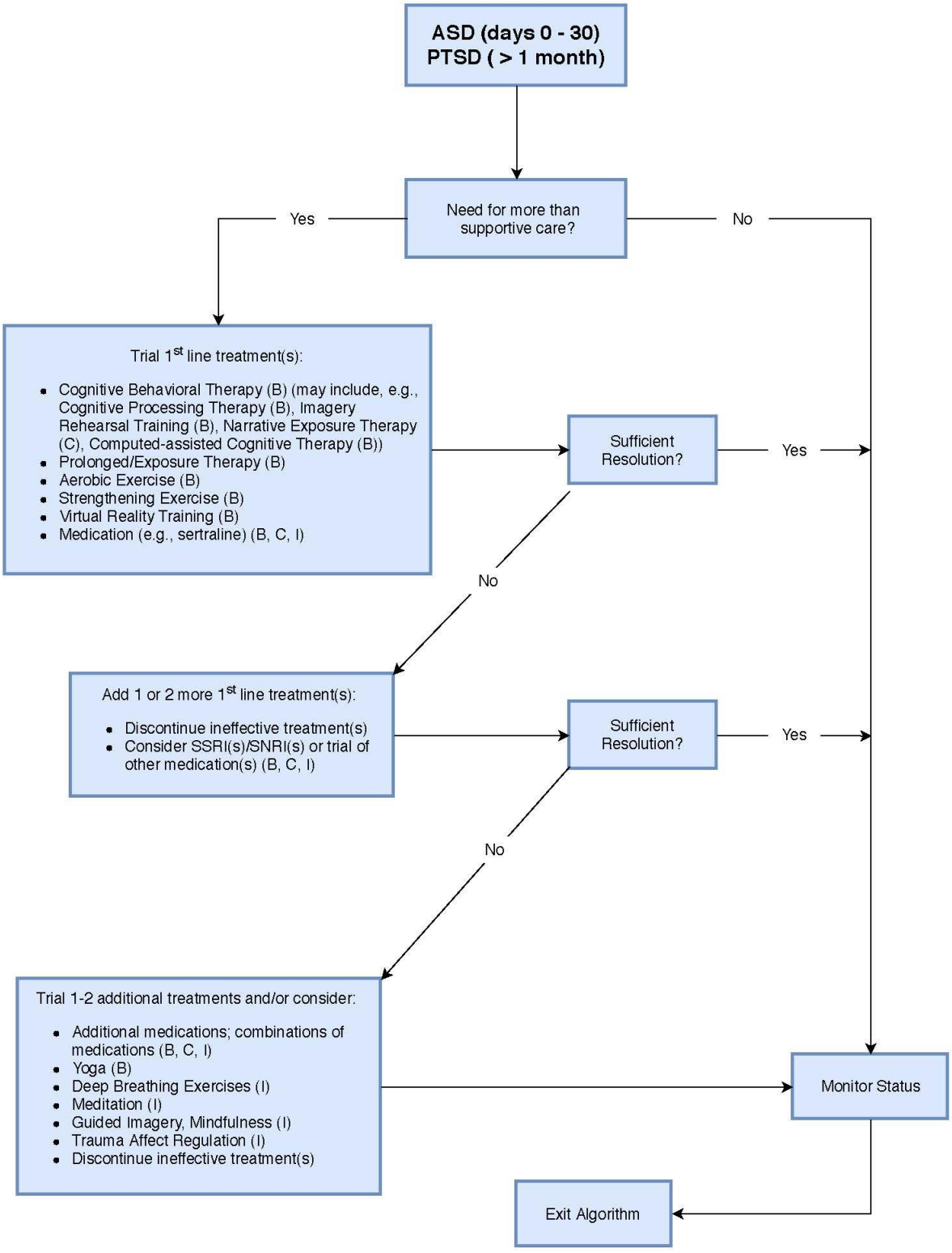
PTSD Algorithm 2



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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.

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

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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). 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.

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

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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

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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.

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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).

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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).

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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

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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.

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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 who 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.

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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].

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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.

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Evidence for the Use of PTSD Screening Tools and Tests

Author Year (Score):	**Dickstein 2015 (score=7.5)**
Category:	Posttraumatic Stress Disorder Checklist
Study type:	Screening
Conflict of Interest:	No COI. Sponsored by the VA Health Service Research and Development Project and by the Marine Corps and the Navy Bureau of Medicine and Surgery.
Sample size:	N = 1,016 Marines and sailors who were on active-duty and deployed to Operations Iraqi and Enduring Freedom (OIF/OEF)
Source of Trauma:	Trauma from military deployment
Age/Sex:	Mean age: 23.36 years; 1,016 males, 0 females
Diagnoses:	Posttraumatic stress disorder (PTSD) and partial PTSD (P-PTSD)
Comparison:	Participants completed both the Posttraumatic Stress Disorder Checklist (PCL) and the Clinician-Administered Scale (CAPS) 3 months after returning from OIF/OEF. PCL cutoffs were compared to three CAPS-based classifications - full PTSD, stringent P-PTSD, and lenient P-PTSD
Results:	Comparison of cutoffs for PCL and CAPS: Full PTSD - sensitivity = 0.60, specificity = 0.97, positive predictive power = 0.40, Stringent P-PTSD - sensitivity = 0.56, specificity = 0.97, positive predictive power = 0.57, Lenient P-PTSD - sensitivity = 0.58, specificity = 0.97, positive predictive power = 0.66
Conclusion:	"Findings suggest that the PCL cutoff that is optimally efficient for detecting PTSD in active- duty Marines and Sailors is substantially lower than the score of 50 commonly used by researchers. In addition, findings provide scores useful for identifying P-PTSD in returning service members."
Comments:	Data support the diagnostic utility of the Posttraumatic Stress Disorder Checklist (PCL) in an active duty military population.

Author Year (Score):	**Quintana 2012 (score=7.5)**
Category:	Composite International Diagnostic Interview (CIDI 2.1)
Study type:	Screening
Conflict of Interest:	No mention of COI. Sponsored by FAPESP.
Sample size:	N = 67, 28 from a specialized outpatient unit for psychiatric diagnosis of PTSD on DSM-4 criteria, 39 volunteers who experienced at least one traumatic event
Source of Trauma:	Trauma source from death of a loved one, witnessing death or violence, physical assault, witnessing violence, childhood violence
Age/Sex:	Mean age: 39.0 years; 24 males, 43 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Participants completed both the Composite International Diagnostic Interview (CIDI 2.1) via DSM-4 criteria and the Structured Clinical Interview (SID)

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Results:	CIDI 2.1 compared to SID: sensitivity = 51.5%, specificity = 94.1%, positive predictive power = 89.5%, negative predictive value = 66.7%, misclassification rate = 26.9%
Conclusion:	"The CIDI 2.1 demonstrated low validity coefficients for the diagnosis of PTSD using DSM IV criteria when compared to the SCID. The main source of discordance in this study was found to be the high probability of false-negative cases with regards to distress and impairment as well as to avoidance symptoms."
Comments:	Data suggest the Composite International Diagnostic Interview (CIDI 2.1) showed low accuracy for PTSD compared to the Structured Clinical Interview (SID)

Author Year (Score):	**Mouthaan 2014 (score=7.0)**
Category:	SPAN, Trauma Screening Questionnaire, Impact of Event Scale-Revised (IES-R)
Study type:	Screening
Conflict of Interest:	No COI. Sponsored by the Netherlands Organization for Health Research and Development and Stichting Achmea Slachtoffer en Samenleving, Aid to Victims
Sample size:	N = 311 who acquired a traumatic injury within 72 hours, injuries sustained in a traumatic event according to DSM-4 A1 criterion for PTSD
Source of Trauma:	Trauma from injury
Age/Sex:	Mean age: 44.9 years; 187 males, 124 females
Diagnoses:	Chronic Posttraumatic Stress Disorder
Comparison:	PTSD diagnosis confirmed by the Clinician-Administered Scale (CAPS). All participants were administered the SPAN (Startle, Physiological arousal, Anger, and Numbness) scale, the Trauma Screening Questionnaire, and the Impact of Event Scale-Revised (IES-R)
Results:	With 80% sensitivity, the SPAN had a specificity = 0.64, positive predictive value (PPV) = 0.08, negative predictive value (NPV) = 0.99, TSQ had specificity = 0.59, PPV = 0.19, NPV = 0.98, and IES-R had specificity = 0.72, PPV = 0.15, NPV = 0.99
Conclusion:	"The SPAN, TSQ and IES-R show similar accuracy in early detection of individuals at risk for PTSD, despite differences in number of items. The modest specificities and low positive predictive values found for all instruments could lead to relatively many false positive cases, when applied in clinical practice."
Comments:	Data suggest that while all 3 screening tools (The SPAN, TSQ, and IES-R) have similar accuracy for detecting PTSD, modest specificites and low positive predictive values may lead to large numbers of false positives.

Author Year (Score):	**de Bont 2015 (score=7.0)**
Category:	Trauma Screening Questionnaire
Study type:	Screening
Conflict of Interest:	No COI. Sponsored by the Dutch Support Foundation 'Stichting tot Steun VCVGZ'.

Sample size:	N = 2,608 patients in secondary or tertiary mental health care with diagnosis of psychotic disorder or mood disorder with psychotic features (DSM-4-TR)
Source of Trauma:	Trauma from witnessing trauma, sexual and physical abuse, accidents, disaster, and war
Age/Sex:	Mean age: 41.9 years; 1,278 males, 1330 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were administered the Trauma Screening Questionnaire (n=2,608). Those with evaluated PTSD scores (TSQ ≥ 6) were given the Clinician-Administered Scale (CAPS) for evaluating PTSD and psychotic disorder was evaluated by the Mini-International Neuropsychiatric Interview-Plus (MINI-Plus) (n=455)
Results:	TSQ cutoff score of 6 yielded mean predictive values: sensitivity (78.8%), specificity (75.6%), and 44.5% correct positive and 93.6% correct negative predictions
Conclusion:	"The TSQ seems to be a valid screening tool for PTSD in patients with a psychotic disorder."
Comments:	Data suggest the TSQ appears appropriate for the screening of PTSD in individuals with a psychotic disorder.

Author Year (Score):	**Kessler 2013 (score=7.0)**
Category:	Composite International Diagnostic Interview Screening Scales (CIDI-SC)
Study type:	Screening
Conflict of Interest:	Sponsored by the Department of the Army and the US Department of Health and Human Services, National Institutes of Health and the National Institute of Mental Health. Authors Colpe and Schoenbaum are employees of NIMH.
Sample size:	N = 460 with active duty Army personnel
Source of Trauma:	Trauma from military exposure
Age/Sex:	No mention of mean age or sex distribution
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Subsample of the Army STARRS All-Army Study (AAS) cross-sectional study. Subsample interviewed within two weeks of completing the AAS study. The subsample was administered the international diagnostic interview screening scales (CIDI-SC) and the posttraumatic stress disorder checklist (PCL). Clinical reappraisal was completed with a modified Research Version, Non-Patient Edition of the Structured Clinical Interview for DMS-4 (SCID-I)
Results:	Diagnostic thresholds set to equalize false positives and negatives. Individual-level concordance was good between CIDI-SC/PCL and SIC diagnoses on diagnostic thresholds. Area under the curve (AUC) = 0.69-0.79.
Conclusion:	"Perhaps the more striking result in light of the challenging Army STARRS field conditions is that the positive CIDI-SC/PCL operating characteristics for dichotomous versions of the scales designed to optimize aggregate concordance with SCID prevalence estimates are generally quite good."

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Comments:	Data suggest good concordance between CIDI-SC/PCL and SCID increasing for PTSD and other disorders.

Author Year (Score):	**Yeager 2014 (score=7.0)**
Category:	Posttraumatic Stress Disorder Checklist
Study type:	Screening
Conflict of Interest:	Sponsored by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development, and the National Center for Research Resources. No mention of COI.
Sample size:	N = 858 veterans who made a healthcare visit during fiscal year 1999
Source of Trauma:	Trauma from military exposure
Age/Sex:	Mean age: 59.6 years; 679 males, 179 females
Diagnoses:	Posttraumatic stress disorder
Comparison:	All participants completed the Posttraumatic Stress Disorder Checklist (PCL) and the Clinician-Administered Scale (CAPS). Participants grouped by age for analysis: age 21-49, age 50-64, and age 65+
Results:	Optimal PCL cutscore for ages 21-49 = 43, ages 50-64 = 34, and ages 65+ = 24. Area under the curve high for all three age groups (87.55% - 88.26%).
Conclusion:	"Recommend use of lower PCL cutscore for older Veterans Administration primary care patients."
Comments:	Data suggest in elderly veterans, the use of a lower cutscore when administering the PCL seems appropriate.

Author Year (Score):	**Kimerling 2004 (score=6.5)**
Category:	Breslau 7-item screen for DSM-4 PTSD
Study type:	Screening
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 134 patients from primary care clinics
Source of Trauma:	Trauma source not specified
Age/Sex:	Mean age: 51.7 years; 52 males, 82 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants completed a 7-item screening tool for DSM-4 PTSD (Breslau) and then PTSD diagnosis verified by Clinician-Administered Scale (CAPS)
Results:	7-item PTSD Screen at cutoff score of ≥ 3: sensitivity = 0.97, specificity = 0.78, score of ≥ 4: sensitivity = 0.85, specificity = 0.84. 7-item screen has test-retest reliability (r=0.84)

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Conclusion:	"Screening for PTSD in primary care is time efficient and has the potential to increase the detection of previously unrecognized PTSD."
Comments:	Data suggest a short screening tool for PTSD in primary care appears beneficial for detecting PTSD in previously unrecognized cases.

Author Year (Score):	**Han 2016 (score=6.5)**
Category:	Abbreviated six-item Posttraumatic Stress Disorder Checklist (PCL-6)
Study type:	Screening
Conflict of Interest:	Sponsored by the National Institute of Mental Health. Author Meredith received grant from National Institute of Mental Health.
Sample size:	N = 760 who receive care from primary care clinician from Federally Qualified Health Centers
Source of Trauma:	Trauma source not specified
Age/Sex:	Mean age: 40.76 years; 179 males, 581 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were administered an abbreviated six-item version of the Posttraumatic Stress Disorder Checklist (PCL-6). PTSD diagnosis was verified by the Clinician-Administered Scale (CAPS)
Results:	Cutoff scores of 15 or lower yields negative predictive value of > 0.90 via PCL-6. Cutoff value of 24 or higher have somewhat high positive predictive value of > 0.80. Strong monotonic relationship between scores and probability of meeting CAPS diagnostic criteria
Conclusion:	"No single cutoff on PCL-6 scores has acceptable reliability on both false positive and false negative simultaneously. An ordinal decision rule (low risk: 12 or less, medium risk: 13 to 16, high risk: 17 to 25 and very high risk: 26 and above) can differentiate the risk of PTSD…"
Comments:	Data suggest the PCL-6 is both cost-effective and feasible to administer as a PTSD screen in primary care settings.

Author Year (Score):	**Dekkers 2010 (score=6.5)**
Category:	Trauma Screening Questionnaire
Study type:	Screening
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 100 victims of civil traumas
Source of Trauma:	Trauma from witnessing crimes, violence, sexual assault, and car accidents
Age/Sex:	Mean age: 37.0 years; 36 males, 64 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants received the Trauma Screening Questionnaire (n=100). One month later the sample was contacted to complete the Clinician-Administered Scale (CAPS), however only 76 individuals completed it

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Results:	Cut-off score of 7 via TSQ correctly identified most subjects with PTSD. Sensitivity = 0.87, specificity = 0.69, positive predictive power = 0.69, negative predictive power = 0.89
Conclusion:	"This study indicants that the Dutch version of the TSQ is a useful instrument for identifying future cases of PTSD."
Comments:	Mixed population of sexual and non-sexual assaults, motor vehicle accidents, and other. Data suggest the TSQ was useful as a screening tool for PTSD in Dutch persons.

Author Year (Score):	**Yeager 2007 (score=6.5)**
Category:	Posttraumatic Stress Disorder Checklist, SPAN
Study type:	Screening
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 840 veterans who made a health care visit during fiscal year 1999
Source of Trauma:	Trauma source not specified
Age/Sex:	Mean age: 59.6 years; 664 males, 176 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were given the Posttraumatic Stress Disorder Checklist (PCL) and the SPAN screen. PTSD diagnosis was confirmed by the Clinician-Administered Scale (CAPS)
Results:	Slight significant difference ($p < 0.0006$) in diagnostic ability between PCL (Area under the curve [AUC] = 0.882) and SPAN (AUC=0.837)
Conclusion:	"Clinicians and researchers should consider lower cutoff scores for the PCL, but the originally suggest cutoff score for the SPAN is appropriate."
Comments:	Data suggest PCL is preferred for PTSD screening over the SPAN unless time constraints make the PCL less attractive.

Author Year (Score):	**Ehring 2007 (score=6.5)**
Category:	Posttraumatic Stress Diagnostic Scale
Study type:	Screening
Conflict of Interest:	Sponsored by Wellcome Prize Studentship and Wellcome Trust Progamme, and Wellcome Trust Principal Fellowships. No mention of COI.
Sample size:	N=775
Source of Trauma:	Trauma from Motor Vehicle Accident (MVA) or a serious physical or sexual assault.
Age/Sex:	Mean age: 35.6 years; 436 males, 339 females.
Diagnoses:	Posttraumatic Stress

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Comparison:	Sample 1 (n=101): who had experience MVA 3-12 months before the study vs. Sample 2 (n=76): participant who had been seriously physically or sexually assaulted 3 months to 7 years before the study vs. Sample 3 (n=140): MVA survivors who were interviewed and completed self-report measures at 2 week and 6 months after accident vs. Sample 4 (n=205): survivors of serious physical or sexual assault who were interview and completed self-report at 2 weeks and 6 months after the assault vs. Sample 5 (n253): MVA survivors recruited 3 months after the accident. Participants completed self-report measures in the second month and at 3 months, and completed a diagnostic interview at 3 months.
Results:	SPAN recommended cutoff of 5, all studies met the minimum quality except sample 1, which result in a lower sensitivity (0.68). All four samples met the PDS total score with a cutoff of 18.New 8-item PDS Subscale cutoff of 9 with all samples meeting the standards.
Conclusion:	"[T]he study suggested that if the full PDS can be given, the symptom cluster scoring plus cutoffs of 18 and 20 performed best in predicting current and future PTSD, respectively."
Comments:	Data suggest no single tool to screen for PTSD risk exists such that utilization of validated screening instruments is important.

Author Year (Score):	**Kimerling 2014 (score=6.0)**
Category:	Participants with PTSD: Composite International Diagnostic Interview (CIDI 3.0)
Study type:	Screening
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 160 female veterans from the Vietnam-era
Source of Trauma:	Trauma from military exposure
Age/Sex:	Mean age: 66.7 years; 0 males, 160 females
Diagnoses:	Lifetime and recent (within the last year) PTSD
Comparison:	All participants were given the Composite International Diagnostic Interview (CIDI 3.0). PTSD diagnosis was assessed by the Clinician-Administered Scale (CAPS) as well
Results:	CIDI correctly identified 78.8% of lifetime PTSD cases (k = 0.56) and 82.0% of recent PTSD (k = 0.51). Sensitivity = 0.61, specificity = 0.91 for lifetime PTSD. Sensitivity = 0.71, specificity = 0.85, recent PTSD
Conclusion:	"Results suggest that the CIDI has good utility for identifying PTSD, though it is a somewhat conservative indicator of lifetime PTSD as compared to the CAPS."
Comments:	Data suggest the CIDI 3.0 PTSD is good in identifying PTSD but is not as good as the CAPS in identifying lifetime PTSD.

Author Year (Score):	**McDonald 2014 (score=6.0)**
Category:	Participants with PTSD: Davidson Trauma Scale
Study type:	Screening

Conflict of Interest:	Sponsored by the VA Mid-Atlantic Mental Illness Research, Education, and Clinical Center, the Department of Veterans Affairs, and a Department of Veterans Affairs, Rehabilitation Research and Development. COI, one or more of the authors have received or will receive benefits for personal or professional sue.
Sample size:	N = 804 military personnel and veterans who participated in the Mid-Atlantic Mental Illness Research, Education and Clinical Center Recruitment Database for the Study of Post-Deployment Mental Health
Source of Trauma:	Trauma from military exposure
Age/Sex:	Median age: 37 years; 636 males, 168 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Structured Clinical Interview of DSM-4-TR Axis I Disorders: Patient Edition (SCID I/P, Version 2.0) as well as the Davidson Trauma Scale (DTS).
Results:	Cut scores from 68-72 had equivalent accuracy (k = 0.54) with specificity = 0.94 and specificity = 0.60-0.63. Additional cute score to symptom cluster methods improved specific and positive predictive power.
Conclusion:	"As expected, adding a cut score criterion to SCM improved specificity and positive predictive power."
Comments:	Data suggest the addition of a cut score criterion to symptom cluster criteria improved the specificity and positive predictive power. A cutscore of 68-72 provided optimal accuracy.

Author Year (Score):	**Freedy 2010 (score=6.0)**
Category:	Participants with PTSD: PTSDS Symptom Checklist – Civilian Version, Span, Breslau's Scale, Primary Care PTSD screen
Study type:	Screening
Conflict of Interest:	Sponsored by the Office of Research and Sponsored Programs at the Medical University of South Carolina in Charleston (JRF). More than one other works at the University of South Carolina.
Sample size:	N = 411 from the Family Practice Center of Trident/Medical University of South Caroline Family Medicine Residency
Source of Trauma:	Trauma source not specified
Age/Sex:	No mean age reported, majority of participants between the ages of 18 to 44; 72 males, 339 females
Diagnoses:	Past month PTSD
Comparison:	All participants were administered the following: PTSD Symptom Checklist (PCL-C), the Primary Care PTSD screen (PC-PTSD), Breslau's scale, and SPAN. PTSD diagnosis confirmed by the Clinician-Administered Scan (CAPS)
Results:	Area under the curve (AUC) values: PCL = 0.897, SPAN = 0.806, Breslau's scale = 0.886, PC-PTSD = 0.885
Conclusion:	"The PC-PTSD screening test (four items) appeared to be the best single screening test. There are few studies to establish the utility of PTSD screening tests within civilian primary care."

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Comments:	Data suggest all 4 PTSD screening tools were adequate with the PC-PTSD (four item test) being the best.

Author Year (Score):	**Gore 2008 (score=6.0)**
Category:	Participants with PTSD: Single-item PTSD screener (SIPS)
Study type:	Screening
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 3,234 from military primary clinics
Source of Trauma:	Trauma source not specified
Age/Sex:	No mean age reported, age range from 18 to 65 years; 1972 males, 1262 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	3,234 were administered the single-item PTSD screener (SIPS) as well as the Primary Care PTSD screen. 213 patients were selected to complete the Posttraumatic Stress Disorder Checklist and a structured diagnostic interview
Results:	Area under the curve (AUC): PC-PTSD = 0.89, SIPS = 0.77
Conclusion:	"A single, user-friendly primary care PTSD screening question with three response options, while sensible and worth further investigation, failed to offer sound test characteristics for PTSD screening."
Comments:	Data suggest SIPS is not as good as the PC-PTSD in terms of sensitivity and specificity for screening of PTSD.

Author Year (Score):	**Hanley 2013 (score=6.0)**
Category:	Participants with PTSD: Primary Care-PTSD Screen, Posttraumatic Stress Disorder Checklist-Civilian Version (PCL-C)
Study type:	Screening
Conflict of Interest:	No COI. No mention of sponsorship.
Sample size:	N = 1,347 patients hospitalized for injury (level I trauma center)
Source of Trauma:	Trauma from motor vehicle crash, gunshot wounds, falls, assault, and other crashes and injuries
Age/Sex:	Mean age: 41.2 years; 956 males, 391 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were administered the Primary Care-PTSD Screen (PC-PTSD) and the Posttraumatic Stress Disorder Checklist-Civilian Version (PCL-C) after admission into the trauma center

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Results:	PCL-C screened 16.1% positively for PTSD compared to 17.2% via the PCL-C. PC-PTSD had sensitivity of 72.4% and specificity of 93.4% compared to PCL-C
Conclusion:	"In trauma patients before hospital discharge, the PC-PTSD is comparable with the PCL-C. Although some sensitivity is lost, the PC-PTSD is a shorter screen, and the loss of sensitivity may be offset by an increased frequency of administration."
Comments:	Data suggest the PC-PTSD is comparable to the PCL-C but some sensitivity is lose while ease and frequency of administration is increased.

Author Year (Score):	**Gardner 2012 (score=6.0)**
Category:	Participants with PTSD: Posttraumatic Stress Disorder Checklist
Study type:	Screening
Conflict of Interest:	No COI. Sponsored by St. John's Rehab Hospital.
Sample size:	N = 132 with burn related-injuries (127 had work-related burn injuries)
Source of Trauma:	Trauma from burn injuries
Age/Sex:	Mean age: 39.0 years; 116 males, 16 females
Diagnoses:	Clinical and Subclinical Posttraumatic Stress Disorder
Comparison:	Participants were administered the Posttraumatic Stress Disorder Checklist (PCL-C). DSM-4 diagnosis made through reviewing chart and clinical interview data.
Results:	PCL-C mean score for clinical PTSD 59.7, for subclinical PTSD 43.5. PCL-C total score of 50+ had sensitivity of 90% and specificity of 79%
Conclusion:	"Our results suggest that PCL-C is a useful screening measure for PTSD in patients with burns."
Comments:	Data suggest the PCL-C has utility for screening burn patients for PTSD.

Author Year (Score):	**Parker-Guilbert 2014 (score=6.0)**
Category:	Participants with PTSD: PTSD Checklist
Study type:	Screening
Conflict of Interest:	Sponsored by the National Institutes of Health's Building Interdisciplinary Research Careers in Women's Health program. Author Marshall is supported by this program.
Sample size:	N = 128 individuals from 64 couples
Source of Trauma:	Trauma source not specified
Age/Sex:	Mean age: 37.06 years; 64 males, 64 females
Diagnoses:	Posttraumatic Stress Disorder

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Comparison:	All patients administered the posttraumatic stress disorder checklist (PCL-S) over the phone followed by diagnostic interview for PTSD and the Clinician-Administered Scale (CAPS) 1.5 months later
Results:	PCL-S overall diagnostic efficiency values (ODE) – 0.78 for men with cut-point at 42 and 0.73 for women with cut-point of 49. ODE of 0.79 for men with cut-point of 47, 0.56 for women at cut-point of 50.
Conclusion:	"These findings suggest that use of the PCL-S to screen fro PTSD among potential study participants may lead to gender biased study results, even when separate diagnostic cut-points for men and women are used."
Comments:	Data suggest that PCL-S screen for PTSD may demonstrate gender bias even when there is implementation of sex-specific cut-points.

Author Year (Score):	**Meltzer-Brody 1999 (score=6.0)**
Category:	Participants with PTSD: SPAN, Davidson Trauma Scale
Study type:	Screening
Conflict of Interest:	Sponsored by the National Institute of Mental Health. Author Davidson received funds from the National Institute of Mental Health.
Sample size:	N = 243 participants of other trauma cohort studies
Source of Trauma:	Trauma from natural disasters, rape, and combat
Age/Sex:	Mean age: 37.0 years; 68 males, 175 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Participants were administered the SPAN screening tool as well as the Davidson Trauma Scale, the Impact of Events Scale (IES), the Sheehan Disability Scale. A structured interview of PTSD was also held
Results:	SPAN results include efficacy = 0.88, sensitivity = 0.84, specificity = 0.91, and positive likelihood ratio of 9.1. SPAN correlated significantly with the IES and the structured interview of PTSD
Conclusion:	"We found that a short four-item version of the DTS closely corresponded to the diagnosis of PTSD by structured clinical interview and believe, therefore, that it could be effectively used to screen for the diagnosis."
Comments:	Data suggest the SPAN correlates well to the Impact of Events Scale, Sheehan Disability Scale and the Structured Interview of PTSD and appears to effectively screen for PTSD.

Author Year (Score):	**Foa 2017 (score=6.0)**
Category:	Participants with PTSD: Posttraumatic Stress Diagnostic Scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship. COI, Brian Marx, Michelle Bovin, and Paola Rodriguez for their training and monitoring of the Clinician-Administered PTSD Scale and thank the staff of the Center for the Treatment and Study of Anxiety at the Perelman School of Medicine for their help with data collection.

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Sample size:	N=242 Participants with PTSD
Source of Trauma:	Trauma source includes: serious, life threatening illness, physical assault, sexual assault, military or combat related, child abuse, accident, natural disaster, and other.
Age/Sex:	Mean age: 39.54 years; 137 male, 101 female.
Diagnoses:	Posttraumatic Stress
Comparison:	Participants complete the PSSI-5 at both visit (n=162): First visit includes completing PCL-S, the BDI-II, and the STAI-T. Second Visit assess test-retest reliability. Vs. Participants completes the PSSI-5 with one visit only (n=80): Participant went to either or of the visits described above.
Results:	PDS-5 results in excellent internal consistency (α=.95) and test-retest reliability (r=.90). Convergent validity of the PDS-5 was significantly correlated with the PSSI–5 total score, $r(213) = .85$ ($p < .001$), and the PCL–S, $r(194) = .90$ ($p < .001$). Discriminant Validity of PDS-5 total severity score was significantly correlated with STAI-T $r(211) = .64$, $p < .001$, and BDI–II, $r(206) = .77$ ($p < .001$).
Conclusion:	"The results of this study indicate that the PDS–5 provides valid and reliable information regarding both probable PTSD diagnosis and PTSD symptom severity per *DSM–5* criteria. The lack of existing PTSD measures with established psychometric properties prevented the examination of concurrent validity."
Comments:	Data suggest PSSI-5 appears to be both valid and reliable to evaluate PTSD for both diagnoses and symptom severity.

Author Year (Score):	**Foa 2000 (score=6.0)**
Category:	Participants with PTSD: Clinically-Administered PTSD scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorships or COI.
Sample size:	N= 64 Patients with PTSD
Source of Trauma:	Trauma source includes, rape, sexual assault, nonsexual assault, fire/explosion, accident, and other trauma.
Age/Sex:	Mean age: 37 years; 30 males, 34 females.
Diagnoses:	Posttraumatic Stress assessed with PSS-I.
Comparison:	Group A interviewed by two clinicians (one clinicians used CAPS the other PSS-I) about trauma history. (n=39) Vs. Group B were interviewed by two Clinician but also completed a PTSD module of the SCID which is administered by a third clinician. (n=25)
Results:	Concurrent validity had a high correlation between the CAPS and PSS-I for the total sore, p= .97 (p< .001). Convergent validity assessed CAPS and PSS-I scored to PTSD section of the SCID with CAPS total score p(23) =.83, p< .001; and PSS-I total score, p(23)=.73 (p<.001).
Conclusion:	"Results of the present study suggest that the PSS-I compares favorably to the CAPS, as evidenced by internal consistency, item-total correlations, intersubscale correlations, and interviewer-rater agreement."

Comments:	Small Sample. Data suggest high degree of correlation between CAPS and PSS-I although CAPS had slightly better specificity and PSS-I had slightly better sensitivity.

Author Year (Score):	**Walters 2007 (score=5.5)**
Category:	Participants with PTSD: Trauma Screening Questionnaire, Davidson Trauma Scale
Study type:	Screening
Conflict of Interest:	No COI. No mention of sponsorship.
Sample size:	N = 562 who entered an emergency unit following an assault
Source of Trauma:	Trauma source includes assault
Age/Sex:	Mean age: 26.0 years; 476 males, 86 females
Diagnoses:	Posttraumatic stress disorder
Comparison:	All participants were given the Trauma Screening Questionnaire 1-3 weeks after entering the hospital. Participants were administered the David Trauma Scale (DTS) 1-6 months after the assault.
Results:	TSQ had sensitivity of 0.85, specificity of 0.89, negative predictive value of 0.98, and efficiency of 0.90
Conclusion:	"This study suggests that the TSQ can be used between 1 and 3 weeks after assault to help identify individuals who will develop PTSD."
Comments:	Data suggest the TSQ may be used 1-3 weeks post assault to screen for PTSD risk with good sensitivity and specificity and an approximate 90% efficiency.

Author Year (Score):	**Ouimette 2008 (score=5.5)**
Category:	Participants with PTSD: Primary Care-PTSD Screen
Study type:	Screening
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 11,230 VA primary care patients
Source of Trauma:	Trauma source from military exposure
Age/Sex:	Mean age: 62.9 years; 10,720 males, 510 females
Diagnoses:	Posttraumatic stress disorder
Comparison:	All participants were given both the Primary Care-PTSD (PC-PTSD) screen and the General Health Questionnaire (GHQ)
Results:	Best cutoff value for PC-PTSD was ≥ 2, sensitivity = 0.45, specificity = 0.96, efficiency = 0.93, positive predictive value = 0.41, negative predictive value = 0.97

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Conclusion:	"The PC-PTSD performed slightly better than the GHQ and provided unique information in identifying PTSD, suggesting that disorder specific screens are important to use in primary care settings."
Comments:	Data suggest the PC-PTSD performed a little better than the FHQ but a combination of that two screens may lead to the most useful information clinically.

Author Year (Score):	**van Dam 2013 (score=5.5)**
Category:	Participants with PTSD: Jellinek-PTSD
Study type:	Screening
Conflict of Interest:	No mention of COI. Sponsored by the Royal Netherlands Academy of Arts and Sciences.
Sample size:	N = 92 self-referrals to large substance abuse treatment center with diagnosis of substance abuse of substance dependence via DSM-4 criteria
Source of Trauma:	Trauma source included accidents, natural disaster, physical assault, sexual assault, rape, war, and violence
Age/Sex:	Mean age: 42.1 years; 70 males, 22 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	PTSD diagnosis was evaluated using the Structured Clinical Interview for DSM-4 (SCIP-I/P). Participants were also administered the Jellinek-PTSD (J-PTSD) screen, a modified version of the Primary Care Posttraumatic Stress Disorder screening questionnaire
Results:	J-PTSD had sensitivity = 0.87, specificity = 0.75, overall efficiency = 0.77
Conclusion:	"An early recognition of PTSD among SUC patients makes it possible to address PTSD symptoms in time, which may ultimately lead to an improvement of symptoms in this complex patient group."
Comments:	Data suggest the J-PTSD has good sensitivity and specificity and is efficient in screening for PTSD in SUD individuals.

Author Year (Score):	**Davidson 1997 (score=5.5)**
Category:	Participants with PTSD: Davidson Trauma Scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 353 participants from four other trauma epidemiological studies
Source of Trauma:	Trauma source included combat, rape victims and natural disaster
Age/Sex:	Mean age: 39.43 years; 205 males, 148 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were administered the Davidson Trauma Scale (DTS), the SCID, the physician-rated Global Assessment of Severity (GASP), the clinician-administered scale (CAPS), the IES, and the SCL-90-R

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Results:	DTS test-retest reliability = 0.86 (P < 0.0001), internal consistency = 0.99. DTS score of 40 lead to diagnostic accuracy of 83%
Conclusion:	"The DTS showed good reliability and validity, and offers promised as a scale which is particularly suited to assessing symptom severity, treatment outcome and in screening for likely diagnosis of PTSD."
Comments:	Mixed population of war victims, rape victims, and natural disaster survivors. Data show the DTS was reliable and moderately valid in screening for a likely PTSD diagnosis.

Author Year (Score):	**Prins 2016 (score=5.5)**
Category:	Participants with PTSD: Primary Care PTSD Screen
Study type:	Screening
Conflict of Interest:	No COI. Sponsored by a VA Health Services Research and Development grant.
Sample size:	N = 398 veterans
Source of Trauma:	Trauma source from military exposure
Age/Sex:	Mean age: 63.3 years; 382 males, 16 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Participants were administered a modified version of the Primary Care PTSD screen (PC-PTSD-5) - modified to incorporate new DSM-5 criteria. A brief psychiatric interview was also held - involving the MINI-International Neuropsychiatric Interview and Acceptability Questionnaire
Results:	PC-PTSD-5 diagnostic accuracy (area under the curve [AUC] = 0.941). Cut score of 4 lead to maximized sensitivity (0.93). Cut score of 4 maximized efficiency (0.63), and cut score of 5 maximized specificity (0.70)
Conclusion:	"The PC-PTSD-5 demonstrated strong preliminary results for diagnostic accuracy, and was broadly acceptable to patients."
Comments:	Data suggest that revised PC-PTSD-5 performed well and was well received by patients.

Author Year (Score):	**Kimerling 2006 (score=5.5)**
Category:	Primary Care-PTSD Screen
Study type:	Screening
Conflict of Interest:	Sponsored by the Veterans Health Administration's Program Evaluation and Resource Center. No COI.
Sample size:	N = 97 patients in a substance use disorder treatment clinic with substance use disorder (SUD)
Source of Trauma:	Trauma source not specified
Age/Sex:	Mean age: 47.9 years; 95 males, 2 females
Diagnoses:	Posttraumatic Stress Disorder

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Comparison:	All participants received the Primary Care PTSD screen (PC-PTSD) and the clinician-administered scale (CAPS)
Results:	PC-PTSD had test-retest reliability of r = 0.80, sensitivity of 0.91, specificity of 0.80, with cut score of 3
Conclusion:	"Screening for PTSD in SUD treatment settings is time efficient and may increase the detection of previously unrecognized PTSD."
Comments:	Data suggest the use of a PTSD screen likely to detect more SUD individuals with PTSD who have subthreshold symptoms.

Author Year (Score):	**McDevitt-Murphy 2005 (score= 5.5)**
Category:	Participants with PTSD: Trauma System Inventory (TSI)
Study type:	Screening
Conflict of Interest:	No mention of Sponsorship. COI, Meghan McDevitt-Murphy, portion of study were presented at the Association for Advancement of Behavior Therapy.
Sample size:	N=62 Participants with PTSD
Source of Trauma:	Trauma source included sexual assault, transportation accident, sudden, unexpected death of a loved one or other violent death, physical assault or assault with a weapon, life-threatening illness or injury, captivity, and other stressful event.
Age/Sex:	No mention of mean age; 7 males, 55 females.
Diagnoses:	Posttraumatic Stress assessed with CAPS.
Comparison:	Both groups PTSD (n=16) vs. Non-PTSD (n=46) went through assessment instruments (included completing the TSI, that consist of structured interviews and self-reported measures of trauma exposures.) that was administered over three session, approximately 2-3 days apart.
Results:	PTSD group had a significantly higher mean profile elevation, $F(1, 60) = 13.75$ ($p < .001$) compare to Non-PTSD group when all 13 TSI scares were used as dependent variables.
Conclusion:	"In sum, the TSI appears to be a valid measure of trauma-related symptoms. It demonstrated good correspondence with the CAPS and several well-established self-report measures of PTSD."
Comments:	Data suggest TSI had good correlation with CAPS when using 5 TSI scales there was correct PTSD classification of 85.5%

Author Year (Score):	**McDonald 2009 (score=5.0)**
Category:	Participants with PTSD: Davidson Trauma Scale
Study type:	Screening
Conflict of Interest:	No mention of COI or sponsorship.

Sample size:	N = 158 military veterans who have served post-9/11
Source of Trauma:	Trauma source from combat
Age/Sex:	Median age: 34 years; 126 males, 32 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Participants were administered the Davidson Trauma Scale (DTS), the Symptom Checklist-90-R and the Structured Clinical Interview for DSM-4-TR Axis I disorders
Results:	DTS internal consistency was good (alpha = 0.97). Area under the curve (AUC) = 0.95 for using DTS to screen those with PTSD and those without
Conclusion:	"The, results illustrate that potency of the DTS as a diagnostic aid was highly dependent on comparison group used for analyses."
Comments:	Data suggest DTS is a good tool to screen from PTSD but its accuracy is dependent upon which comparison group is used in the analyses.

Author Year (Score):	**Tiet 2013 (score=5.0)**
Category:	Participants with PTSD: Posttraumatic Stress Disorder Checklist, Primary Care-PTSD Screen
Study type:	Screening
Conflict of Interest:	Sponsored by the Department of Veterans Affairs Program Evaluation and Resource Center/Mental Health Strategic Healthcare Group. No mention of COI.
Sample size:	N = 400 outpatients from VA medical centers - three substance use disorder clinics and one general mental health clinic (158 from substance use (SUD) clinics, 242 from general mental health (MH) clinics)
Source of Trauma:	Trauma source from military exposure
Age/Sex:	Mean age: 48.48 years; 362 males, 38 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were administered the PTSD Checklist-Civilian version (PCL-C), 5 abbreviated versions of the PCL, and the Primary Care PTSD Screen (PC-PTSD)
Results:	All 7 screening tools had adequate psychometric properties to screen PTSD. Area under the curve (AUC) for SUD clinic patients range from 0.80-0.86, AUC for MH clinic patients range from 0.77-0.80
Conclusion:	"Results of this study provide confirmation of the validity of using the PCL, PC-PTSD, PC-Bliese-4, and the PCL-LS-2 to help identify PTSD among patients seen in SUD and MH treatment settings."
Comments:	Data suggest the PCL, PC-PTSD and five shortened versions of the PCL have adequate screening properties for PTSD in SUD patients.

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Author Year (Score):	**Boscarino 2011 (score=5.0)**
Category:	Participants with PTSD: New York PTSD Risk Score
Study type:	Screening
Conflict of Interest:	Sponsored by the National Institute of Mental Health, the Pennsylvania Department of Health, and the Geisinger Clinic Endowment
Sample size:	N = 3298 participants from either a World Trade Center disaster study (WTCD), a chronic pain study, and a trauma center validation study
Source of Trauma:	Trauma source from the World Trade Center disaster or other types of unspecified traumas
Age/Sex:	Mean age: 45.90 years; 1372 males, 1926 females
Diagnoses:	Posttraumatic Stress DIsorder
Comparison:	The New York PTSD Risk Score was developed by created various prediction models. The Short Screening Scale for PTSD (SSSP) and the Primary Care PTSD Screen (PCPS) were utilized to develop these prediction models
Results:	Best prediction model was PCPS alone (AUC = 0.88, specificity = 0.822, sensitivity = 0.937). The additional of care status, sleep disturbance, depression and trauma exposure lead to increased AUC (AUC = 0.943, specificity = 0.857, sensitivity = 0.931) - significant AUC improvement ($p < 0.0001$)
Conclusion:	"The New York PTSD Risk Score is a multifactor prediction tool that includes the Primary Care PTSD Screen, depression symptoms, access to care, sleep disturbance, trauma history and demographic variables and appears to be effective in prediction PTSD among patients seen in health settings."
Comments:	Data suggest the New York PTSD Risk Score is an appropriate PTSD screening tool.

Author Year (Score):	**Breslau 1999 (score=5.0)**
Category:	Participants with PTSD: Breslau's 7-symptom screen
Study type:	Screening
Conflict of Interest:	Sponsored by the NIMH. No mention of COI.
Sample size:	N = 1830 randomly sampled participants from the Detroit Area Survey of Trauma
Source of Trauma:	Trauma source not specified
Age/Sex:	No mention of mean age or sex distribution
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were assessed with a structured interview following the National Institute of Mental Health Diagnostic Interview Schedule for DSM-4 and the Composite International Diagnostic Interview 2.1. Regression analyses were used to identify a subset of items from the interview that predicted scale for PTSD
Results:	Best predictive model included five symptoms of avoidance and numbing and two symptoms of hyperarousal. Cutoff score of 4 or above led to sensitivity of 80%, specificity of 97%, positive predictive value of 71%, negative predictive value of 98%

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Conclusion:	"The short screening scale is an efficient method to screen for PTSD in epidemiologic and clinical studies, given limitations on resources and burden on respondents."
Comments:	Data suggest a shortened (7-symptom) screening scale for PTSD is an efficient tool with a sensitivity of 80% and a specificity of 97%

Author Year (Score):	**Pupo 2011 (score=5.0)**
Category:	Participants with PTSD: Clinically-Administered PTSD scale
Study type:	Screening
Conflict of Interest:	Sponsored by State of Sao Paulo Funding Agency and the Millennium Institute grant from the Brazilian research Council, MCP received a scholarship from the Ministry of Education/ COI, Professor Jair Mari a CNPq level 1 researcher, and refugees for contribution of the language and content of the paper.
Sample size:	N= 98 participants with PTSD
Source of Trauma:	Exposed to violence in the city of Sao Paulo.
Age/Sex:	Mean age: 39 years; 24 males, 74 females.
Diagnoses:	Posttraumatic Stress assessed with SCID/PTSD module.
Comparison:	Participant with PTSD (n=50): completed the BDI and BAI questionnaires and SCID-I was administered by a trained psychiatrist. Vs. Participants with no PTSD: victims of urban violence, but did not develop PTSD (n=48). Completed the BDI and BAI questionnaires and SCID-I was administered by a trained psychiatrist.
Results:	Validity comparison between the CAPS scores and SCID/PTSD module with a cutoff point of 45/46 in the CAPS scale, provided the best balance between sensitivity and specificity: sensitivity=90.0% (95% confidence interval (C.I.)=81.68%;98.3%); specificity=95.8% (95% C.I.=90.1%;100%); positive predictive value=95.7% (95% C.I.=90.1%;100%); negative predictive value=79.3 (95% C.I.=81.9%;98.4%); and misclassification rate=7.1%.
Conclusion:	"[T]he CAPS showed to be an accurate scale to identify cases of PTSD, with good reliability and high internal consistency…"
Comments:	Predominantly female participants. Data suggest CAPS as an accurate scale to identify PTSD.

Author Year (Score):	**Vaishnavi 2006 (score=5.0)**
Category:	Participants with PTSD: Clinically-Administered PTSD scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship. COI, Rita Davison, Nabila Danish, and Becky Smith for their help with screening and assessing the patients in this study. Erik Churchill for his help with the statistical analyses.
Sample size:	N=20 Patients with PTSD
Source of Trauma:	Death of husband by suicide, Assault, Rape, Brother shot, Motor vehicle accident ,Workplace accident, Unexpected death of mother, Mother beaten and left for dead, Assault while in military

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	(noncombat), Son committed suicide, Physical abuse, Witnessed shooting, Incest, Witnessed suicide attempt
Age/Sex:	Only average age provided: 18 years ≥; 3 males, 17 females.
Diagnoses:	Posttraumatic Stress
Comparison:	Patients assessed (by two trained interviewers) with both SPRINT and CAPS rate jointly (n=8) Vs Patient's assessed (by the two same trained interviewers with both SPRINT AND CAPS separately. (n=12)
Results:	The two clinicians showed no significant difference in CAPS or SPRINT scores over all 20 patients (50.1 and 46.6; P5.72) and in SPRINTscores (16.9 and 18.7, P5.57). The total CAPS and the SPRINT scores pooled over all 20 patients demonstrated a strong correlation (.781, P=.0003).
Conclusion:	"[O]ur findings do provide additional validation for the SPRINT as a brief assessment of PTSD symptoms. Although the SPRINT cannot substitute for the much more extensive CAPS, the data suggest potential utility of the SPRINT in settings where rapid assessment is desired."
Comments:	Predominately female patient, small sample. Data suggest comparable accuracy between SPRINT and CAPS for PTSD but SPRINT takes less time.

Author Year (Score):	**Calhoun 2010 (score=4.5)**
Category:	Participants with PTSD: Primary Care-PTSD Screen, Davidson Trauma Scale, SPAN
Study type:	Screening
Conflict of Interest:	No COI. No mention of sponsorship.
Sample size:	N = 220 veterans with military service post-9/11
Source of Trauma:	Trauma source from combat
Age/Sex:	Mean age: 35.7 years; 176 males, 44 females
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	All participants were administered the Primary Care-PTSD Screen (PC-PTSD), the Davidson Trauma Scale (DTS), and the SPAN. PTSD diagnosis was confirmed by a structured interview with DSM-4 criteria
Results:	Cutting score of 3 maximized PC-PTSD efficiency (efficiency = 85%, sensitivity = 83%, specificity = 85%). Area under the curve (AUC): PC-PTSD = 0.875, DTS = 0.944, SPAN = 0.931
Conclusion:	"Results suggest that the PC-PTSD is an acceptable screen for PTSD among veterans. Within primary care settings, the PC-PTSD may be most advantageously employed in the context of staged screening, given the measure's relative susceptibility of false positives."
Comments:	Data suggest the PC-PTSD may be appropriate for use in staged screening of PTSD but it is susceptible to false positives.

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Author Year (Score):	**Hunt 2017 (score=4.5)**
Category:	Participants with PTSD: Clinically-Administered PTSD scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N= 309 Patients who survived injured trauma.
Source of Trauma:	Trauma source includes Motor vehicle crash, fall, stabbing, industrial accident, recreational, blunt assault, gunshot wound, motorcycle crash, and pedestrian struck by vehicle.
Age/Sex:	Mean age: 42.03 years; 221 males, 88 females.
Diagnoses:	Posttraumatic Stress and Violent Trauma
Comparison:	Participants administered the CAPS-5 as 1 month post injury (n=139) Vs. Participants administered the CAPS-5 as 6 month post injury (n=170)
Results:	PTSD prevalence rates were not statistically significantly different in comparisons of the DSM–5 and ICD-11 in the full sample (28.5% vs. 23.6%, z = 1.4, p =.17; k = .724).
Conclusion:	"These findings indicate that the CAPS-5 can be seen as measuring 2 distinct phenomena: posttraumatic stress disorder and general posttraumatic dysphoria. This is an important contribution to the current debate on which latent factors constitute PTSD and may reduce discordance."
Comments:	Data suggest CAPS-5 to measure posttraumatic stress and post traumatic dysphoria. Data suggest the CAPS-5 may be used as well as CFA to distinguished PTSD from other mental health issues.

Author Year (Score):	**Foa 2016 (score= 4.5)**
Category:	Participants with PTSD: Clinically-Administered PTSD scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship. COI, Brian Marx, Michelle Bovin, and Paola Rodriguez for their training and o monitoring of the Clinician-Administered PTSD Scale administration, the staff of the Center for the Treatment and Study of Anxiety at the Perelman School of Medicine for their help with data collection.
Sample size:	N=242 Patient with PTSD
Source of Trauma:	Trauma source includes: serious, life threatening illness, physical assault, sexual assault, military or combat related, child abuse, accident, natural disaster, and other
Age/Sex:	Mean age: 39.54 years; 137 male, 101 females.
Diagnoses:	Posttraumatic Stress
Comparison:	Group A (n=161): participants completed two visits, schedule over 3-10 days of taking the PSSI-5 with a different interviewer at each visit to asses test-retest reliability. Vs. Group B (n=62): participants (from Pen and VAAAHS) completed two visits, schedule over 3-10 days were randomized to complete either the CAPS-5 or the PSSI-5 at the first visit and the other at the second visit.

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Results:	PSSI-5 resulted in a good test-retest reliability total score (n=141), r (141) =.87 (p< .001). PSSI-5 total severity score highly correlated with PDS-5, r(213)=.85 (p < .001), and the PCL-S, r(195) = .85 (p < .001)
Conclusion:	"In summary, the results of this study indicate that the PSSI–5 provides valid and reliable assessment of *DSM–5* PTSD diagnosis and symptom severity."
Comments:	Data suggest PDS-5 has utility for measuring DSM-5 PTSD symptoms.

Author Year (Score):	**Snyder 2009 (score=4.5)**
Category:	Participants with PTSD: Trauma System Inventory
Study type:	Screening
Conflict of Interest:	Sponsored by Research Catalyst Award to the second author, from the Office of Research and Graduate Education. No mention of COI.
Sample size:	N=221 Military veterans with PTSD
Source of Trauma:	Trauma source includes anxious, depression, intrusive experiences, defense avoidance, dissociation, impaired self-reference, anger/ irritability, sexual concerns, dysfunctional sexual behavior, tension reduction behavior.
Age/Sex:	Mean age: 52.07 years; 203 males, 18 females.
Diagnoses:	Posttraumatic Stress
Comparison:	Patient completed the M-PTSD (given to only combat-exposed participants) (n=150) with a semi-structured interview addressed psychosocial, military and trauma history vs. Patients completed the PAI (n=101, with the same interview listed above vs. Patients completed the BDI (n=99), with the same interview listed above vs. Patient completed the BAI (n=97), with the same interview listed above
Results:	TSI resulted in an acceptable internal consistency score (α=0.83).
Conclusion:	"The current study extended the Trauma Symptom Inventory's (TSI) psychometric findings through investigation with a veteran sample. The TSI performs well not only with civilian trauma victims, but also with military trauma survivors as well."
Comments:	Data suggest good performance of TSI with both civilian and non-civilian populations in detecting PTSD symptoms.

Author Year (Score):	**Hoge 2014 (score=4.0)**
Category:	Participants with PTSD: Posttraumatic Stress Disorder Checklist mapped to DMS-5, Posttraumatic Stress Disorder Checklist specific stress version
Study type:	Screening
Conflict of Interest:	No COI. Sponsored by the US Army Military Operational Medicine Research Program (MOMRP)

Sample size:	N = 1822 US infantry soldiers
Source of Trauma:	Trauma source combat
Age/Sex:	No mention of mean age;
Diagnoses:	Posttraumatic Stress Disorder
Comparison:	Posttraumatic Stress Disorder Checklist mapped to DMS-5 criteria (PCL-5) (n=911) vs. Posttraumatic Stress Disorder Checklist specific stress version (PCL-S) (n=911)
Results:	13% (224) screened positive for PTSD by PCL-S versus 12% by PCL-5 (k=0.67). For soldiers exposed to combat 19% (177) screened positive by PCL-5 versus 18% (165) by PCL-S (k=0.66). Score of 15-38 in PCL-5 had similar performance as PCL-S scores of 30-50
Conclusion:	"Our findings showed the PCL-5 to be equivalent to the validated PCL-S."
Comments:	Data suggest the original version of the PCL-S is equivalent to the new version of the PCL-5 but the newer version of PTSD symptom criteria does not always match the older version of symptom criteria.

Author Year (Score):	**Foa 1997 (score=4.0)**
Category:	Participants with PTSD: Posttraumatic Stress Diagnostic Scale
Study type:	Screening
Conflict of Interest:	Sponsored by National Institute of Mental Health (MH 42178) and National Computer Systems, Posttraumatic Stress Diagnostic Scale is available from National Computer Systems (1-800-627-7271). COI, one or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=264 Patient with PTSD
Source of Trauma:	Source of Trauma includes: accident or fire, natural disaster, nonsexual assault (known assailant), nonsexual assault (unknown assailant), sexual assault (known assailant), Sexual assault (unknown assailant)m, Combat or war zone, Sexual abuse, Imprisonment, Torture, Life-threatening illness, Other
Age/Sex:	Mean age: 38.49 years; 136 males, 112 females.
Diagnoses:	Post - traumatic Stress
Comparison:	Participants with PTSD (n=128): PTDS was re-administered to a subsample between 1 ½ and 3 weeks after the initial assessment, with a mean of 16 days Vs. Participants non- PTSD (n=120): was re-administered to a subsample between 1 ½ and 3 weeks after the initial assessment, with a mean of 16 days
Results:	The Means for the entire sample were 23.41 *(SD* = 14.68) on the total PTDS score; Re-experiencing subscale, 6.38 (SD = 4.35); Avoidance subscale, 9.23 (SD = 6.60), Arousal subscale: 7.80 (SD = 5.01)
Conclusion:	"The satisfactory validity of the PTDS was further supported by its high correlations with other measures of trauma related psychopathology. Therefore, the PTDS appears to be a useful tool for screening and assessing current PTSD in clinical and research settings."

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Comments:	Data suggest the Post traumatic Diagnostic Scale (PTDS) showed good correlation with the structured Clinical Interview (SCID) with a sensitivity of 89% and a specificity of 75%.

Author Year (Score):	**Winters 2014 (score=4.0)**
Category:	Participants with PTSD: Posttraumatic Stress diagnostic Scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship. COI: IS designed the study, LW and SF performed the analyses.
Sample size:	N=105 Participants with PSTD, and alcohol dependency.
Source of Trauma:	Trauma source includes nonsexual assault by known assailants, nonsexual assault by unknown assailants, and accidents.
Age/Sex:	Mean age: 41.3 years; 73 males, 32 females.
Diagnoses:	Posttraumatic Stress
Comparison:	Patients diagnosed with PTSD assessed with PDS (n=21) vs Patients diagnosed without PTSD assessed with PDS (n=84)
Results:	Patient with diagnosed PTSD had a significantly higher symptom severity vs. patients without PTSD (M=22.19 vs. 5.39; t(23.9) = 6.03; p<.001). Of all participants, n=87 (83%) were classifies by the PDS (.46), with a sensitivity of .57, and specificity .89.
Conclusion:	"These findings confirm previous results suggesting that the psychometric properties of self-report measures of PTSD in patients with SUDs might differ from those in the general population."
Comments:	Data suggest use of PDS in patients with concomitant alcohol abuse may need cutoff score modifications to increase the test sensitivity, thus improving diagnostic accuracy.

Author Year (Score):	**Lee 1996 (score=4.0)**
Category:	Participants with PTSD: Clinically Administered PTSD Scale
Study type:	Screening
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=125 combat veterans with PTSD
Source of Trauma:	Trauma from previous combat experience.
Age/Sex:	Mean age: 69.6 years; no mention of sex.
Diagnoses:	Posttraumatic Stress
Comparison:	Patients from selected medical outpatients clinics as control (non psychiatric group, n=87): Assessed with CAPS-1 and SCID-DTREE (computer-assisted diagnostic instrument) Interview testing time lasted around 2 hours. Vs. Patients from psychiatric out patients' clinics (n=38): Assessed the same as Control group.
Results:	Internal consistency on the CAPS-1 directed excellence (.95). An overall 93% efficiency rate- prevalence at 40%, sensitivity at 90%, and specificity at 95%.

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Conclusion:	"Even those in the psychiatric clinics did not have major problems and tended to have used these clinics only in recent years. These older veterans seemed to enjoy themselves and were eager to tell their story. The CAPS-1 appears to be a measure that reflects "problems" in this story."
Comments:	Data suggest CAPS may be used to assess PTSD in older combat veterans.

Author Year (Score):	**Bryant 2000 (score=4.0)**
Category:	Participants with PTSD: Acute Stress Diagnostic Scale (ASDS)
Study type:	Screening (Multiple studies contained in 1 reference)
Conflict of Interest:	No mention of COI. Sponsored by the National Health and Medical Research Council
Sample size:	N = 99 civilian trauma victims N = 107 survivors of bushfires in Sydney or Hobart, Australia
Source of Trauma:	Study A: Motor vehicle accidents, nonsexual assault, industrial accidents Study B: Bushfire-related trauma Study C: Subset of sample population in Study B
Age/Sex:	Study A: Mean age: 31.59 years; 65 males, 34 females. Study B: Mean age: 38.56 years; 49 males, 58 females. Study C: Mean age: 39.91 years; 32 males, 50 females
Diagnoses:	Posttraumatic Stress Disorder, Acute Stress Disorder
Comparison:	Study A: Participants administered the ASDI 2-24 days posttrauma, between 2-10 days later completed battery of self-report measures including the Dissociative Experiences Scale-Taxon (DES-T), Impact of Event Scale (IES), and Beck Anxiety Inventory (BAI) (n=99) Study B: Participants completed the ASDS between 19-24 days posttrauma, 2-7 days later completed ASDS for second time Study C: Participants contacted 6-7 month posttrauma. PTSD evaluated via the Clinician Administered PTSD Scale (CAPS).
Results:	Study A: Intercorrelations fo ASDS with Validity Measures – DES-T (0.18, $p > 0.001$), IES-Intrusion (0.81, $p < 0.001$), IES-Avoidance (0.87, $p < 0.001$), BAI (0.78, $p < 0.001$). Participants with ASD scored higher on ASDS than those without ASD (65.11 vs. 36.97, $t(97) = 6.88$, $p < 0.001$). Study B: Internal validity calculated via alpha coefficients for ASDS total and each symptom clusters. ASDS total alpha = 0.96, Dissociation alpha = 0.84, Reexperiencing alpha = 0.87, Avoidance alpha = 0.92, Arousal alpha = 0.93. ASDS total scores correlated 0.94 Study C: 13% of participants satisfied criteria for PTSD. Predictive validity based on ASDS cutoff. 90% who developed PTSD initial diagnosed with ASD. 80% of those without PTSD did not present ASD. 58% of those identified with ASD did not develop PTSD and 2% between two assessments
Conclusion:	"The ASDS shows promise as a screening instrument to identify acutely traumatized individuals who warrant more thorough assessment for risk of PTSD."
Comments:	Data suggest the ADSD has a sensitivity of 95% and specificity of 83% to accurately identify ASD by comparing it to the ASD Interview.

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Author Year (Score):	**Edmondson 2010 (score=4.0)**
Category:	Participants with PTSD: Acute Stress Diagnostic Scale (ASDS)
Study type:	Screening
Conflict of Interest:	No mention of COI. Sponsored by the National Center for Research Resources (NCRR), a component of the National Institutes of Health (NIH), and the NIH Roadmap for Medical Research
Sample size:	N = 132 adult evacuees from parishes surrounding New Orleans
Source of Trauma:	Hurricane Katrina evacuees relocated to a Red Cross Shelter in Austin Texas
Age/Sex:	Mean age: 43.0 years; 74 males, 58 females
Diagnoses:	Posttraumatic Stress Disorder, Acute Stress Disorder, Depression, Anxiety, Schizophrenia, Bipolar Disorder & Other
Comparison:	Acute Stress Disorder symptoms assessed via ASDS for all participants (n=132). Three confirmatory factor analysis (CFA) were conducted as follows: 1. 4-factor with all subscales (Dissociation, Reexperiencing, Avoidance, Arousal) 2. 3-factor with avoidance and dissociation as separate first-order factors and reexperiencing and arousal as second-order distress factor 3. 2-factor with dissociation as first-order factor and re-experiencing, arousal, and avoidance as second-order distress factor
Results:	4-factor ASDS reported not to be good fit: χ^2 (146) = 310.76 ($p < 0.01$); χ^2/df = 2.13; Bollen-Stine bootstrap χ^2 p = 0.02; Comparative fix index (CFI) = 0.86; Root-mean-square error of approximation (RMSEA) = 0.09 (90% CI (0.08–0.11)); Akaike Information Criterion (AIC) = 436.76 3-factor ASDS reported not to be good fit: χ2 (142) = 242.35 ($p < 0.01$); χ2/df = 1.71; Bollen-Stine bootstrap χ2 p = 0.14; CFI = 0.92; RMSEA = 0.07 (90% CI (0.06–.09); PClose = 0.01); AIC= 338.35 2-factor ASDS reported not a good fit: χ2 (139) = 225.77 ($p < 0.01$); χ2/df = 1.62; Bollen-Stine bootstrap χ2 p = 0.23; CFI = 0.93; RMSEA = 0.07 (90% CI (0.05–0.09); PClose = 0.03); AIC= 327.77
Conclusion:	"In spite of these limitations, the present findings represent the most thorough examination of the factor structure of the ASDS to date and provide important information on this scale, which has implications for the ASD construct itself."
Comments:	Data suggest an alternate two factor model confirms the ASD better than the original four factor model by Harvey & Bryant in 2002.

Author Year (Score):	**Fuglsang 2004 (score=3.5)**
Comments:	Data suggest a significant lack of precision in predicting who will and will not develop PTSD when comparing the ASDS to the PDS.

Author Year (Score):	**Tanja 2016 (score=3.5)**
Comments:	Data suggest direct threats appear to be more closely associated with impaired post traumatic cognitions to have a greater probability of developing into full or partial PTSD.

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Author Year (Score):	**Steele 2014 (score=3.5)**
Comments:	Data suggest short form Posttraumatic Stress Disorder Checklist (PCL) was better than the Primary Care—Posttraumatic Stress Disorder Screen (PC-PTSD) for replacing the longer PCL.
Author Year (Score):	**Reese 2012 (score=3.5)**
Comments:	Data suggest the Primary Care PTSD (PC-PTSD) screening tool plus one screen found a large number of PTSD individuals in an urban trauma setting. Unclear of what the screen is compared to or how the PTSD screen is validated.
Author Year (Score):	**Bisson 2010 (score=3.0)**
Comments:	Data question feasibility of implementing a simple screening tool for PTSD post violent crimes/trauma due to cost and poor response rate.
Author Year (Score):	**Betemps 2003 (score=3.0)**
Comments:	Data suggest a Rasch model may assist in assessing severity and identify out points in PTSD patients.
Author Year (Score):	**Blanchard 1995 (score= 2.5)**
Comments:	Data suggest changes in scoring rules for the CAPS in diagnosing PTSD in MVA victims' results in changes of prevalence estimates.
Author Year (Score):	**Hendrix 1994 (score= 2.5)**
Comments:	The PPS "may" aid in the prediction of PTSD and its associated long term impacts.
Author Year (Score):	**Ella 2006 (score=2.5)**
Comments:	Small sample with inconclusive results. Data suggest a large members of participants produced invalid TSI profiles according to ATR validity scales.
Author Year (Score):	**Luftman 2017 (score=2.0)**

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Comments:	Data suggest PTSD risk appears underreported in injured patient caregivers.

Author Year (Score):	**Edens, 1998 (score=5.5)**
Category:	Trauma Symptom Inventory
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 155 students from a university psychology department and a local community college.
Source of Trauma:	None of the participants were recruited for true sources of trauma. They were assigned to feign either an automobile accident or sexual assault under either honest or malingering conditions.
Age/Sex:	Mean age: 25.6 years; 119 males, 36 females
Diagnoses:	PTSD
Comparison:	TSI under honest conditions (N=155) vs TSI under malingering conditions (N=155)
Results:	Elevated TSI profiles on all subscales, $F(10,144) = 60.56$, $p<0.0001$. MANOVA of the three validity scales, $F(3,151) = 121.42$, $p<0.0001$. ATR score of overall correct classification rate was 87% (sensitivity = 82%, specificity = 92%).
Conclusion:	"Overall, results of this preliminary study are encouraging. Individuals who are provided with basic descriptive information about PTSD appear quite capable of successfully producing trauma-related symptomatology on the TSI. Despite being provided with this information, however, the majority of participants were unable to avoid detection on the ATR scale when attempting to malinger."
Comments:	Data suggest TSI produced good sensitivity and specificity for determining malingering and numbers of false positives were low suggesting few true PTSD individuals positives would get classified as malingerers.

Author Year (Score):	**Rosen, 2006 (score=4.5)**
Category:	Trauma Symptom Inventory
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 161 college students receiving research course credit for participating.
Source of Trauma:	None of the participants were recruited for true sources of trauma.
Age/Sex:	Mean age: 21.7 years; 60 males, 91 females
Diagnoses:	PTSD
Comparison:	TSI under honest conditions (N=60) vs TSI under malingering conditions (N=101)

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Results:	Optimal balance between sensitivity and specificity was 68.3 % and 80% using an ATR cut score of T>60 with a correct classification score of 72.7%. At Edens et al's score of T>61 for profiles with two or more elevated scales, sensitivity was 85.9% and specificity was 57.9% with false positive rate of 42%.
Conclusion:	"In this study, using an analogue design to experimentally manipulate honest and malingered responses on the TSI, we found that proposed ATR cut scores produce a significant risk of false positives. Furthermore, the functioning of proposed cut scores worsened when we used posttraumatic stress disorder relevant samples and low estimates of malingering base rates. In light of these findings, the TSI should be used with caution when assessing claims of posttraumatic stress in forensic or disability settings."
Comments:	Data suggest TSI should be used cautiously to asses PTSD claims in forensic or disability settings. It is difficult to develop a test for correctly identifying PTSD malingerers.

Author Year (Score):	**Elhai, 2005 (score=4.0)**
Category:	Trauma Symptom Inventory
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 136 participants either clinically diagnosed with PTSD or psychology students feigning PTSD.
Source of Trauma:	True trauma was sexual or physical victimization, child physical abuse, domestic violence, and adult sexual assault.
Age/Sex:	Mean age: 25.7 years; 44 males, 92 females
Diagnoses:	PTSD
Comparison:	PTSD simulators feigning either an attempt to obtain money or avoid prosecution (N=63) vs diagnosed PTSD patients (N=47)
Results:	Discriminant Function Analysis with group status as the criterion variable had a sensitivity of 47.6% and a specificity of 74.5% Overall correct classification was 59.1%.
Conclusion:	"Discriminant Function analysis using ATR revealed 75% correct patient classification but only 48% correct simulator classification, with an overall correct classification rate of 59% (positive predictive power [PPP] = .71; negative predictive power [NPP] = .51). Individual ATR cutoff scores did not yield impressive classification results, with the optimal cutoff (T score = 61) correctly classifying only 61% of simulators and patients (PPP = .66, NPP = .54). Although ATR was not developed as a malingered PTSD screen, instead serving as a general validity screen, caution is recommended in its current clinical use for detecting malingered PTSD."
Comments:	Data suggest ARS not sufficient for accurately detecting PTSD and if used for the detection of malingering, other tests should be used to test for malingering.

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Pharmacogenomic testing has been used to attempt to customize treatment for patients with PTSD [120-122].

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.

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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.

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Evidence for the Use of Education: Trauma Affect Regulation

Author Year (Score):	**Ford 2013 (score=5.5)**
Category:	Trauma Affect Regulation
Study type:	RCT
Conflict of Interest:	Sponsored by Grants from Department of Justice Office of Juvenile Justice and Delinquency Programs. No mention of COI.
Sample size:	N=72 incarcerated women with full or partial PTSD
Source of Trauma:	Physical abuse, sexual abuse, domestic violence, community violence, accident/illness trauma, sexual trauma, physical assault
Age/Sex:	Mean age: 36.2 years; 0 males, 72 females
Comparison:	TARGET group: (n=38) received trauma affect regulation guide for education and therapy in 12 75- minute group therapy sessions vs SGT group: (n=34) received supportive group therapy in 12 75-minute sessions that did not use therapeutic mechanisms (as in TARGET)
Follow-up:	No mention of follow-up.
Results:	Improvement in CAPS PTSD and CORE-OM psychosocial symptoms for both groups showed medium effect sizes. TARGET group showed small-medium effect size compared to SGT group with no change for NMR. TSI subscales showed small effect size for both treatments. Symptoms worsened in 6 SGT participants and 4 in TARGET group. Group differences showed no significance (p>.30).
Conclusion:	"TARGET was more effective than SGT in increasing sense of forgiveness toward others who have caused harm in the past. Group therapy that teaches affect regulation may enhance incarcerated women's ability to achieve affective resolution (forgiveness) while also reducing their victimization-related PTSD and associated symptoms. Experiential-focused supportive group therapy also may reduce victimization-related PTSD and associated symptoms."
Comments:	Data suggest both treatments led to decreased PTSD symptom severity and self-efficacy. TARGET better than SGT in terms of forgiveness.

Author Year (Score):	**Ford 2011 (score=4.0)**
Comments:	Some baseline differences and sparse demographic data by groups. Low compliance, high dropouts are sufficiently concerning to potentially invalidate conclusions re. possible efficacy.

Author Year (Score):	**Frisman 2008 (score=3.5)**
Comments:	Usual care bias. Some baseline characteristic dissimilarities significant attrition rates.

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Education about a disorder is routine and customary in healthcare. However, educational training goes beyond mere education and may involve teaching posttraumatic stress disorder patients skills to help deal with symptoms. Educational programs use various methods including online training to conduct motivational interviewing, teaching goal setting, and behavioral task assignments [134-136].

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.

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Evidence for the Use of Educational Training

Author Year (Score):	**Scholes 2007 (Score=4.0)**
Category:	Education
Study type:	RCT
Conflict of Interest:	Supported by a British Association for Accident and Emergency Medicine Research Grant. No mention of COI.
Sample size:	N=227 patients attended accident and emergency.
Source of Trauma:	Accident or emergency attending
Age/Sex:	Mean age: 37.3 years; 71 males, 156 females.
Comparison:	Group 1: Patients attended accident and emergency with ASDS score above cut-off point who received a self-help booklet (n=116) vs. Group 2: Patients attended accident and emergency with ASDS score above cut-off point who did not received a self-help booklet (n=111) vs. Group 3: patients with ASDS score below cut-off point who did not receive booklet (n=120).
Follow-up:	Follow-up at 6 months.
Results:	PDS severity changed indicated in time effect ($p<0.001$). Other effects were not significant in PDS severity change ($p>0.47$). Time effects were significant for anxiety and depression ($p<0.001$); and other effects were not ($p>0.43$).
Conclusion:	"This trial failed to support the efficacy of providing self-help information, as a preventative strategy to ameliorate PTSD."
Comments:	Data suggest lack of efficacy.

Author Year (Score):	**Ruzek 2014 (Score=4.0)**
Category:	Education
Study type:	RCT
Conflict of Interest:	Supported by the U.S. Army Medical Research and Materiel Command grant. No mention of COI.
Sample size:	N=168 full-time Veterans Health Administration clinicians.
Source of Trauma:	combat
Age/Sex:	Mean age: 48.8±10.4 years; 51 males, 117 females.
Comparison:	Group 1: Web based training in intervention skills including motivation enhancement, goal setting, and behavioral task assignment (n=57) vs. Group 2: web training and consultation allocated to and received intervention lasted 6 weeks with each phone-based weekly consultation lasted 45 to 60 minutes (n=55) vs. Group 3: traditional continuing training which allowed participants to freely participate any activities including local continuing conferences and other formal training, with no web training (n=56).
Follow-up:	No mention of specific follow-up time length.
Results:	Standardized patient (SP) ratings was improved in both active training groups, compared to control group ($p<0.001$). In control group, no SP change was found.
Conclusion:	"Overall, these findings support the use of web-based dissemination for large-scale training programs for trauma providers in health care delivery systems. Further studies are needed to clarify the specific role of consultation as an adjunct to web-based training."

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Comments:	Data suggest web based plus connotation group improved more than either web based alone or control groups.

Author Year (Score):	**Freyth 2010 (Score=3.5)**
Comments:	Data suggest lack of efficacy.

Author Year (Score):	**Bugg 2009 (Score=3.0)**
Comments:	Data suggest lack of efficacy.

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Exercise has been used to treat PTSD symptoms [138-140]. Those with PTSD are reportedly more likely to participate in unhealthy behaviors such as smoking, alcohol consumption, lack of exercise or have comorbid conditions such as diabetes or obesity [141-147].

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.

Evidence for the Use of Exercise

Author Year (Score):	**Rosenbaum 2014 (score=6.0)**
Category:	Exercise
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by St John of God Healthcare and by the Australian National Health and Medical Research Council.
Sample size:	N = 81 participants with DSM-IV-TR diagnosis of primary PTSD
Source of Trauma:	A majority of participants experience work-related trauma, no details specified type
Age/Sex:	Mean age: 47.8 years; 68 males, 13 females
Comparison:	Exercise group: Weekly supervised exercise sessions with two unsupervised sessions in the same week, sessions consisted of 30 minutes of resistance training along with a walking program, for 12 weeks (n=39) vs. Usual care group: combination of psychotherapy, pharmaceutical interventions, and group therapy (n=42)
Follow-up:	12 weeks after randomization
Results:	Intervention group had improved primary outcome in PTSD checklist-civilian (PCL-C) compared to the usual care group: MD = -5.4, 95% CI (-10.5 to -0.3) (p=0.04)
Conclusion:	"This study provides the first evidence that an exercise intervention is associated with reduced PTSD and depressive symptoms, reduced waist circumference, and improved sleep quality."
Comments:	Usual care bias. Usual care involved psychotherapy, medications and group therapy. Data suggest significant improvement in PTSD symptom reduction in the interventional group as well as significant between group changes in symptoms of depression, improved sleep quality as well as decreased waist circumferences.

Author Year (Score):	**Powers 2015 (score=4.5)**
Category:	Exercise
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by the National Institute on Drug Addiction.
Sample size:	N = 9 with diagnosis of PTSD via DSM-IV criteria
Source of Trauma:	No trauma source specified
Age/Sex:	Mean age: 34.0 years; 1 male, 8 females
Comparison:	Prolonged exposure (PE) therapy with an acute bout of exercise prior to each session, 12 sessions total – exercise sessions were 30 minutes each, PE sessions being 90 minutes each (n=NA) vs. Prolonged exposure therapy with no exercise prior to sessions, 12 sessions total, PE sessions being 90 minutes each (n=NA). Each treatment took 12 weeks. The comparison group sizes were not specified.
Follow-up:	No follow-up after post-treatment
Results:	Pre- and post- brain-derived neurotrophic factor (BDNF) means: PE and exercise = 1.77, 1.75, respectively. PE alone = 1.38, 3.73, respectively. Pre- and post-PTSD Symptom Scale-Interview means: PE and exercise = 42.00, 5.20. PE alone = 37.00, 8.25. PE with exercise experienced increased BDNF compared to PE alone (d = 1.08, SE = 0.72). PE with exercise experienced increased PTSD symptom reduction compared to PE alone (d = 2.65, SE = 0.92)

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Conclusion:	"This pilot study provides initial support for further investigation into exercise augmented exposure therapy."
Comments:	Pilot study with very small sample (n=9). Exercise consisted of 30 minutes of moderate intensity treadmill prior to prolonged exposure sessions for 12 total sessions. Data suggest E+PE showed improvement in PTSD symptoms and an elevated (BDNF) compared to PE alone.

Author Year (Score):	**Fetzner 2015 (score=4.0)**
Category:	Exercise
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by the Canadian Institute of Health Research Vanier Canada Graduate Scholarship and the President's Research Chair of Adult Mental Health at the University of Regina.
Sample size:	N = 33 with either primary diagnosis of full (N=25) or subsyndromal (n=8) PTSD
Source of Trauma:	Most common index traumas were death of a loved one or motor vehicle accidents
Age/Sex:	Mean age: 36.9 years; 8 males, 25 females
Comparison:	Cognitive distraction (CD) – aim to direct attention away from uncomfortable and potentially distressing somatic sensations caused by aerobic exercise, each participant watched a nature documentary and answered three questions regarding said video every five minutes (n=11) vs. Interoceptive prompts (IP) – aim to increase attention to somatic sensations from aerobic exercise, participants watched themselves in real-time video and received three IP every five minutes (n=11) vs. Exercise group – stationary bike for six 20-minute aerobic session in two weeks (n=11)
Follow-up:	Follow-up at 1 week and 1 month post-treatment
Results:	PTSD Checklist-Civilian: Effect sizes for PTSD symptom change during treatment for CD group (total d = 1.18), IP group (total d = 1.25), and exercise group (total d = 0.98). AS Index-3: Effect sizes for AS change during treatment for CD (d = 2.53), IP group (d = 0.69), and exercise group (d = 0.96). Center for epidemiological studies-depression scale: Effect size for depression change during treatment for CD (d = 0.87), IP (d = 1.02), and exercise group (d = 0.42).
Conclusion:	"Findings suggest, regardless of attentional focus, aerobic exercise reduces PTSD symptoms."
Comments:	Aerobic exercise was 2 weeks of stationary biking for 6 sessions. Data suggest aerobic exercise does improve PTSD symptoms regardless of attentional focus as was reported by 89% of all participants.

Author Year (Score):	**LeBouthillier 2017 (score=4.0)**
Category:	Exercise
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by a Canadian Institutes of Health Research Doctoral Research Award, by the University of Regina President's Chair for Academic Excellent in Adult Mental Health Research.

Sample size:	N = 56 with a diagnosis of one of the following anxiety disorders: phobias, social anxiety, panic disorder, agoraphobia, OCD, or PTSD
Source of Trauma:	No source specified
Age/Sex:	Mean age: 32.59 years; 13 males, 43 females
Comparison:	Aerobic exercise – 40 minute sessions on spin cycle (n=15) vs. Resistance training – 2-3 sets of 10-12 repetitions on various weight lifting machines (n=23) vs. Waitlist control (n=18). Exercise completed three times per week for four weeks with supervision of a personal trainer
Follow-up:	Follow-up at 1 week and 1 month
Results:	No significant change in symptoms over time in waitlist control group or in aerobic group (Cohen's d = 0.05, 95% CI (-0.26, 0.36)). Resistance training associated with reduction of symptoms (7.6 score reduction, Cohen's d = -0.39, 95% CI (-0.72, -0.07)) compared to aerobic exercise. Resistance training had significant different at 1 week (b = 3.49, 95% CI (-13.47, 19.60), p = 0.650) and 1 month follow-up (b = -2.19, 95% CI (-12.82, 7.17), p = 0.658) compared to post-intervention.
Conclusion:	"Results highlight the efficacy of different exercise modalities in uniquely addressing anxiety-related disorder symptoms and constructs."
Comments:	Mixed population of anxiety disorders including PTSD. Only a small portion of the sample had a diagnosis of PTSD (8.92%). Waitlist control bias. Partial crossover design. Relatively small sample. Data suggest both the aerobic group and the resistance training group showed improved psychological well being (decreased stress and anxiety), and the resistance group reported improved disorder specific symptoms such as anxiety sensitivity, distress tolerance and intolerance of uncertainty.

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Yoga has been used as an adjunctive therapy to address the cognitive, emotional, and physiological symptoms associated with PTSD [152-165].

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.

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† 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.

Evidence for the Use of Yoga

Author Year (Score):	**van der Kolk 2014 (score=6.5)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by the United States National Center for Complementary and Alternative Medicine (NCCAM).
Sample size:	N = 64 with chronic, treatment-resistant PTSD
Source of Trauma:	No specific source of trauma described.
Age/Sex:	Mean age: 42.9 years; 0 males, 64 females.
Comparison:	Yoga Group: 10 weeks of an hour long trauma-informed yoga class. This yoga incorporate elements of meditation and breathing techniques (n=32) vs. Control Group: 1 hour educational session weekly for ten weeks (n=32). All participants were required to engage in ongoing therapy and continue any existing pharmacological treatment
Follow-up:	No follow up after post treatment.
Results:	16 of 31 yoga participants and 6 of 29 control participants no longer met criteria for PTSD via the Clinician-Administered PTSD Scale (CAPS) ($\chi 2_1 = 6.17$, p = .013). Effect size range for decreased in CAPS – yoga, d=1.07, control d=0.66. Significant decrease from pretreatment to midtreatment (yoga – b = −9.21, t = −2.34, P = .02, d = −0.37, control – b = −22.12, t = −3.39, P = .001, d = −0.54)
Conclusion:	"Yoga significantly reduced PTSD symptomatology, with effect sizes comparable to well-researched psychotherapeutic and psychopharmacologic approaches. Yoga may improve the functioning of traumatized individuals by helping them to tolerate physical and sensory experiences associated with fear and helplessness and to increase emotional awareness and affect tolerance."
Comments:	Data suggest 10 weeks of yoga reduced PTSD symptoms compared to supportive therapy alone.

Author Year (Score):	**Rhodes 2016 (score=6.5)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No COI. No sponsorship.

Sample size:	N = 64 with chronic, treatment-resistant PTSD
Source of Trauma:	No specific source of trauma described.
Age/Sex:	Mean age: 42.9 years; 0 males, 64 females.
Comparison:	Yoga Group: 10 weeks of an hour long trauma-informed yoga class (n=32) vs. Control Group: 1 hour educational session weekly for ten weeks (n=32). All participants were required to engage in ongoing therapy and continue any existing pharmacological treatment
Follow-up:	Follow up at 1.5 years after posttreatment.
Results:	Only 49 participants from original study completed long-term follow-up. Higher frequency of yoga practice after treatment significant associated with loss of PTSD diagnosis ($r = -0.283$, $p < 0.05$) and decreased in depression symptom severity ($r = 0.348$, $p < 0.05$)
Conclusion:	"Yoga appears to be a useful treatment modality; the greatest long-term benefits are derived from more frequent yoga practice."
Comments:	Follow up to van der Kolk 2014. Data suggest continuing the practice of yoga was predictive for maintaining gains 18 months after original treatment.

Author Year (Score):	**Carter 2013 (score=6.0)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by The Art of Living Foundation.
Sample size:	N = 31 male veterans
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 58.5 years; 25 males, 0 females.
Comparison:	SKY Group: 22 hours of guided Sudarshan Kriya Yoga (SKY) modified for Veterans over 5 days, followed by a 2 hour group session for four weeks and monthly afterwards for 5 months. This yoga incorporated elements of mindfulness and psychoeducation as well as breathing techniques (n=14) vs. Control Group: 6-week wait-list, receiving the SKY intervention later on (n=11). All participants treated with multiple medications prior to yoga, which were left unaltered during study
Follow-up:	Follow-up at 6 months.
Results:	CAPS pretreatment score – Yoga group, 56.3 (SD=12.3), Control group, 56.6 (SD=18.7). CAPS posttreatment score – yoga, 42.1 (SD=18.2, $t(13)=3.19$, 95% CI (4.6-23.7), $p<0.01$). CAPS score at 6 month follow-up – yoga, 26.2 (SD=14.8, $t(13)=3.59$, 95% CI (6.4-25.5, $p<0.01$)
Conclusion:	"The results indicate that multi-component interventions with yoga breath techniques may offer a valuable adjunctive treatment for veterans with PTSD."
Comments:	Wait list control bias. Data suggest intervention group exhibited decreased CAPS scores which were maintained at 6 months. .

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Author Year (Score):	**Quiñones 2015 (score=5.0)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by the Fundación Bolivar Davivienda and Agencia Colombiana para la Reintegreación (ACR)
Sample size:	N = 100 with PTSD diagnosed via PCL-C score
Source of Trauma:	Exposure to Colombian armed conflict
Age/Sex:	No mean age provided 73 males, 27 females.
Comparison:	Intervention Group: Satyananda Yoga classes twice a week for 16 weeks, plus mandatory ordinary assistance protocol for reintegrating individuals. This yoga incorporate elements of mindfulness, breathing techniques and relaxation (n=50) vs. Mandatory ordinary assistance protocol only, while on the wait list for yoga intervention (n=50)
Follow-up:	No follow-up after post-treatment.
Results:	Pretreatment and posttreatment PCL-C Total scores for control and yoga groups, respectively: 54.9 to 48.26 (unstandardized regression coefficient b for score change = 0.20, $p < 0.005$, $t = 3.407$), 56.3 to 38.84 ($b = 0.50$, $p < 0.001$, $t = 9.593$)
Conclusion:	"The data suggest that Satyananda Yoga methodology is an effective therapy for reintegrating adults diagnosed with PTSD. Further research is needed in order to evaluate prolonged effects of this alternative therapy."
Comments:	Data suggest Satyananda Yoga may be effective for reducing PTSD symptoms.

Author Year (Score):	**Reinhardt 2017 (score=4.5)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by the US Department of Defense Awards and the Institute of Extraordinary Living of the Kripalu Center for Yoga & Health.
Sample size:	N = 51 with PTSD diagnosis
Source of Trauma:	No specific source of trauma mentioned
Age/Sex:	Mean age: 47.76 years; 45 males, 6 females.
Comparison:	Yoga Intervention90 minute sessions of Kripalu Yoga twice a week for 10 consecutive weeks. This yoga incorporate elements of breathing, meditation and relaxation (n=26) vs Control Group: No treatment, assessment only. These participants were offered the opportunity to do the yoga intervention after completing the study (n=25). Some of the participants had ongoing medication or psychotherapy treatments
Follow-up:	Follow-up at 10 weeks.
Results:	CAPS Past Week pre and post scores for yoga and control groups, respectively: 70.33 to 58.22, 67.33 to 61.17. Repeated measures analysis of variance for group differences: by group – $F_{1,13} = 0.00$ ($p = 1.0$), by time – $F_{1,13} = 3.41$ ($p = 0.09$), by group*time – $F_{1,13} = 0.36$ ($p = 0.56$). CAPS Past Month pre and post scores for yoga and control groups, respectively: 73.33 to 63.56, 69.17 to 67.83. Repeated measures analysis of variance for group differences: by group – F1,13 = 0.00 ($p = 1.0$), by time – F1,13 = 0.93 ($p = 0.35$), by group*time – F1,13 = 0.54 ($p = 0.48$).

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Conclusion:	"These results are consistent with recent literature indicating that yoga may have potential as a PTSD therapy in a veteran or military population. However, additional larger sample size trials are necessary to confirm this conclusion."
Comments:	Small sample. Waitlist control bias. Both the yoga and control group showed improvement in re-experiencing PTSD symptoms.

Author Year (Score):	**Mitchell 2014 (score=4.0)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 38 with subthreshold or full PTSD diagnosis via the PTSD Symptom Scale-Interview
Source of Trauma:	Physical assault, sexual abuse, sexual assault, unexpected death of a loved one
Age/Sex:	Mean age: 44.4 years; 0 males, 38 females.
Comparison:	Kripalu-based Hatha yoga, 75 minutes sessions, given the option to either attend 12 weekly sessions of 12 biweekly sessions over 6 weeks. This yoga incorporate elements of mindfulness and breathing techniques (n=20) vs. Control group: Met once per week for 12 weeks in groups of 4-5 to complete questionnaires (n=18)
Follow-up:	Follow-up at 1 month.
Results:	PTSD Checklist total score slope means for yoga and control groups, respectively: *B* = -0.10, t = -2.96 (p = 0.003), *B* = -0.09, t = -2.42 (p = 0.02).
Conclusion:	"Although more research is needed, yoga may be an effective adjunctive treatment for PTSD."
Comments:	Sparse methods. All female population. Pilot study. Data suggest yoga diminished hyperarousal but control group showed decreased anxiety and re-experiencing symptoms.

Author Year (Score):	**Reddy 2014 (score=4.0)**
Category:	Yoga
Study type:	RCT
Conflict of Interest:	No COI. No mention of sponsorship.
Sample size:	N = 38 with subthreshold or full PTSD diagnosis via the PTSD Symptom Scale-Interview
Source of Trauma:	Physical assault, sexual abuse, sexual assault, unexpected death of a loved one
Age/Sex:	Mean age: 44.4 years; 0 males, 38 females.
Comparison:	Kripalu-based Hatha yoga, 75 minutes sessions, given the option to either attend 12 weekly sessions of 12 biweekly sessions over 6 weeks. This yoga incorporated elements mindfulness and dialectical behavioral therapy (n=20) vs. Control group: No intervention. Participants completed weekly assessments and were offered yoga classes after the study (n=18)

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Follow-up:	Follow-up at 1 month.
Results:	At follow-up 69% of yoga participants reported a decrease in PTSD symptoms and over 80% of control participants reported no difference in or an increase in symptoms. 92% of yoga participants reported better coping of symptoms while 9% of control participants the same (Fisher's exact test t = 0.000016, p < 0.001)
Conclusion:	"Results from this pilot study suggest that a specialized yoga therapy may play a role in attenuating the symptoms of PTSD, reducing risk of alcohol and drug use, and promoting interest in evidence-based psychotherapy."
Comments:	Data suggest yoga may reduce symptoms of PTSD. Secondary analysis for Mitchell 2014.

Author Year (Score):	**Jindani 2015 (score=3.5)**
Comments:	Waitlist control bias. Data suggest both groups showed PTSD symptoms improvement with greater improvement in yoga group.

Author Year (Score):	**Dick 2014 (score=3.5)**
Comments:	Data suggest yoga may decrease a suppression of expression in PTSD compared to control.

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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.

Evidence for the Use of Group Therapy

Author Year (Score):	**Sautter 2015 (score=5.0)**
Category:	Group Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by Merit Review Grant from VA Research Rehabilitation and Development program and a supplemental funding award from South Central Mental Illness Research Education and Clinical Center to Frederic J. Sautter. No mention of COI.
Sample size:	N=69 OIF and OEF veterans with PTSD and their partners
Age/Sex:	Mean age: 33.1 years; 56 males, 1 female
Comparison:	PFE Group: (n=28) received 12 60-minutes sessions that avoid skills training and other therapeutic interventions vs SAT Group: (n=29) received 12 60-minute sessions with therapist, veteran, and partner doing emotion activation and skills training phases
Follow-up:	12 weeks
Results:	Treatment effect was observed in CAPS and PCL-M for both SAT and PFE groups (CAPS: p<.001, p=.01, respectively; PCL-M p=.0007, p=.004, respectively). SAT group showed greater improvement than PFE. PTSD criteria was not met after treatment for 15 veterans in SAT and 2 veteran in PFE (p=.003).
Conclusion:	"This couples-based treatment for combat-related PTSD appears to have a strong therapeutic effect on combat-related PTSD in recently returned veterans."
Comments:	Couples based PTSD intervention. Data suggest self-rated PTSD symptoms decreased more in SAT group than education group.

Author Year (Score):	**Sundquist 2015 (score=4.0)**
Category:	Group Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by J.S. and K.S. from the Swedish Research Council, ALF funding from Region Ska˚ ne and The Swedish Research Council for Health, Working Life and Welfare (in Swedish: Forte). No COI.
Sample size:	N=215 patients with depression, anxiety, stress, and adjustment disorders
Age/Sex:	Mean age: 41.5 years; 29 males, 171 females
Comparison:	Mindfulness Group: (n=110) received mindfulness based group therapy or cognitive therapy for 2 hour sessions once a week for 8 weeks as well as 20min/day at home vs Control Group: (n=105)

	received TAU which included pharmacological treatment and psychotherapy or counseling
Follow-up:	8 weeks
Results:	For MADRS-S, HADS-D, and HADS-A scales, scores decreased for both groups ($p<0.001$). Absolute differences in mean change for MADRS-S was 2.55, 1.00 for HADS-D, 2.80 for HADS-A, and 4.31 for PHQ-9 comparing 6-8 mindfulness sessions vs 1-5 sessions.
Conclusion:	"Mindfulness-based group therapy was non-inferior to treatment as usual for patients with depressive, anxiety or stress and adjustment disorders."
Comments:	Usual care bias. Data suggest comparable efficacy in both groups.

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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**

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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**

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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.

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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

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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.

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Evidence for the Use of Cognitive Behavioral Therapies

Author Year (Score):	**Monson 2012 (score=7.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health. COI, one or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N = 40 couples (80 individuals)
Source of Trauma:	Military Service, Motor Vehicle Collision, Sexual and nonsexual assault.
Age/Sex:	Mean age: 34.5 years; 27 males, 53 females.
Comparison:	Group 1: received Cognitive behavioral couple therapy (N=20 couples) vs. Group 2: placed on a waitlist for the same treatment. (N=20 couples) Biweekly sessions for phases 1 and 2 and then weekly sessions for phase 3 for a total of 15 sessions of unspecified lengths of time.
Follow-up:	Baseline, 4 weeks, 12 weeks, and 3 months.
Results:	Group 1 vs Group 2, PTSD CAPS score mean change baseline to week 12: -35.42 (95% CI -47.84 to -23.00) vs -12.20 (95% CI -21.51 to -2.89) (p=0.004). Group 1 vs Group 2, patient-reported relationship satisfaction score mean change baseline to 12 weeks: 12.22 (95% CI 5.72 to 18.72) vs 2.79 (95% CI -3.95 to 9.53) (p=0.049)
Conclusion:	"Among couples in which one partner was diagnosed as having PTSD, a disorder-specific couple therapy, compared with a wait list for the therapy, resulted in decreased PTSD symptom severity and patient comorbid symptom severity and increased patient relationship satisfaction."
Comments:	Population comprised of a mix of various types of trauma leading to PTSD. Waitlist control bias. Small sample. Data suggest CBT improved clinician evaluated PTSD symptoms as well as patient relationship satisfaction.

Author Year (Score):	**Talbot 2014 (score=7.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	No Sponsorship. No COI.
Sample size:	N=45 participants with at least 3 months chronic PTSD.
Source of Trauma:	Military Service
Age/Sex:	Mean age: 37.2±10.5 years; 14 males, 31 females.
Comparison:	Group 1: Cognitive behavioral therapy (CBT) (N=29) vs. Group 2: Monitored waitlist group (Control) (N=16) Sessions occurred weekly for 8 total weeks and treatment session time was unspecified.
Follow-up:	Baseline, mid and post treatment, and 6 months.
Results:	No significant difference in PTSD CAPS scale between groups post treatment. Group 1 subjective insomnia score change mid treatment and post treatment: (t(40)=-2.27, p=0.029) and (t(40)=-6.82, p<0.001). Group 1 vs group 2, post treatment insomnia remissions: 41% vs 0%.
Conclusion:	"In summary, CBT-I was efficacious in the treatment of insomnia and disruptive nocturnal behaviors in PTSD, and the improvements

	in sleep were sustained. The initial evidence regarding CBT-I and nightmares is promising but further evaluation is needed."
Comments:	All female participants. Waitlist control bias. Data suggest CBT improved insomnia in PTSD patients and gains were maintained at 6 months.

Author Year (Score):	**McGovern 2015 (score=7.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by the National Institute on Drug Abuse. No COI.
Sample size:	N=221 individuals with PTSD and substance use disorder.
Source of Trauma:	Childhood sexual assault and adult physical assault.
Age/Sex:	Mean age: 35.3±10.42 years; 90 male, 131 females.
Comparison:	Group 1: received integrated cognitive behavioral treatment and standard care with outpatient services and medication. (N=73) vs Group 2: received individual addiction counseling and standard care. (N=75) vs Group 3: received standard care only (N=73)
Follow-up:	Baseline, 3 months, 6 months.
Results:	All groups showed reduction in PTSD symptoms. Group 1 vs Group 2: toxicology (substance abuse), ANOVA parameter difference: 1.10; CI 0.17-2.04. Group 1 vs Group 3, toxicology ANOVA parameter difference: 1.13; CI 0.18 – 2.08.
Conclusion:	"[C]ontrary to hypothesis, ICBT demonstrated no clear advantage over the other treatments at 6-months on PTSD symptom severity. However, ICBT did demonstrate superior outcomes on drug use, as measured by positive urine drug screens and frequency of reported drug use."
Comments:	Data suggest comparable efficacy in PTSD symptom reduction in all groups.

Author Year (Score):	**Bryant 2008, a (score=6.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by National Health and Medical Research Council Program. No COI.
Sample size:	N=90 consecutive civilian trauma survivors referred to a traumatic stress clinic.
Source of Trauma:	Nonsexual assault and motor vehicle accident.
Age/Sex:	Mean age: 39.13±10 .87 years; 48 males, 52 females
Comparison:	Group 1: received imaginal exposure (N=31) vs Group 2: received in vivo exposure (N=28) vs Group 3: received both Imaginal exposure and in vivo exposure. (N=31) vs Group 4: received imaginal exposure, in vivo exposure, and cognitive restructuring. (N=28) Treatments lasted for 100 minute sessions for 8 weeks.
Follow-up:	Follow up at baseline, 3 months and 6 months.
Results:	Group 1 vs group 2 vs group 3 vs group 4, 6 month follow up participants with PTSD: 75% vs 69% vs 63% vs 31% ($p<0.01$). Group 4 showed significantly superior reductions in CAPS score compared to all other groups using ANOVA analyses ($p<0.05$).
Conclusion:	"[t]he current results suggest that therapists should consider implementing cognitive restructuring techniques in conjunction with exposure-based therapies."

Comments:	At 6 months, combination therapy resulted in fewer PTSD individuals. Data suggest a combination of CR with exposure therapy may be the best treatment for treating PTSD.

Author Year (Score):	**Ehlers 2014 (score=6.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Wellcome Trust. No COI.
Sample size:	N=121 patients referred to an anxiety disorder hospital.
Source of Trauma:	Majority of traumatic events revolved around violence, accidents/disaster, and death or harm of others.
Age/Sex:	Mean age: 38.95 years; 50 males, 71 females.
Comparison:	Group 1: received standard cognitive Therapy for PTSD 3 months (N=31) vs. Group 2: received 7 Intensive Cognitive Therapy sessions over the span of one week (N=30) vs. Group 3: received support therapy, no focus on cognition (N=30) vs. Group 4: were placed on a waitlist for 14 weeks.
Follow-up:	Baseline, 6, 14, 27, and 40 weeks.
Results:	Group 1, PTSD CAPS scores pretreatment vs 40 weeks: 70.60±13.45 vs 20.96±27.71. Group 2, PTSD CAPS scores pretreatment vs 40 weeks: 78.72±19.80 vs 35.33±35.11. Group 3: PTSD CAPS scores pretreatment vs 40 weeks: 74.60±15.39 vs 49.04±38.01. Group 4: PTSD CAPS scores pretreatment vs 40 weeks 69.95±14.17 vs 65.28±20.64. Group 1, PTSD symptoms score, pretreatment vs 40 weeks: 32.44±6.94 vs 9.63±11.26. Group 2, PTSD symptoms score, pretreatment vs 40 weeks: 33.21±7.66 vs 13.03±13.99. Group 3, PTSD symptoms score, pretreatment vs 40 weeks: 34.26±7.40 vs 20.94±15.40. Group 4, PTSD symptoms score, pretreatment vs 40 weeks: 32.46±7.60 vs 29.24±9.36.
Conclusion:	"Cognitive therapy for PTSD delivered intensively over little more than a week is as effective as cognitive therapy delivered over 3 months. Both had specific effects and were superior to supportive therapy. Intensive cognitive therapy for PTSD is a feasible and promising alternative to traditional weekly treatment."
Comments:	Data suggest comparable efficacy suggesting intensive CBT (CBT delivers over 7 days) is as effective as CBT delivered over 3 months.

Author Year (Score):	**Schnurr 2007 (score=6.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by VA cooperative Studies Program and Department of Defense. COI: One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=283 females veterans/active duty personnel.
Source of Trauma:	Military service.
Age/Sex:	Mean age: 44.7 years; 0 males, 284 females
Comparison:	Group 1: received prolonged exposure therapy for 10 weeks. (N=141) vs Group 2: received present-centered therapy for ten sessions (N=143).
Follow-up:	Baseline, post treatment, 3 and 6 months.

Results:	Group 1, PTSD CAPS sale, posttreatment vs 6 month follow-up: 52.9 (47.7-58.0) vs 50.4 (45.0 – 55.8). Group 2, PTSD CAPS sale, posttreatment vs 6 month follow-up: 60.1 (55.3 – 64.8) vs 54.5 (49.3 – 59.7). Between group 1 and group 2 effect for PTSD CAPS scale p<0.05.
Conclusion:	"Prolonged exposure is an effective treatment for PTSD in female veterans and active-duty military personnel. It is feasible to implement prolonged exposure across a range of clinical settings."
Comments:	Data suggest prolonged exposure was better than present-centered therapy for reducing PTSD symptoms showing statistical significant at p=0.03.

Author Year (Score):	**Bryant 2008, b (score=6.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by grant 300304 from the National Health and Medical Research. No COI.
Sample size:	N=90 consecutive civilian trauma survivors referred to a traumatic stress clinic.
Source of Trauma:	Motor vehicle accident and non-sexual assault.
Age/Sex:	Mean age: 35.4 years; 38 males, 52 females
Comparison:	Group 1: received prolong exposure therapy for 5 weeks (N=30) vs Group 2: received cognitive therapy for 5 weeks (N=30) vs Group 3: was a waitlisted control group (n=30)
Follow-up:	Baseline, 6 weeks, 3 and 6 months.
Results:	Group 1 vs Group 2, PTSD CAPS effect size comparison (0.80 considered significant) at 3 months: 0.42 (95% CI -0.09 to 0.92). Group 1 vs Group 3 PTSD CAPS effect size comparison at 3 months: 0.95 (95% CI 0.42-1.49). Group 2 vs group 3, PTSD CAPS effect size comparison at 3 months: 0.50 (95% CI -0.01 to 1.10).
Conclusion:	"Exposure-based therapy leads to greater reduction in subsequent PTSD symptoms in patients with ASD when compared with cognitive restructuring. Exposure should be used in early intervention for people who are at high risk for developing PTSD."
Comments:	Data suggest an early intervention of exposure based therapy is superior to cognitive restructuring for preventing PTSD in high risk individuals.

Author Year (Score):	**Cottraux 2008 (score=5.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by a grant from the French Ministry of Health. No COI.
Sample size:	N=60 patients with PTSD.
Source of Trauma:	Motor vehicle accident, physical and sexual assault, violence.
Age/Sex:	Mean age: 40.2 years; 10 males, 32 females.
Comparison:	Group 1: received cognitive behavioral therapy for 16 weeks (N=27) vs Group 2: received supportive therapy
Follow-up:	Baseline, post treatment (16 weeks), and 52 week, 104 weeks. .
Results:	No significant differences between group 1 and group two for PTSD Checklist Scale
Conclusion:	"Bearing in mind all these limitations, in such chronic PTSD patients, CBT was a more acceptable treatment as it had a higher

Comments:	patient retention rate (87%) than ST (52%). However, in the long run, the CBT and ST completers did equally well." Data suggest comparable results in both groups but CBT had a higher retention rate.

Author Year (Score):	**Bryant 1998 (score=5.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by grants from the NSW Health Department and the National Health and Medical Research Council. No COI.
Sample size:	N=20 patients with acute stress disorder (ASD).
Source of Trauma:	Motor vehicle accidents, industrial accidents.
Age/Sex:	Mean age: 32.75 years; 10 males, 14 females.
Comparison:	Group 1: received cognitive behavioral therapy (N=12) vs Group 2: received supportive counseling (N=12)
Follow-up:	Baseline, post treatment, and 6 months.
Results:	Group 1 vs group 2, Trait anxiety interview baseline to 6 months: 47.08±17.21 to 38.00±9.26 vs 49.08 (9.71) to 47.50 (12.41) ($p<0.05$). Group 1 vs group 2, impact of event scale intrusion baseline to 6 months: 24.17±7.45 to 8.58±8.70 vs 25.08±5.56 to 17.92±8.98 ($p<0.05$). Group 1 vs group 2, cases of PTSD baseline to 6 months: 12 to 2 vs 12 to 8 ($p<0.05$).
Conclusion:	"[T]his study represents the 1st demonstration of successful treatment of ASD with CBT and its efficacy in preventing chronic PTSD."
Comments:	Very small sample. Data suggest CBT superior for ASD, a precursor of PTSD. At 6 months fewer cases of PTSD seen in CBT group with both clinically and statistically significant reduction in depressive, avoidance, and intrusive symptoms.

Author Year (Score):	**Bryant 2013 (score=5.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by a National Health and Medical Research Council Program grant. COI: Authors have received payment for CBT training.
Sample size:	N=70 civilian trauma survivors.
Source of Trauma:	Motor vehicle accident or assault.
Age/Sex:	Mean age: 39.51 years; 32 males, 38 females.
Comparison:	Group 1: received Cognitive behavioral therapy and social support (N=34) vs Group 2: received skills from therapists on how to combat distress (N=36)
Follow-up:	Baseline, post treatment, and 6 months.
Results:	Group 1 vs Group 2, CAPS scores baseline to 6 month follow up: 67.69±16.26 to 47.54±22.45 vs 73.75±17.79 to 37.47±23.49 ($p<0.001$).
Conclusion:	"This evidence suggests that response to CBT may be enhanced in PTSD patients by preparing them with emotion regulation skills. High attrition of participants during the study limits conclusions from this study."

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Comments:	Significant dropout rate limiting conclusions. Data suggest CBT plus emotion tolerance training "may" be better than CBT plus support for PTSD.

Author Year (Score):	**Mills 2012 (score=5.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the Australian National Health and Medical Research Council. No mention of COI.
Sample size:	N = 103 participants with a DSM-IV-TR diagnoses of PTSD and substance dependence.
Source of Trauma:	Physical assault, threatened or held captive, witnessed injury or death, sexual assault, accident or disaster, torture and combat exposure.
Age/Sex:	Mean age: 33.7 years; 39 males, 64 females.
Comparison:	COPE plus usual treatment (N=55) vs only usual treatment (N=48)
Follow-up:	Follow up at baseline 6 weeks, 3 and 9-months
Results:	Mean difference CAPS score for COPE + usual care was -38.24 (95% CI -47.93,-28.54) vs -22.14 (95% CI -30.33,-13.95) for only usual treatment.
Conclusion:	"Among patients with PTSD and substance dependence, the combined use of COPE plus usual treatment, compared with usual treatment alone, resulted in improvement in PTSD symptom severity without an increase in severity of substance dependence."
Comments:	Data suggest COPE and usual care resulted in improved PTSD symptoms without a concomitant substance dependence increase.

Author Year (Score):	**Back 2016 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Department of Defense. No COI.
Sample size:	N=35 veterans in substance abuse treatment clinic.
Source of Trauma:	Military Service
Age/Sex:	Mean age: 49.0±8.2 years; 26 males, 1 females.
Comparison:	Group 1: Received N-Acetylcysteine (NAC) and cognitive behavioral therapy (N=14) vs Group 2: Received placebo pills and cognitive behavior therapy. (N=13)
Follow-up:	Baseline and 8 weeks.
Results:	Group 1 vs Group 2, change in self-report PTSD scale, baseline to week 8: 45.7 to 31.2 (32%) vs 43.4 to 41.9 (3%) ($p<0.001$). Group 1 vs Group 2, clinician-rated PTSD symptoms change from baseline to week 8: 58.8 to 32.0 (46%) vs 68.6 to 51.5 (25%) ($p<0.05$). Group 1 vs Group 2, craving for substance use (VAS) change baseline to week 8: 3.7 to 0.7 (81%) vs 4.1 to 2.8 (32%) ($p<0.001$).
Conclusion:	"In summary, the current data provide encouraging preliminary support for combining NAC and cognitive-behavioral therapy to reduce PTSD symptoms, craving, and depression over 8 weeks."

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Comments:	Data suggest NAC may be appropriate for treating PTSD symptoms and substance use disorders.

Author Year (Score):	**Blanchard 2003 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from NIMH. No mention of COI.
Sample size:	N = 78 motor vehicle accident survivors with a diagnosis of PTSD according to DSM-IV for at least 6 months.
Source of Trauma:	Motor vehicle accident survivors.
Age/Sex:	Mean age: 41.1 years; 21 males, 57 females
Comparison:	8-12 weeks of CBT (N=27) vs the same amount of SUPPORT (N=27) vs waitlist control (N=24)
Follow-up:	Follow up at pre-treatment, post-treatment, and 3 months
Results:	Mean CAPS score pre-treatment for the CBT group were 68.2 vs the SUPPORT group which were 65.0 and changed to 23.7 and 40.1 post treatment respectively ($F(1,50)=9.78$, $p=0.003$, $\eta^2=0.164$)
Conclusion:	"Regardless of these limitations, we think the study clearly shows the benefits of CBT as a treatment for chronic PTSD secondary to motor vehicle accidents."
Comments:	Chronic PTSD in motor vehicle accident survivors. Waitlist control bias. Waitlist population allowed crossing over post assessment of the 2 treatment groups. Data suggest CBT superior to SUPPORT at 3 months. Support was better than waitlist.

Author Year (Score):	**Difede 2007 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a NIMH RAPID grant. No mention of COI.
Sample size:	N = 31 disaster workers exposed to the World Trade Center attack and/or its aftermath and a DSM-IV TR PTSD diagnosis.
Source of Trauma:	World Trade Center attack.
Age/Sex:	Mean age: 45.77 years; 30 male, 1 female
Comparison:	Weekly 75 minute sessions of CBT for 12 weeks (N=15) vs treatment-as-usual (N=16)
Follow-up:	Follow up at baseline and 3 months.
Results:	Dropouts less well educated than completers ($p=0.044$), had lower levels of income ($p=0.042$), and had higher MAST scores ($p=0.091$). Mean pre-treatment CAPS scores for the CBT group was 44.43 vs 19.57 post treatment ($p=0.011$).
Conclusion:	"This study provides useful preliminary empirical evidence that could inform treatment planning and service delivery to disaster workers after future terrorist incidents or natural disasters. Future studies might improve retention by focusing on variables associated with dropout."
Comments:	Pilot study. Usual care bias. Dropout rates associated with higher alcohol use, lower income and educational status. Data suggest

	CBT delivered as a brief intervention may be beneficial for PTSD in disaster workers.

Author Year (Score):	**Mueser 2015 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the National Institute of Mental Health.
Sample size:	N = 201 participants with a DSM-IV diagnosis of severe mental illness, a diagnosis of sever PTSD based on CAPS, and significant functional limitations within the last 3-6 months as a result.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 43.7 years; 63 males, 138 females.
Comparison:	A brief 3 session treatment of breathing retraining and education (N=97) vs 12-16 weeks of CBT (N=104)
Follow-up:	Follow up at baseline, post-treatment, 6 and 12 months.
Results:	Mean CAPS total CBT vs Brief treatment effect size -.29 F(1,170)=6.51, p=0.01.
Conclusion:	"Cognitive restructuring has a significant impact beyond breathing retraining and education in the CBT programme, reducing PTSD symptoms and improving functioning in people with severe mental illness."
Comments:	Participants with PTSD combined with mental illness such as major mood disorder, schizophrenia, and borderline personality. Data suggest CBT significantly decreases PTSD symptoms and those patients receiving the complete CBT program for 12-16 weeks showed superior results in PTSD symptom improvement.

Author Year (Score):	**Van Emmerick 2008 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the Netherlands Organization for Health Research and Development. No mention of COI.
Sample size:	N = 126 participants with a DSM-IV diagnosis of PTSD.
Source of Trauma:	Traffic accident, non-sexual violence, and sexual violence.
Age/Sex:	Mean age: 40.2 years; 41 males, 85 females.
Comparison:	Weekly 1.5 hour treatment with CBT (N=41) vs structured writing therapy (N=44) vs waitlist control (N=41)
Follow-up:	Follow up at baseline, posttest, and mean of 381 days.
Results:	Mean IES-T score interaction between time and group for CBT vs SWT was F(1.79, 134.51)=0.44, p=0.62. Treatment vs waitlist control for the same was F(1.72,188.86)=6.72. p<0.01.
Conclusion:	"The present study confirmed the efficacy of CBT for ASD and PTSD and identified SWT as a promising alternative treatment."
Comments:	High dropout rate. Chronic PTSD subjects. Data suggest comparable efficacy between CBT and SWT.

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Author Year (Score):	**Johnson 2017 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by The National Program for Integrated Clinical Specialist and PhD-training for psychologists in Norway. No mention of COI.
Sample size:	N = 74 participants with a DSM-IV diagnosis of PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 42.0 years; 29 males, 45 females.
Comparison:	Average of 9.4 sessions of wither 90 minutes of CBT (N=38) vs 50 minutes of metacognitive therapy (N=36)
Follow-up:	Follow up pretreatment and 1 year.
Results:	Mean BAI score pre-treatment to one year follow up for CBT was 24.8 to 15.8 (d=0.86 95% CI .38-1.32) vs the same for MCT 26.7 to 17.4 (d=0.84 95% CI 0.35,1.31) No significant different between the groups was found.
Conclusion:	"MCT seems to have a more rapid effect on anxiety symptoms, but there were no significant differences in the long term for patients with comorbid anxiety disorders."
Comments:	At one year, data suggest comparable efficacy. Dropout rate reasons due to each of motivation and alcohol use. Reasons were the same for both groups.

Author Year (Score):	**Margolies 2013 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a United States Department of Veterans Affairs Predoctoral Rehabilitation Research Fellowship. No mention of COI.
Sample size:	N = 40 veterans of either OEF and/or OIF diagnosed with PTSD by either the PTSD Clinic and/or the Mental Health Service Clinic and current sleep disturbances.
Source of Trauma:	Combat related.
Age/Sex:	Mean age: 37.7 years; males 36, females 4
Comparison:	4 sessions of CBT-I with adjunctive IRT (N=20) vs waitlist control (N=20)
Follow-up:	Follow up every day for 2 weeks before treatment, 6 weeks during treatment and 2 weeks after treatment in the form of a sleep journal.
Results:	Significant condition x time interaction across the four sleep variables $F(4,29) = 5.4$, $p=.002$, $\eta_p^2=.43$. Sleep efficacy for the treatment group was 11% at baseline and 75% posttreatment vs 6% and 21% for the waitlist group (Chi-squared(1) = 50.2, p<.001)
Conclusion:	"The findings from this first controlled study with OEF/OIF veterans suggest that CBT-I combined with adjunctive IRT may hold promise for reducing both insomnia and PTSD symptoms. Given the fact that only half of the patients with nightmares fully implemented the brief IRT protocol, future studies should

	determine if this supplement adds differential efficacy to CBT-I alone."
Comments:	Waitlist control bias. Data suggest at 6 weeks OEF/OIF veterans may benefit from CBT-I and IRT to reduce PTSD symptom severity, nightmares and depression and associated symptoms compared to control.
Author Year (Score):	**Kuhn 2017 (score=5.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 120 participants who were exposed to a traumatic event more than 1 month ago and scored 35 or greater on the PCL-C and with no current PTSD treatment.
Source of Trauma:	Physical Assault, sexual assault, serious accident, life-threatening illness or injury, disaster exposure, combat exposure.
Age/Sex:	Mean age: 39.3 years; 37 males, 83 females
Comparison:	PTSD coach app group (N=62) vs waitlist control (N=58)
Follow-up:	Follow up at baseline, posttreatment and 3 months.
Results:	Condition x Time interaction for mean PCL-C score d = 0.41, p<0.05.
Conclusion:	"PTSD Coach use resulted in significantly greater improvements in PTSD symptoms and other outcomes relative to a waitlist condition. Given the ubiquity of smartphones, PTSD Coach may provide a wide-reaching, convenient public health intervention for individuals with PTSD symptoms who are not receiving care.'
Comments:	Waitlist control bias. Data suggest using a PTSD coach improved PTSD symptoms compared to control.
Author Year (Score):	**Johnson 2011 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from NIMH. No mention of COI.
Sample size:	N = 70 women from one of two inner-city battered women's shelters who had experienced an incident of IPV on the Conflict Scales-Revised in the month prior to admission to the shelter and meet IPV-related PTSD or sub threshold criteria on the Clinician Administered PTSD Scale.
Source of Trauma:	Intimate partner violence.
Age/Sex:	Mean age: 32.6 years; 0 males, 70 females
Comparison:	Up to 12 sessions of Helping to Overcome PTSD through Empowerment (HOPE) group (N=35) vs standard shelter service (SSS) control group (N=35)
Follow-up:	Follow up at 1 week, 3 and 6 months.
Results:	Re-abuse rates at 6 months in the ITT group were 46.9% in the HOPE group vs 81.8% for SSS control (OR = 5.1, 95% CI [1.66-15.7], RR = 1.75, 95% CI [1.17-2.61]) CAPS Emotional Numbing Treatment x Time interaction had an effect size of d=0.41 with p<0.05.
Conclusion:	"Results support the acceptability and feasibility of HOPE and suggest that HOPE may be a promising treatment for IPV victims in

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	shelter. However, results also suggest that modifications to HOPE may be required to improve treatment outcomes."
Comments:	Data suggest at 6 months, HOPE was better than SSS as HOPE was associated with significantly lower probability of re-abuse and experienced less PTSD symptoms.

Author Year (Score):	**Possemato 2016 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Department of Veterans Affairs, Veterans Health Administration, Center for Integrated Healthcare Research Pilot Award. No mention of COI.
Sample size:	N = 20 VA primary care patients with a positive screening for PTSD on the Primary Care – PTSD screen.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 42 years; 19 males, 1 females
Comparison:	Clinician Supported (CS) PTSD coach group (N=10) vs Self-Managed (SM) PTSD coach group (N=10)
Follow-up:	Follow up at 8, 12, and 16 weeks.
Results:	Mean PCL score at baseline for the CS group was 56.0 vs 49.8 posttreatment (p=0.02) Mean PCL score at baseline for the SM group was 51.0 vs 40.0 posttreatment (p<0.01). Group x time effect of the same was not significant (p=0.30)
Conclusion:	"Both PTSD Coach interventions are feasible and potentially helpful. The addition of clinician support appears to increase the effectiveness of self-management alone."
Comments:	Pilot RCT. Data suggest comparable efficacy for both interventions.

Author Year (Score):	**Duffy 2007 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by Northern Ireland Victims Liaison Unit. No COI.
Sample size:	N = 58 consecutive patients with chronic PTSD.
Source of Trauma:	Terrorism and other civil conflict in Northern Ireland.
Age/Sex:	Mean age: 43.9 years; 35 males, 23 females.
Comparison:	Immediate cognitive therapy group (n=29) – received CBT treatment form five therapists for 12 weeks. Vs. Waiting list group (n=29) – patients waited for 12 weeks followed by cognitive therapy.
Follow-up:	1, 4, and 12 months after treatment.
Results:	Posttraumatic stress diagnostic scale mean score at 12 months post-treatment was 15.1 for the immediate therapy group (ITG), 33.1 for the waiting list group (WLG), 16.9 95% CI mean score, and p<0.001. The Beck Depression Inventory mean score was 17.9 for ITG, 33.6 for WLG, 13.2 95% CI, and p<0.001. The Sheehan Disability Scale mean score was 4.2 for the ITG, 7.4 for WLG, 2.4 95% CI, and p<0.001.
Conclusion:	"Cognitive therapy is an effective treatment for posttraumatic stress disorder related to terrorism and other civil conflict."
Comments:	Waitlist control bias. Data suggest a statistically significant improvement in PTSD, stress and social functioning at 12 weeks in CBT group. At 12 months, treatment gains were well maintained.

Author Year (Score):	**Thrasher 2010 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Wellcome Trust (035091), London, and by the UK Medical Research Council. No COI.
Sample size:	N = 77 participants with chronic PTSD.
Source of Trauma:	Trauma, personal, use of weapon, injury, disability, disfigurement, bereavement.
Age/Sex:	Mean age: 38 years; 24 males, 53 females.
Comparison:	Active treatment (n=57) – patients received either cognitive restructuring and/or exposure therapy. Vs. Relaxation only (n=20) –
Follow-up:	No mention of follow up.
Results:	Active treatment, compared with relaxation, CAPS change scores (mean, SD) were: 34.8, 22.8, compared with 13.2, 23.1. Overall, higher Significant others scale (SOS) scores (better social support) were significantly associated with greater improvement in CAPS, r = 0.36, df = 75, P <0.001. The SOS did not predict outcome with relaxation, r = 0.14, df = 18, P = 0.57. For active treatment, however, higher SOS strongly predicted better outcome, r = 0.46, df = 55, P<0.001.
Conclusion:	"Better social support is associated with significantly greater gain following cognitive restructuring and (or) exposure therapy for PTSD. Future interventions should consider augmenting social support as an adjunct to treatment."
Comments:	Data suggest increased social support is predictive for better gain post exposure therapy or cognitive restructuring in the treatment of PTSD.

Author Year (Score):	**Sijbrandij 2007 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by Stichting Achmea Slachtoffer en Samenleving (SASS), Aid to Victims, Zeist, the Netherlands, and the Netherlands Organization for Health Research and Development. No COI.
Sample size:	N = 143 patients with acute PTSD.
Source of Trauma:	Assault, witnessing assault, sexual assault, accidental injury, sudden death of loved one.
Age/Sex:	Mean age: 37.6 years; 57 males, 86 females.
Comparison:	Brief Cognitive Behavioral Therapy (n=79) – patients participated in four weekly 120 minute sessions containing education, relaxation exercises, imaginal exposure, in vivo exposure, and cognitive restructuring. Vs. Waitlist group (n=64) – patient didn't receive the intervention, but were assessed with the same follow-up times. They were offered intervention at the 4-month follow up.
Follow-up:	1 week and 4 months.
Results:	At 1 week posttreatment, the mean PTSD total score was 22.1 for the cognitive behavioral group (CBG), 29.4 for the waiting list group (WLG), -9.94 to -2.79 95% CI, p=0.001. At 4 month posttreatment, the mean PTSD total score was 15.9 for CBG, 20.5 for WLG, -7.71 to -2.62 95% CI, p=0.33.

Conclusion:	"Brief early cognitive behavioral therapy accelerated recovery from symptoms of acute PTSD but did not influence long-term results. Brief early cognitive behavioral therapy showed enhanced efficacy in patients with baseline comorbid depression and patients who were included within 1 month after their traumatic experience."
Comments:	Waitlist control bias. Data suggest brief CBT, while decreasing PTSD symptoms initially did not sustain long-term results.

Author Year (Score):	**Maercker 2006 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Deutsche Forschungsgemeinschaft. No COI.
Sample size:	N = 42 participants with chronic or sever subsyndromal PTSD.
Source of Trauma:	Motor vehicle accident.
Age/Sex:	Mean age: 40.35 years; 10 males, 32 females.
Comparison:	CBT (n=21) – patients received 8-12 weekly sessions focused three exposures: reading personal description of MVA, sensu exposure, and in vivo exposure to fear arousing cues. Vs. Wait List (n=21) – treatment was delayed 2-3 months. They were given the option of CBT treatment aft the post-treatment assessment.
Follow-up:	3 month follow up.
Results:	The mean CAPS scores for the CBT group at pre-treatment, post-treatment, and 3-month follow up were 47.6, 18.8, and 18.9, respectively. The mean CAPS scores for the wait list group at pre-treatment and post-treatment were 41.8 and 35.2, respectively. (Group × time interaction effect size d = 1.61). Intent-to-treat analysis supported the outcome (d = 1.34).
Conclusion:	"The degree of improvement in our treatment group was comparable to that in previously reported treatment
Comments:	Small sample. Waitlist control bias. Data suggest CBT was effective in reducing PTSD symptoms at 3 months via CAPS-scores.

Author Year (Score):	**Ruglass 2017 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the National Institute on Drug Abuse. Drs. T. Killeen and S. Back report they receive royalties from Oxford University Press for a treatment manual they wrote on utilizing COPE.
Sample size:	N = 110 patients with PTSD.
Source of Trauma:	Physical assault, sexual assault, accident or disaster, or sudden injury or death of other.
Age/Sex:	Mean age: 44.56 years; 70 males, 40 females.
Comparison:	COPE (n=39) – patients received an integrated program of PE for PTSD and RPT for SUD for 90-min weekly sessions for 12 weeks. Vs. RPT (n=43) – patients received a cognitive-behavioral SUD intervention focusing on coping strategies to manage situations that increase the risk of substance use relapse for 90-mins weekly for 12 weeks. Vs. AMCG (n=28) – patients met with research assistant weekly for 12 weeks to complete self-report measures,

	urine toxicology, alcohol breathalyzer, and to confirm general health/safety.
Follow-up:	1, 2, and 3 month.
Results:	Results for PTSD outcome: MPSS-SR total scores by the end-of-treatment session for COPE = -42.99, 95% CI -56.30 to -29.68, p<0.001 and for RPT = -31.51, 95% CI -40.64 to -22.38, p<0.001. Symptom reduction between groups: COPE-AMCG = –34.06, 95% CI –51.36 to –16.75, p < 0.001; RPT-AMCG = –22.58, 95% CI –36.92 to –8.24, p = 0.002; COPE-RPT = –11.48, 95% CI –27.62 to 4.67, p = 0.16. CAPS total severity score at 1 month follow up: COPE = -27.12, 95% CI –35.84 to –18.40, p<0.001; RPT = –25.38, 95% CI –33.12 to –17.64, p<0.001. CAPS total severity score at 3 month follow up: COPE = –28.31, 95% CI –36.01 to –20.60, p < 0.001; RPT = –26.71, 95% CI –34.28 to –19.14, p<0.001).
Conclusion:	"COPE and RPT reduced PTSD and SUD severity in participants with PTSD + SUD. Findings suggest that among those with full PTSD, COPE improves PTSD symptoms more than a SUD-only treatment. The use of PE for PTSD was associated with significant decreases in PTSD symptoms without worsening of substance use."
Comments:	Data suggest COPE better than SUD-only treatment as it decreases PTSD symptoms without escalating substance abuse and treatment gains for both groups were stable at 3 months.

Author Year (Score):	**Maguen 2017 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by VA Health Services Research and Development RRP 12–237 (PI: Maguen); University of California, San Francisco REAC 525014–36248 (PI: Maguen); and VA Health Sciences Research and Development Research Career Development Award 06–042 (PI:Maguen). No mention of COI.
Sample size:	N = 33 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 61.2 years; 33 males, 0 females.
Comparison:	IOK (N=17) – patients attended 6-8 weekly, 90 minute individual sessions of CBT that focused on the physiology of killing responses, moral injury, self-forgiveness, spirituality, making amends, and improved functioning. Vs. Waitlist Condition (N=16) – patients were placed in the 6-week waitlist condition and served as a control group.
Follow-up:	Study did conduct a follow-up, but the time is not specified.
Results:	The mean PCL Total Score in the waitlist group was 52.9 at baseline and 50.7 at the follow-up, 95% CI = -5.97 to -1.71, p=0.2534. The mean PCL Total score in the treatment group was 48.6 at baseline, 41.3 at follow-up, 95% CI = -14.71 to -0.05, p=0.0512. The PCL total score in the treatment vs. waitlist between group difference was -7.27 [-13.89, -0.64], between group P-value = 0.033, and the partial omega-squared [95% CI] = 0.119 [0.007, -0.342].
Conclusion:	"These results provide preliminary evidence that Veterans can benefit from a treatment focused on the impact of killing after initial trauma therapy."
Comments:	Waitlist control bias. Pilot study. Data suggest CBT can help war veterans and reduce symptoms associated with PTSD such as

depression, anxiety, phobia, OCD and interpersonal anxiety. Treatment completers expressed the desire for longer treatment.

Author Year (Score):	**Ziemba 2014 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Human Research Protection Office, Office of Human Research Protections, U.S. Army Medical Research and Materiel Command. R.N.C. is a partner in Clinical Psychology Consultants, Ltd. S.J.Z., N.S.B., L.A.P.L., C.H.R., and L.S.P. declare no competing financial interests exist.
Sample size:	N = 18 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age not specified; gender not specified.
Comparison:	Telemedicine-administered CBT (n=7) – subjects received 10 weekly therapy sessions with a telemedicine approach. Vs. Face-to-face administered CBT (n=6) – subjects received 10 weekly therapy sessions with a face-to-face approach.
Follow-up:	No follow up.
Results:	The average Clinician Administered Posttraumatic Stress Disorder Scale Score for the face-to-face modality was 90 pretherapy, 68 post therapy, with a percent change of -24.2% and for the telemedicine modality was 95 pretherapy, 72 post therapy, with a -24.4% percent change.
Conclusion:	"Findings reveal a trend expressing the equivalence of telemedicine and face-to-face therapy when treating OEF/OIF veterans with PTSD among rural populations by a community provider. It further demonstrates the successful collaboration between a community healthcare provider and the military healthcare system."
Comments:	Small sample. Data suggest telemedicine may be as effective as face-to-face treatment for PTSD and patient satisfaction increased as access to treatment was not as challenging.

Author Year (Score):	**Ulmer 2011 (score=4.5)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a Department of Veterans Affairs HSR&D Career Development Award CDA 09-218. Dr. Edinger has received research support from Philips Respironics and has consulted for Philips Respironics and Kingsdown, Inc. The other authors have indicated no financial conflicts of interest.
Sample size:	N = 22 veterans with PTSD.
Source of Trauma:	Combat-related
Age/Sex:	Mean age: 48.38 years; 13 males, 8 females.
Comparison:	Sleep Intervention for PTSD (SIP) (N=12) – patients received the usual care treatment and additional 6 bi-weekly 1-h individual sessions with an interventionist, 3 sessions of CBT, and 3 sessions of imagery rehearsal therapy (IRT). Vs. Usual Care (TAU) (N=9) – patients were treated by their primary care provider for sleep disturbance and PTSD symptoms.
Follow-up:	No follow up.

Results:	The comparison of means and treatment effect sizes for participants with complete base and post-intervention data on outcome questionnaires for the PCL-M mean scores were 62.39 at baseline, 44.00 for the SIP group, and 66.22 for the TAU. Cohen's D value = -1.85.
Conclusion:	"Findings demonstrate that an intervention targeting trauma-specific sleep disturbance produces large short term effects, including substantial reductions in PTSD symptoms and insomnia severity. Future research should focus on the optimal approach to the treatment of comorbid PTSD and sleep disturbance in terms of sequencing, and should assure that sleep-focused interventions are available and acceptable to our younger veterans, who were more likely to drop out of treatment."
Comments:	Usual care bias. Data suggest interventional group achieved large short-term reductions in PTSD symptoms severely and sleep disturbance.

Author Year (Score):	**Ehlers 2003 (score=4.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Wellcome Trust, London, England and the Oxfordshire NHS Trust Research and Development Fund, Oxford, England. COI: Dr. Ehlers is a Wellcome Trust Principal Research Fellow.
Sample size:	N = 97 participants with PTSD.
Source of Trauma:	Motor vehicle accident.
Age/Sex:	No mention of mean age or gender.
Comparison:	Cognitive Therapy (n=28) – patients received 12 weekly 90 minutes sessions of cognitive therapy during 3 months. Vs. Self-Help Booklet (n=28) – patients received at 64-page booklet that follows cognitive behavioral principles for PTSD. A clinician met with the patient for 40 minutes to explain uses of the book. Vs. Repeated Assessments (n=27) – patients were informed about repeated assessments in a 20-minute session with a clinician.
Follow-up:	6 months.
Results:	CT group showed better outcome than RA at posttreatment and follow up (at 3 months: PTSD symptoms, F(4,46)=9.474, P<0.001; associated symptoms, F(2, 50)=13.136, P<0.001; disability, F(2, 50)=13.054, P<0.001; at 9 months: PTSD symptoms, F(2, 45)=7.602, P<0.001; associated symptoms, F(2,49)=6.897, P=0.002; disability, F(2, 49)=4.840, P=0.01). The CT group also showed better outcome than SH at posttreatment and follow up (at 3 months: PTSD symptoms, F(4, 44)=8.044, P<0.001; associated symptoms, F(2, 48)=14.189, P<0.001; disability, F(2, 48)=9.042, P<0.001; at 9 months: PTSD symptoms, F(4, 44)=7.674, P<0.001; associated symptoms, F(2, 48)=12.509, P<0.001; disability, F(2, 48)=7.887, P=0.001).
Conclusion:	"Cognitive therapy is an effective intervention for recent-onset PTSD. A self-help booklet was not effective. The combination of an elevated initial symptom score and failure to improve with self-monitoring was effective to in identifying a group of patients with early PTSD symptoms who were unlikely to recover without intervention."
Comments:	Lack of efficacy for self-help booklet. Data suggest CBT superior to self-help for PTSD.

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Author Year (Score):	**Zatzick 2011 (score=4.0)**
Category:	Cognitive Behavior Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by grants from National Institute of Mental Health. No mention of COI.
Sample size:	N=207 patients acutely injured trauma survivors with PTSD symptoms
Source of Trauma:	No mention of specific source of trauma.
Age/Sex:	Mean age: 38.4±13.1 years; 109 males, 98 females
Comparison:	Stepped Collaborative Care: (n=104) received cognitive behavioral therapy, pharmacotherapy, and trauma focused case management vs Usual Care: (n=103)
Follow-up:	1, 3, 6, 9, 12 months
Results:	Results indicate that collaborative care combined with cognitive behavioral therapy and pharmacotherapy helped to target PTSD. No results indicate true efficacy of treatment.
Conclusion:	"Stepped care protocols targeting PTSD may enhance the population impact of early interventions developed for survivors of individual and mass trauma by extending the reach of collaborative care interventions to acute care medical settings and other nonspecialty posttraumatic contexts."
Comments:	Usual care bias. Predominantly female subjects. Data suggest a collaborative care model for PTSD utilizing early stepped care may benefit individual and mass trauma survivors.

Author Year (Score):	**Teng 2008 (score=4.0)**
Category:	Cognitive Behavior Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by startup funds to Ellen J. Teng from South Central Mental Illness, Research, Education and Clinical Center as part of the VA Office of Academic Affiliations Special MIRECC Fellowship Program in Advanced Psychiatry and Psychology. No mention of COI.
Sample size:	N=49 outpatients with PTSD
Source of Trauma:	No mention of specific source of trauma.
Age/Sex:	Mean age: 51.94±8.44 years; 30 males, 5 females
Comparison:	PCT Group: (n=18) received cognitive behavior therapy of education, cognitive restructuring, and behavior exercises vs PE-SUP Group: (n=17) received control therapy which provided information about nature, etiology, and course of anxiety disorder with supportive framework
Follow-up:	3 months
Results:	Between group differences were significant at follow-up for panic severity and fear, as PCT group showed less reporting of panic symptoms than the PE-SUP group (p=.008). PCT group showed less severe anxiety sensitivity than PE-SUP group and 63% of PCT group were panic free by follow-up.
Conclusion:	"These findings indicated that PCT was superior to an active control therapy in reducing the frequency, severity, and distress associated with panic disorder and suggested that brief cognitive–behavioral therapy for panic is effective for persons with chronic PTSD."

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Comments:	Data suggest PCT significantly decreased panic, fear, and anxiety at 3 months compared to PE-SUP group.

Author Year (Score):	**Beidel, 2011 (score=4.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health (NIMH). No mention of COI.
Sample size:	N = 35 veterans.
Source of Trauma:	Combat related.
Age/Sex:	Mean age: 59.3 years; 35 males, 0 females.
Comparison:	Trauma Management Therapy (TMT) (n=14) – patients received TMT, a multicomponent behavioral treatment that consisted of intensive EXP, programmed practice, and social and emotional rehabilitation. Treatment consisted of 14 90-minute sessions. Vs. Exposure Therapy Only (EXP) (n=16) – patients received 1 session of psychoeducation/treatment orientation and 14 sessions of EXP.
Follow-up:	No follow up.
Results:	The CAPS total score for PTSD symptoms in the TMT group was 84.9 pre-tx and 69.0 in post-tx; in the EXP group was 90.6 pre-tx and 65.5 post-tx; p=0.001. The PCL-M score for PTSD symptoms in the TMT group was 67.0 pre-tx and 60.9 post-tx; in the EXP group was 68.2 pre-tx and 63.6 post-tx; p=0.01. There were significant main effects for time for the CAPS Total Score ($F (df = 1, 28) = 34.08$, $p < .001$) and the PCLM ($F (df = 1, 28) = 6.72$, $p < .01$).
Conclusion:	"This study demonstrates efficacy of exposure therapy for treating the core symptoms of PTSD among combat veterans with a severe and chronic form of this disorder. Moreover, multi-component CBT shows promise for improving social functioning beyond that provided by exposure therapy alone, particularly by increasing social engagement/interpersonal functioning in a cohort of veterans with severe and chronic PTSD."
Comments:	Participants all male combat veterans. Data suggest comparable efficacy between both groups for statistically significant improvement in PTSD symptoms.

Author Year (Score):	**Bryant 1999 (score=4.0)**
Category:	Cognitive Behavior Therapy & Prolonged Exposure
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from National Health and Medical Research Council. No mention of COI.
Sample size:	N=45 trauma survivors with acute stress disorder
Source of Trauma:	Motor vehicle accident, non-sexual assault
Age/Sex:	Mean Age: 40.0 years; 22 males, 23 females
Comparison:	CBT & PE Group: (n=15) received 5 1.5 hour sessions once weekly of cognitive behavior therapy and prolonged exposure therapy vs PE Group: (n=14) received 5 1.5 hour sessions once weekly of only prolonged exposure therapy vs Supportive Counseling: (n=16) received 5 1.5 hour sessions once weekly of supportive counseling and general problem-solving skills avoiding technique for other 2 groups
Follow-up:	6 months

Results:	Higher avoidance ANOVA scores were observed in the Supportive counseling group than both CBT & PE group and the PE group ($p<0.01$, $p<0.001$ respectively). A similar observation was made for STAI anxiety (CBT & PE $p<0.02$, PE $p<0.05$). Supportive counseling patients reported higher intensity and frequency of PTSD symptoms than PE group and the CBT &PE group (Intensity $p<0.001$, $p<0.01$ respectively) (Frequency $p<0.01$, $p<0.01$ respectively).
Conclusion:	"These findings suggest that PTSD can be effectively prevented with an early provision of cognitive behavior therapy and that prolonged exposure may be the most critical component in the treatment of acute stress disorder."
Comments:	Data suggest PTSD may be prevented via a combination of early CBT and PE may be key in the treatment of acute stress disorder.

Author Year (Score):	**Zoellner 2011 (score=4.0)**
Category:	Cognitive Behavioral Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=40 motor-vehicle accident survivors with PTSD
Source of Trauma:	Motor vehicle accident
Age/Sex:	Mean age: 41.2±10.7 years; 10 males, 20 females
Comparison:	CBT group: (n=20) received 8-12 weekly 2-3 hour sessions of cognitive behavioral therapy with trained therapist vs WLC group: (n=20) placed on waitlist
Follow-up:	3 months
Results:	CBT group showed growth effect increase of d=.42 for new possibilities and d=.69 for personal strength. WLC group showed effect increase of d=.53 for spiritual change and personal strength; however, showed a decrease in appreciation for life in both groups (CBT d=.19, WLC d=-.26).
Conclusion:	"The results of this study caution researchers to naively expect PTG as a uniformly positive outcome to evaluate treatment effectiveness."
Comments:	Crossover RCT. Waitlist control bias. Data suggest CBT was effective in reducing PTSD symptoms.

Author Year (Score):	**Franklin 2017 (score=3.5)**
Comments:	Pilot RCT, Small sample suggesting telephone-delivered CBT may decrease insomnia due to PTSD.

Author Year (Score):	**Wu 2014 (score=3.5)**
Comments:	Baseline differences in group age (35.72-43.07). Data suggest at 6 months, B-CBT showed increased reductions in PTSD symptoms anxiety and depression versus self-help booklets in MVC survivors.

Author Year (Score):	**Akbarian 2015 (score=3.5)**
Comments:	All female subjects. Data suggest CBT significantly reduced PTSD symptoms of anxiety and depression vs control.

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Author Year (Score):	**Possemato 2011 (score=3.5)**
Comments:	Pilot study. Data suggest WED may decrease PTSD symptoms.
Author Year (Score):	**Polak 2015 (score=3.5)**
Comments:	Small sample pilot study. Data suggest faster reduction of PTSD symptoms in TF-CBT group.
Author Year (Score):	**Steel 2017 (score=3.5)**
Comments:	Usual care bias. At 6 months data suggest comparable efficacy for CBT in schizophrenia, individuals with PTSD as both groups exhibited decreased PTSD symptoms over time.
Author Year (Score):	**Macdonald 2016 (score=3.5)**
Comments:	Primarily female population. Waitlist control bias. Data suggest CBCT improved trauma-related beliefs, guilt and PTSD symptoms compared to control.
Author Year (Score):	**Tecic 2011 (score=3.5)**
Comments:	Data suggest a longer (extended) treatment plan extending into outpatient care may be better than only brief inpatient care for treating trauma patients with anxiety, depression, and PTSD one year post-treatment.
Author Year (Score):	**Tarrier 1999 (score=3.5)**
Comments:	Data suggest similar efficacy.
Author Year (Score):	**Frueh 2007 (score=3.5)**
Comments:	Data suggest comparable efficacy for outcomes in both groups but treatment adherence and patient comfort better in same-room group.
Author Year (Score):	**Litz 2007 (score=3.5)**
Comments:	Internet-based therapy may be a method of delivering care to large numbers and those who have obstacles receiving in person care.
Author Year (Score):	**Stecker 2014 (score=3.0)**
Comments:	At 6 months data suggest comparable efficacy for PTSD symptom reduction but utilization of a telephone-based intervention accelerated treatment engagement.
Author Year (Score):	**Gallegos 2016 (score=3.0)**
Comments:	Data suggest suicidal participants were twice as likely to attend treatment as non-suicidal participants and to attend the 1 and 6 month follow-up interviews.

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Author Year (Score):	**Bryan 2016 (score=2.5)**
Comments:	Primarily male active duty soldiers. Data suggest suicide related outcomes were primarily related to depression and were similar in both groups.
Author Year (Score):	**Rabe 2008 (score=2.0)**
Comments:	Waitlist control bias. Data suggest CBT may cause adaptive brain changes in PTSD patients.
Author Year (Score):	**Ahmadizadeh 2013 (score=2.0)**
Comments:	Sparse methods. Little baseline information, no data on dropouts or compliance.
Author Year (Score):	**Ivarsson 2014 (Score=6.0)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by Linkoping University. No mention of COI.
Sample size:	N = 62 Swedish patients with chronic PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 46±11.7 years; 11 males, 51 females.
Comparison:	ICBT group: received 8 weekly Internet-based cognitive behavior treatment included breathing retraining, psychoeducation, IE and in vivo exposure, relapse prevention, and cognitive restructuring (n = 31) vs. control group: received 8 weekly delayed treatment attention control with self-report questionnaire and phone based interview (n = 31).
Follow-up:	Follow-up at 1 year.
Results:	78.6% participants in treatment group and 25.9% participants in control group indicated improvement on Impact of Event Scale Revised (IES-R) scores, and significant difference was found between the two groups (p<0.001; 95%CI=3.01 to 36.45).
Conclusion:	“In sum, these results suggest that ICBT with therapist support can reduce PTSD symptoms significantly.”
Comments:	Data suggest ICBT showed significant reductions in PTSD symptoms, depression, anxiety and quality of life compared to control, and these results were stable for one year.
Author Year (Score):	**Spence 2011 (Score=5.0)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the New South Wales Institute of Psychiatry. No mention of COI.
Sample size:	N=44 Australian participant with telephone-administered diagnosis of PTSD.
Source of Trauma:	Physical or sexual assault, traffic accidents, or other stressful events.
Age/Sex:	Mean age: 42.6±13.1 years; 8 males, 34 females.

Comparison:	iCBT group: received 7 lessons of internet-based cognitive behavioral therapy in 8 weeks (n=23) vs. control group: received unstructured treatment after assessment as waitlist control (n=21)
Follow-up:	Follow-up at 3 months.
Results:	For PCL-C scores, the primary outcome, treatment group indicated significantly greater improvement than control group ($p<0.03$). No difference on PCL-C scores was found between post-treatment and follow up in the treatment group ($p=0.79$).
Conclusion:	"Results provide preliminary support for Internet-based CBT as an efficacious treatment for individuals with a confirmed primary diagnosis of PTSD."
Comments:	Waitlist control bias. Data suggest internet based CBT may be an effective treatment delivery method for PTSD.

Author Year (Score):	**Knaevelsrud 2007 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Supported by the German organization "Weisser Ring" for crime victims. The authors declared no COI.
Sample size:	N=96 German participant with posttraumatic stress reactions.
Source of Trauma:	Sexual abuse (i.e. rape), accident, physical disease, or death of close person.
Age/Sex:	Mean age: 35 years; 10 males; 86 females.
Comparison:	CBT group: received 10 sessions of internet-based cognitive behavioral therapy in 5 weeks (n=49) vs. control group: received waiting list control (n=47).
Follow-up:	Follow-up at 3 months.
Results:	Treatment group indicated large effect size for PTSD symptoms (d=0.98 to 1.41). For the IES-R scores, treatment group indicated superior to control group ($x^2=9.29$; $p=0.002$).
Conclusion:	"A stable and positive online therapeutic relationship can be established through the Internet which improved during the treatment process."
Comments:	Waitlist control bias. Data suggest internet delivered therapy may be a viable alternative to face to face therapy for PTSD.

Author Year (Score):	**Knaevelsrud 2010 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Supported by the German organization "Weisser Ring" for crime victims. The authors declared no COI.
Sample size:	N=96 German PTSD patients.
Source of Trauma:	Death of close person, sexual abuse/rape.
Age/Sex:	Mean age: 34 years; 4 males, 30 females.
Comparison:	CBT group: received 10 sessions of internet-based cognitive behavioral therapy over 5 weeks (n=41) vs. control group: received wait-list control (n=55).
Follow-up:	Follow-up at 3months and 1.5 year.

Results:	PTSD symptoms were improved after intervention; constructs included intrusion (t (33) =8.5), hyper-arousal (t (33) = 9.4), and avoidance (t (33) =6.1) (p< 0. 001). Physical functioning indicated no significant improvement (p=0.727).
Conclusion:	"Therefore, effective and accessible treatment alternatives such as Interapy are of substantial interest from the viewpoint of public health."
Comments:	Data suggest at 18 months, there were maintained gains for PTSD symptoms, anxiety and depression from internet based treatment.

Author Year (Score):	**Hobfoll 2015 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Supported by the McCormick Foundation, Pepsi-Cola Company, Goldman Sachs Gives, Robin Hood Foundation, Bristol-Myers Squibb Foundation, and Wallach Family Donation.
Sample size:	N=303 veterans with PTSD who served 911 in 2001
Source of Trauma:	911 attack in 2001.
Age/Sex:	Mean age: 34 years; 247 males, 56 females.
Comparison:	Vets Prevail group: received 6 weeks Vets Prevail included 7 online cognitive behavioral therapy lessons, community message board, and peer support (n=209) vs. AAU group: received 6 weeks adjustment as usual (n=94).
Follow-up:	Follow-up at 6 and 12 weeks.
Results:	Significant interaction of time and condition on PTSD reduction was found (p<0.001). Significant difference between pre-intervention and post-intervention in PTSD symptoms reduction was found (p=0.03).
Conclusion:	"Vets Prevail circumvents many barriers to care and effectively addresses the dire mental health needs of veterans."
Comments:	Usual care bias. Data suggest online interventions for PTSD in veterans with mild-moderate symptoms may benefit from a program like vets prevail.

Author Year (Score):	**Brief 2013 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N= 600 veterans served in operation enduring freedom or operation Iraqi freedom.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 32 years; 518 males, 92 females.
Comparison:	IIG group: received 8 modules of Initial VetChange intervention included motivational, self-control training, and cognitive behavioral training to change veterans drinking problem with 20 minutes per module (n=404) vs. DIG group: received delayed VetChange intervention after 8 weeks wait (n=196).
Follow-up:	Follow-up at 1 and 3 months.
Results:	Compared with DIG group participants, veterans in IIG group indicated significant greater reduction in PTSD symptoms (p=0.009), drinks per drinking day (DDD) (P<0.0001), average weekly drinks (p<0.0001), and percent heavy drinking days (p<0.0001).

Conclusion:	"VetChange is effective in reducing drinking and PTSD symptoms in OIF/OEF veterans."
Comments:	Waitlist control bias. Data suggest VET change may reduce PTSD and drinking in OIIF/OEF veterans and results maintained at 3 months.

Author Year (Score):	**Knaevelsrud 2015 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by German Foreign Ministry. The authors declared no COI.
Sample size:	N= 159 war-traumatized Arab patients.
Source of Trauma:	War
Age/Sex:	Mean age: 28.1±7.43 years; 45 males, 114 females.
Comparison:	Treatment group: received 10 sessions internet-based cognitive behavioral intervention treatment with 45 minutes per 2 weekly sessions over 5 weeks (n=79) vs. control group: received the same intervention as treatment group after 6 weeks wait (n=80).
Follow-up:	Follow-up at 3 months.
Results:	First outcome PDS includes intrusion (8.32 to 5.09), hyperarousal (9.52 to 6.42), and avoidance (12.49 to 8.78) in treatment group significantly indicated greater reduction than in the control group: intrusion (8.33 to 8.06), hyperarousal (9.52 to 9.07), and avoidance (12.80 to 13.04) ($p<0.001$).
Conclusion:	"[E]ven in unstable and insecure settings with ongoing exposure to human rights violations through war and dictatorships, people with posttraumatic stress symptoms benefit from a cognitive behavioral treatment provided entirely through the Internet."
Comments:	Waitlist control bias. Data suggest benefit from web-based CBT for war victims with PTSD.

Author Year (Score):	**Engel 2015 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=80 veterans with PTSD.
Source of Trauma:	Military conflict
Age/Sex:	Mean age: 36.4 years; 65 males, 15 females,
Comparison:	DESTRESS-PC group: received 6 weeks delivery of self-training and education for stressful situations intervention included a variant of cognitive behavioral therapy-based stress inoculation training with 3 times logins to a website to self-evaluate PTSD symptoms per week (n=43) vs. OUC group: received 6 weeks optimized usual care included usual primary care treatment for PTSD and 3 times of phone-based nurse check-ins to evaluate 0TSD symptoms (n=37).
Follow-up:	Follow-up at 6, 12, and 18 weeks.
Results:	Total PCL scores and treatment gains greatly improved in DESTRESS-PC group than OUC group ($p=0.012$); time effects ($p<0.001$); and recruitment site effect on PTSD improvement ($p=0.005$).
Conclusion:	"DESTRESS-PC shows promise as a means of delivering effective, early PTSD treatment in primary care. Larger trials are needed."
Comments:	Data suggest a trend towards the improvement of depression.

Author Year (Score):	**Spence 2014 (Score=4.5)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the National Health and Medical Research Council, and the New South Wales Institute of Psychiatry. The authors declared no COI.
Sample size:	N=125 participants with PTSD.
Source of Trauma:	Sexual or physical assault, injury, traffic accident, death of close person, combat, or natural disaster.
Age/Sex:	Mean age: 41±11.4 years; 17 males, 108 females.
Comparison:	EXP group: received 8 weeks of 4 lessons included stress management, cognitive restructuring and exposure components, and psychoeducation (n=59) vs. NoEXP group: received 8 weeks of 6 lessons included same components as treatment group except exposure component (n=66).
Follow-up:	Follow-up at 3 months.
Results:	Significant changes were found in the two groups after treatment, for PSS-I score ($p<0.001$), IES-R score ($p<0.001$). No significant differences were found between post-treatment and follow-up for the PTSD patients or the overall participants ($p>0.05$).
Conclusion:	"[T]rauma-focused cognitive behavioral therapy for PTSD with or with our exposure components can be safe and efficacious."
Comments:	Primary female participants. Data suggest comparable efficacy between groups.

Author Year (Score):	**Lewis 2017 (Score=4.0)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. The authors declared no COI.
Sample size:	N=42 patients who meet diagnostic criteria for mild to moderate DSM-5 PTSD.
Source of Trauma:	Sudden death witnessing, traffic accidents, sexual or physical assault, traumatic childbirth, being held hostage,
Age/Sex:	Mean age: 38.3 years; 17 males, 25 females.
Comparison:	Guided self-help group: received 8 weeks internet-based self-help treatment included 8 online steps focused on psychoeducation, behavioral reactivation, imaginal exposure rationale, cognitive behavioral techniques and etc. (n=21) vs. waitlist group: received 14 weeks delayed treatment (n=21).
Follow-up:	Follow-up at 1 month.
Results:	Compared to the control group, the treatment group indicated significantly lower PTSD symptoms after intervention (Mean difference= 18.60, 95% CI=-24.65 to -13.41). No significant differences on CAPS were found for the two groups: treatment group: 35.99 to 15.77; control group: 37.12 to 14.8.
Conclusion:	"Internet-based trauma-focused guided self-help for PTSD is a promising treatment option that requires far less therapist time than current first line face-to-face psychological therapy."
Comments:	Crossover trial. Waitlist control bias. Data suggest decreased clinically assessed PTSD symptoms in intervention group.

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Author Year (Score):	**van Dam 2013 (Score=4.0)**
Category:	Computer-Assisted Cognitive Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Royal Netherlands Academy of Arts and Sciences. The authors declared no COI.
Sample size:	N=34 patients from Netherland with PTSD and substance use disorder (SUD).
Source of Trauma:	Severe substance abuse.
Age/Sex:	Mean age: 42.3 ±9.0 years; 23 males, 11 females.
Comparison:	TAU & SWT group: received 6 weeks 45 to 60 minutes weekly structured writing therapy for PTSD included writing assignments, cognitive reappraisal, and social sharing of trauma and treatment as usual based on cognitive behavioral therapy (n=19) vs. TAU only group: patients received 6 to 12 weeks only treatment as usual with 4 times per week (n=15).
Follow-up:	Follow-up at 3 months.
Results:	Significant decrease in PTSD severity was found in SWT and TAU group from mid-treatment to post-treatment (p=0.007). No significant decreases in PTSD symptom severity were found in TAU group (p>0.05).
Conclusion:	"[A]dding a trauma-focused treatment on to standard SUD treatment may be beneficial."
Comments:	Waitlist control bias. Preliminary data suggest TAU+SWT better than TAU for treating symptoms of PTSD combined with SUD.

Author Year (Score):	**Wagner 2012 (Score=3.5)**
Comments:	Waitlist control bias. Data suggest online treatment for war victims with PTSD may provide a therapeutic platform for treatment.

Author Year (Score):	**Acosta 2017 (Score=3.0)**
Comments:	Usual care bias. Data suggest web-delivered CBT significantly decreased heavy drinking but did not improve PTSD or quality of life.

Author Year (Score):	**Lange 2001 (Score=2.5)**
Comments:	Waitlist control bias. 80% of treatment group completers showed improvement compared to controls.

Author Year (Score):	**Resick 2008 (score=6.0)**
Category:	Cognitive Processing Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by National Institute of Mental Health Grant. No mention of COI.
Sample size:	N = 162 Adult females with PTSD
Source of Trauma:	Various sources of trauma
Age/Sex:	Mean age: 35.4 years; 0 males, 162 females
Comparison:	CPT (cognitive processing therapy; Therapy focused on anxiety and other emotions from traumatic events) patients (n=41). 12 sessions of 60 minute therapy, twice a week vs CPT-C; same

	treatment as previous except for WA component (N =40) vs Written accounts (WA; therapy via writing through traumatic experiences) patients (N=40). Each treatment lasted 6 weeks with two hours of therapy per week.
Follow-up:	3-month follow up
Results:	The CPT group showed significantly more change in CAPS scores than the CPT-C group (estimated improvement difference: −53.87, *SE* = 4.51, *z* = −11.96, *p* < .0001). The CPT-C group also showed significantly greater change in CAPS score over time than the CPT-C group (estimated improvement difference: −50.51, *SE* = 4.57, *z* = −11.06, *p* < .0001), but the CPT and CTp-C groups were not significantly different from each other.
Conclusion:	"Participants improved on most of the supplementary measures of symptoms and functioning included in this study, whether assessed by standardized assessor interviews or self-report scales across the three conditions."
Comments:	Waitlist control bias. Data suggest all 3 groups improved in PTSD and depression but the CPT-C group showed better PTSD improvement than WA.

Author Year (Score):	**Monson 2006 (score=6.0)**
Category:	Cognitive processing therapy
Study type:	RCT
Conflict of Interest:	Supported by a Clinical Research Career Development Award to Candice M. Monson from the VA Cooperative Studies Program. No mention COI.
Sample size:	N= 60 military personnel with PTSD
Source of Trauma:	Chronic military related PTSD
Age/Sex:	Mean age: 54 years; 54 males, 6 females
Comparison:	CPT treated (Therapy focused on anxiety and other emotions from traumatic events) (n=30). 12 sessions over 6 weeks. vs Waiting list control (n=30). Patients asked to wait 10 weeks to start the CPT treatment.
Follow-up:	1-month
Results:	Change in total CAPS in the CPT versus wait-list conditions, respectively, at posttreatment, 50% (n = 15) versus 10% (n = 3) had reliable improvement, 50% (n = 15) versus 80% (n = 24) had no reliable change, and 0% (n = 0) and 10% (n = 3) had reliable deterioration in their symptoms.
Conclusion:	"The current study suggests that substantial improvements can be made in a group of patients considered to be among the most chronic and treatment recalcitrant. We are hopeful for them, as well as for the new generation of veterans who have not suffered for decades."
Comments:	Waitlist control bias. Data suggest significant improvement in PTSD symptoms in CPT group.

Author Year (Score):	**Forbes 2012 (score=5.5)**
Category:	Cognitive Processing therapy
Study type:	RCT
Conflict of Interest:	COI; The Australian Centre for Posttraumatic Mental Health is partially funded by the Australian Government, Department of Veterans Affairs. Sponsored by the Australian Government, Department of Veterans Affairs

Sample size:	N=59 military veterans with PTSD
Source of Trauma:	Military-related PTSD
Age/Sex:	Mean age: 53.38 years; 57 Males, 2 Females
Comparison:	CPT (Therapy focused on anxiety and other emotions from traumatic events) treated (n=30) 12 twice weekly 1 hour sessions vs Treatment as Usual (TAU; therapy that the therapist administered from prior protocol) (n=29). Same treatment period as CPT.
Follow-up:	3-month follow up
Results:	At baseline, CPT and TAU groups differed only on CAPS total severity score, which was greater for the CPT group ($F(1,57) = 2.35$, $p < 0.05$). No significant differences were evident between the two conditions in treatment credibility (CPT: M = 18.96, SD = 5.91; TAU: M = 19.64, SD = 4.90).
Conclusion:	"This trial reports the first RCT evidence that CPT (recently rolled out across US veterans services) is a highly effective treatment for military-related PTSD and co-morbidity when administered by community practitioners to regular clients in veterans' community based mental health services under fully controlled conditions."
Comments:	Usual care bias. At 3 months, CPT showed significantly greater improvement in PTSD.

Author Year (Score):	**Bolton 2014 (score=5.0)**
Category:	Cognitive processing therapy
Study type:	RCT
Conflict of Interest:	Sponsored by USAID Victims of Torture Fund. No mention of COI.
Sample size:	N=281 Adult survivors of systematic violence
Source of Trauma:	Systematic Violence
Age/Sex:	Mean age: 41.08 years; 79 Males, 202 Females
Comparison:	Behavioral activation treatment for depression (BATD; therapy based on Skinnerian models for behavior change) (n=82) vs CPT (n=67) (Therapy focused on anxiety and other emotions from traumatic events) vs Basic supportive counseling program (n=53). Each treatment followed the 12-session model.
Follow-up:	6 month follow up
Results:	Estimated effect sizes for depression and dysfunction were 0.60 and 0.55 respectively, comparing BATD participants to all controls and 0.84 and 0.79 respectively, compared to BATD controls only. Estimated effect sizes for depression and dysfunction were 0.70 and 0.90 respectively comparing CPT participants to all controls and 0.44 and 0.63 respectively compared to CPT controls only.
Conclusion:	"Both interventions showed moderate to strong effects on most outcomes. This study demonstrates effectiveness of these interventions in low resource environments by mental health workers with limited prior experience."
Comments:	Data suggest comparable efficacy in both treatment groups compared to control

Author Year (Score):	**Nixon 2012 (score=4.5)**
Category:	Cognitive Processing therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a Flinders Research Grant. No mention of COI.
Sample size:	N=30 with acute stress disorder

Source of Trauma:	Physical or sexual assault
Age/Sex:	Mean age: 40.55 years; 16 Males, 14 Females
Comparison:	CPT (Therapy focused on anxiety and other emotions from traumatic events) (n=17) vs supportive counseling therapy aimed to reduce uncomfortable emotions associated with trauma (n=13). 6 weekly 90 minute sessions.
Follow-up:	6 month follow up
Results:	Testing (CAPS) showed that there was no significant difference between the two groups at posttreatment. For the ITT sample: CPT – M=23.83, SD=15.81; SC – M=42.36, SD=27.74, t(21)=1.99, and for the completer sample: CPT – M=23.83, SD=15.81; SC – M=39.63, SD=28.04, t(18)=1.62
Conclusion:	"In summary, CPT showed promise as a useful intervention for ASD. It was reasonably tolerated and resulted in significant reductions in posttraumatic and depressive symptoms, as well as a reduction in trauma-related cognitions. To date, the effectiveness as opposed to efficacy of CBT interventions for ASD is unknown, with all studies being conducted in the context of research or university treatment centers."
Comments:	Small pilot sample, high dropout rates. Data suggest at 6 months, similar efficacy between groups.

Author Year (Score):	**Resick 2017 (score=4.0)**
Category:	Cognitive Processing Therapy
Study type:	RCT
Conflict of Interest:	Supported by the US Department of Defense through the US Army Medical Research and Materiel Command. No COI.
Sample size:	N= 268 active duty service members with PTSD
Source of Trauma:	Military related PTSD
Age/Sex:	Mean age: 33.2 years; 244 Males, 24 Females
Comparison:	Group CPT: This therapy is focused on anxiety and other emotions from traumatic events, groups were allocated into group therapy sessions where CPT was the course of treatment. 12 session of 1 hour each, usually twice a week. (n=133) vs Individual CPT: same treatment as before, except patients allocated into individual sessions (n=135).
Follow-up:	6 month follow up
Results:	Improvement in PTSD severity at posttreatment was greater when CPT was administered individually compared with the group format (mean [SE] difference on the PSS-I, −3.7 [1.4]; Cohen d = 0.6; P = .006).
Conclusion:	"Individual treatment resulted in greater improvement in PTSD severity than group treatment. Depression and suicidal ideation improved equally with both formats. However, even among those receiving individual CPT, approximately 50% still had PTSD and clinically significant symptoms. In the military population, improving existing treatments such as CPT or developing new treatments is needed"
Comments:	Data suggest PTSD symptoms improved more with CPT administered individually rather than in a group format. However suicidal depression improved in both groups.

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Author Year (Score):	**Morland 2015 (score=3.5)**
Comments:	Data suggest comparable efficacy for PTSD in telemedicine (VTC) group and in-person (NP) group
Author Year (Score):	**Macdonald 2011 (score=3.5)**
Comments:	Waitlist control bias. Sparse methods. Data suggest improved PTSD symptoms following CPT with those treated earlier showing a faster decline following a slower rate of PTSD symptom improvement.
Author Year (Score):	**Suris 2013 (score=3.5)**
Comments:	Data suggest patient reported PTSD symptoms (not clinician evaluated symptoms) improved more in CPT group compared to PCT. However, concerns of the treatment fidelity (standard CPT delivery) resulted in diminishing data integrity and removal of his/her data.
Author Year (Score):	**Galovski 2016 (score=3.5)**
Comments:	Participant flow diagram is unclear as numbers of completers/dropouts do not add up/ data suggest sleep and depression improved but not symptoms of PTSD.
Author Year (Score):	**Resick 2015 (score=3.0)**
Comments:	Data suggest improvement in both group but greatest in CPT-C group.
Author Year (Score):	**Lee 2002 (Score=4.5)**
Category:	Stress Inoculation Training
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=24 participants with PTSD.
Source of Trauma:	Sexual or physical assault, traffic accidents, murder encounter, or combat.
Age/Sex:	Mean age: 35.3 years; 13 males, 11 females.
Comparison:	SITPE group: received 7 sessions of Stress inoculation training with prolonged exposure with 90 minute per weekly session (n=12) vs. EMDR group: received 7 sessions of eye movement desensitization and reprocessing with 90 minute per weekly session (n=12).
Follow-up:	Follow-up at 3 months.
Results:	Both groups indicated effective outcome in reduction of PTSD diagnostic status. In EMDR group, 83% participants showed no symptoms of PTSD; and in SITPE group, 75% participants also showed no PTSD symptoms. The two groups indicated significantly difference in improvement ($p<0.05$).
Conclusion:	"EMDR did significantly better than SITPE. At follow-up EMDR was found to lead to greater gains on all measures."
Comments:	Wait control bias. Data suggest comparable efficacy on global PTSD measures but on subscale measures, EMDR was better than SITPE like for the degree of intrusion. All measures showed EMDR better than SITPE at 3 month follow-up.

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Author Year (Score):	**Hensel-Dittman 2011 (score=4.5)**
Category:	Stress Inoculation Training
Study type:	RCT
Conflict of Interest:	Sponsored by the European Refugee Fund and the Deutche Forschungsgemeinschaft. No COI.
Sample size:	N = 28 individuals who had a history of experiencing organized violence and a current PTSD diagnosis.
Source of Trauma:	Organized violence such as war and torture.
Age/Sex:	No mention of age or gender.
Comparison:	Ten 90 min sessions of either narrative exposure therapy (N =15) vs stress inoculation training (N =13)
Follow-up:	Follow up before treatment, 4 weeks, 6 months, and 1 year.
Results:	For CAPS sum score there was a main effect of time ($F(3,52)=4.2$; $p=0.01$) and time-treatment interaction ($F(3.52)=3.08$;$p<0.05$). Symptom reduction in the NET group between pretest and 6-months (d=1.42, 95%CI 0.57-2.27) and between pretest and 1 year (d=1.59, 95% CI 0.62-2.57)
Conclusion:	"The results indicate that exposure treatments like NET lead to a significant PTSD symptom reduction even in severely traumatized refugees and asylum seekers."
Comments:	Data suggest NET led to PTSD symptom reduction and gains remained up to 1 year post treatment.

Author Year (Score):	**Lewis 2015 (score=3.5)**
Comments:	Sample predominately male. Data suggest PRESTINT lowered aroused and may be useful in coping with military stress.

Author Year (Score):	**Hourani 2016 (score=3.5)**
Comments:	Small Sample. PRESIT shows promise for being a tool used for prevention of stress in military personnel pre-deployment.

Author Year (Score):	**Foa 1999 (score=3.5)**
Comments:	Data suggest PE better than PE-SIT and SIT for post treatment anxiety and depression. PE-SIT and SIT showed comparable results.

Author Year (Score):	**Cook 2010 (score=5.5)**
Category:	Imagery Rehearsal Training
Study type:	RCT
Conflict of Interest:	Sponsored by the Office of Research and Development, Department of Veterans Affairs. No mention of COI.
Sample size:	N = 156 male U.S Vietnam War Veterans receiving mental health services at the Philadelphia VA Medical Center with current PTSD due to combat in Vietnam according to the DSM-IV criteria.
Source of Trauma:	Combat related.
Age/Sex:	Mean age: 59.4 years; 156 males, 0 females.
Comparison:	Weekly 90 min group sessions of imagery rehearsal (N=61) vs sleep and nightmare management (N=63) each for six weeks
Follow-up:	Follow up at baseline, 1, 3, and 6 months.

Results:	Pooled Pittsburg Sleep Quality Index Wald test: $\chi 2(1)=10.37$ ($p=.001$), and CAPS score, Wald test: $\chi 2(1)=20.97$ ($p<.001$)
Conclusion:	"Six sessions of imagery rehearsal delivered in group format did not produce substantive improvement in Vietnam War veterans with chronic, severe PTSD."
Comments:	Data suggest comparable efficacy in both groups for improved sleep quality but imagery rehearsal was not superior to conventional methods nor did either method substantially decrease the frequency of nightmares.

Author Year (Score):	**Ulmer 2011 (score=4.5)**
Category:	Imagery Rehearsal Training
Study type:	RCT
Conflict of Interest:	Sponsored by a Department of Veterans Affairs HSR&D Career Development Award CDA 09-218. Dr. Edinger has received research support from Philips Respironics and has consulted for Philips Respironics and Kingsdown, Inc. The other authors have indicated no financial conflicts of interest.
Sample size:	N = 22 veterans with PTSD.
Source of Trauma:	Combat-related
Age/Sex:	Mean age: 48.38 years; 13 males, 8 females.
Comparison:	Sleep Intervention for PTSD (SIP) (N=12) – patients received the usual care treatment and additional 6 bi-weekly 1-h individual sessions with an interventionist, 3 sessions of CBT, and 3 sessions of imagery rehearsal therapy (IRT). Vs. Usual Care (TAU) (N=9) – patients were treated by their primary care provider for sleep disturbance and PTSD symptoms.
Follow-up:	No follow up.
Results:	The comparison of means and treatment effect sizes for participants with complete base and post-intervention data on outcome questionnaires for the PCL-M mean scores were 62.39 at baseline, 44.00 for the SIP group, and 66.22 for the TAU. Cohen's D value = -1.85.
Conclusion:	"Findings demonstrate that an intervention targeting trauma-specific sleep disturbance produces large short term effects, including substantial reductions in PTSD symptoms and insomnia severity. Future research should focus on the optimal approach to the treatment of comorbid PTSD and sleep disturbance in terms of sequencing, and should assure that sleep-focused interventions are available and acceptable to our younger veterans, who were more likely to drop out of treatment."
Comments:	Usual care bias. Data suggest interventional group achieved large short-term reductions in PTSD symptoms severely and sleep disturbance.

Author Year (Score):	**Krakow 2001 (score=4.0)**
Category:	Imagery Rehearsal Training
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the National Institute of Mental Health and a grant from the University of New Mexico Health Sciences Center Research Allocation Committee. No mention of COI.

Sample size:	N = 168 female sexual assault survivors with self-reported nightmares, insomnia and posttraumatic stress symptoms coupled with a criterion A trauma link.
Source of Trauma:	Sexual assault.
Age/Sex:	Mean age: 36.9 years; 0 males, 168 females.
Comparison:	3 sessions of cognitive imagery treatment over 4 weeks (N=88) vs waitlist control (N=80)
Follow-up:	Follow up at baseline, 3 and 6 months.
Results:	Change in number of nightmares for treatment was -2.55 vs -0.40 for control (p=0.001). Change in nightmares per week was -3.94 for treatment and 0.56 for control (p=0.001)
Conclusion:	"Imagery rehearsal therapy is a brief, well-tolerated treatment that appears to decrease chronic nightmares, improve sleep quality, and decrease PTSD symptom severity."
Comments:	All participants female. Waitlist control bias. Data suggest imagery rehearsal therapy appears to significantly decrease nightmares associated with PTSD in sexual assault victims.

Author Year (Score):	**Thünker 2012 (score=4.0)**
Category:	Imagery Rehearsal Training
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 69 patients with nightmares, nightmares and depression, and nightmares and PTSD.
Source of Trauma:	No mention of trauma source.
Age/Sex:	Mean age: 37.3 years; 22 males, 47 females.
Comparison:	Primarily nightmare sufferers with nightmare therapy based on IRT (N=22) vs nightmares and depression with nightmare therapy based on IRT (N=21) vs nightmares and PTSD with nightmare therapy based on IRT (N=14) vs PTSD waitlist control (N=12)
Follow-up:	Follow up at baseline prior to therapy, post therapy and at 10 weeks.
Results:	Reduction in the number of nightmares in the treatment group ($t(13)=3.01$, $p<0.01$). Reduction of anxiety for treatment group ($t(13)=2.11$, $p<0.1$).
Conclusion:	"Thus, those who suffered primarily from nightmares showed the strongest benefit from the nightmare treatment."
Comments:	Mixed population of nightmare sufferers, PTSD sufferers and major depressives. Waitlist control bias in PTSD group. Data suggest manualized IRT improved nightmare frequency and anxiety in all groups.

Author Year (Score):	**Nijdam 2012 (score=6.0)**
Category:	Brief Eclectic Therapy
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by the Academic Medical Centre, Amsterdam, The Netherlands.
Sample size:	N = 140 with PTSD diagnosis via DSM-IV
Source of Trauma:	Assault, sexual assault, accident, disaster, war-related
Age/Sex:	Mean age: 37.8 years; 61 males, 79 females.

Comparison:	Eye movement desensitization and reprocessing – weekly 90 minutes sessions for 17 weeks (n = 70) vs. Brief eclectic psychotherapy – weekly 45-60 minute sessions for 17 weeks (n = 70)
Follow-up:	No follow-up reported
Results:	Mixed-model analysis showed significant main effect of time (F = 17.99, dF = 1065, p < 0.001), treatment condition (F = 12.20, dF = 169, p < 0.005), and significant interaction between time and treatment condition (F = 4.0, dF = 1065, p < 0.001). Response difference between groups (t = 3.49, dF = 169, p < 0.005). Mean difference on Impact of Event Scale-Revised score = 13.1 (95% CI 5.69-20.5).
Conclusion:	"Although both treatments are effective, EMDR results in a faster recovery compared with the more gradual improvement with brief eclectic psychotherapy."
Comments:	Data suggest comparable efficacy.

Author Year (Score):	**Nijdam 2013 (score=NA)**
Category:	Brief Eclectic Therapy
Study type:	Secondary Analysis to Nijdam 2012
Conflict of Interest:	No mention of COI. Sponsored by the Academic Medical Centre, Amsterdam, The Netherlands.
Sample size:	N = 140 with PTSD diagnosis via DSM-IV
Source of Trauma:	Assault, sexual assault, accident, disaster, war-related
Age/Sex:	Mean age: 37.8 years; 61 males, 79 females.
Comparison:	Eye movement desensitization and reprocessing – weekly 90 minutes sessions for 17 weeks (n = 70) vs. Brief eclectic psychotherapy – weekly 45-60 minute sessions for 17 weeks (n = 70)
Follow-up:	No follow-up reported
Results:	Data analysis focused on brief eclectic psychotherapy participants. 64 hotspots identified, with at least one hotspot was identified. Mean number of unique hotspots per patient = 3.20 (SD = 1.61). Did not differ significantly between successfully and unsuccessfully treated groups (U = 39.00, p = .218)
Conclusion:	"Repeatedly focusing on hotspots and looking for associated characteristics of hotspots may help clinicians to enhance the efficacy of imaginal exposure for patients who would otherwise show insufficient response to treatment."
Comments:	Secondary analysis of Nijdam 2012. Data point to "hotspots" and their associated characteristics to augment efficacy of imaginal exposure.

Author Year (Score):	**Nijdam 2015 (score=NA)**
Category:	Brief Eclectic Therapy
Study type:	Secondary Analysis to Nijdam 2012
Conflict of Interest:	No mention of COI. Sponsored by the Academic Medical Centre, Amsterdam, The Netherlands.
Sample size:	N = 140 with PTSD diagnosis via DSM-IV
Source of Trauma:	Assault, sexual assault, accident, disaster, war-related
Age/Sex:	Mean age: 37.8 years; 61 males, 79 females.
Comparison:	Eye movement desensitization and reprocessing – weekly 90 minutes sessions for 17 weeks (n = 70) vs. Brief eclectic

	psychotherapy – weekly 45-60 minute sessions for 17 weeks (n = 70)
Follow-up:	No follow-up reported
Results:	No difference found between treatment types, except for the Impact of Event Scale-Revised total score (Brief Eclectic Psychotherapy higher than Eye Movement Desensitization Reprocessing, t = 2.25, p = 0.03). Significant correlations between pretreatment PTSD symptom severity and California Verbal Learning Test (CVLT) sum of trials 1-5, CVLT long-term retrieval, CVLT long-term cued retrieval, Rivermead Behavioral Memory Test (RBMT) short-term retrieval, and RBMT long-term retrieval (all P ≤ 0.028)
Conclusion:	"Poor verbal memory performance represents a risk factor for worse treatment response to trauma-focused psychotherapy. Memory measure can be helpful in determining which patients are unable to benefit from trauma-focused psychotherapy."
Comments:	Secondary analysis of Nijdam 2012. Data suggest memory responses (memory performance) is correlated to trauma-focused psychotherapy treatment response such that poor performance equals poor response.

Author Year (Score):	**Lindauer 2005 (score=4.0)**
Category:	Brief Eclectic Therapy
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by Netherlands Organisation for Scientific Research (NOW) Grant.
Sample size:	N = 24 Dutch participants referred to outpatient clinic for further diagnosis and treatment of PTSD
Source of Trauma:	Interpersonal violence, accidents, disasters
Age/Sex:	Mean age: 38.95 years; 11 males, 13 females.
Comparison:	Brief Eclectic Psychotherapy – weekly 45-60 minute sessions for 16 weeks (n = 12) vs. Waitlist control (n = 12)
Follow-up:	Follow-up at 2 weeks post treatment
Results:	Intentional-to-treat, Pretest and Posttest scores for intervention and control groups, respectively: Reexperiencing score – 3.4 to 1.2, 3.9 to 3.1 (Test for Treatment Effects: F=4.97, p<0.05), Avoidance score – 3.9 to 1.6, 3.5 to 3.2 (F=3.60, p>0.05), Hyperarousal score – 3.8 to 1.3, 3.8 to 2.7 (F=5.82, p<0.05)
Conclusion:	"By posttest, BET had effectively reduced PTSD as well as general anxiety symptoms in the treated group of outpatients as compared to the waitlist group."
Comments:	Small samples. Wait-list control biases. Time since trauma in years different (2.7 vs. 6.2). Waitlist control bias. Data suggest BET reduced PTSD symptoms and symptoms of anxiety.

Author Year (Score):	**Gersons 2000 (score=3.5)**
Comments:	Population of Dutch police officers. Waitlist control bias. At 3 months the BEP groups showed significant improvement in PTSD symptoms except for hostility.

Author Year (Score):	**Van Emmerick 2008 (score=5.0)**
Category:	Narrative Exposure Therapy
Study type:	RCT

Conflict of Interest:	Sponsored by a grant from the Netherlands Organization for Health Research and Development. No mention of COI.
Sample size:	N = 126 participants with a DSM-IV diagnosis of PTSD.
Source of Trauma:	Traffic accident, non-sexual violence, and sexual violence.
Age/Sex:	Mean age: 40.2 years; 41 males, 85 females.
Comparison:	Weekly 1.5 hour treatment with CBT (N=41) vs structured writing therapy (N=44) vs waitlist control (N=41)
Follow-up:	Follow up at baseline, posttest, and mean of 381 days.
Results:	Mean IES-T score interaction between time and group for CBT vs SWT was F(1.79, 134.51)=0.44, p=0.62. Treatment vs waitlist control for the same was F(1.72,188.86)=6.72. p<0.01.
Conclusion:	"The present study confirmed the efficacy of CBT for ASD and PTSD and identified SWT as a promising alternative treatment."
Comments:	High dropout rate. Chronic PTSD subjects. Data suggest comparable efficacy between CBT and SWT.

Author Year (Score):	**Hensel-Dittman, 2011 (score=4.5)**
Category:	Narrative Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the European Refugee Fund and the Deutche Forschungsgemeinschaft. No COI.
Sample size:	N = 28 individuals who had a history of experiencing organized violence and a current PTSD diagnosis.
Source of Trauma:	Organized violence such as war and torture.
Age/Sex:	No mention of age or gender.
Comparison:	Ten 90 min sessions of either narrative exposure therapy (N =15) vs stress inoculation training (N =13)
Follow-up:	Follow up before treatment, 4 weeks, 6 months, and 1 year.
Results:	For CAPS sum score there was a main effect of time (F(3,52)=4.2; p=0.01) and time-treatment interaction (F(3.52)=3.08;p<0.05). Symptom reduction in the NET group between pretest and 6-months (d=1.42, 95%CI 0.57-2.27) and between pretest and 1 year (d=1.59, 95% CI 0.62-2.57)
Conclusion:	"The results indicate that exposure treatments like NET lead to a significant PTSD symptom reduction even in severely traumatized refugees and asylum seekers."
Comments:	Data suggest NET led to PTSD symptom reduction and gains remained up to 1 year post treatment.

Author Year (Score):	**Alghamdi, 2015 (score=4.5)**
Category:	Narrative Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by Taif University. No COI.
Sample size:	N = 34 firefighters who met DSM-IV criteria for PTSD.
Source of Trauma:	Related to firefighting.
Age/Sex:	Mean age: 30.4 ± 5.1 years; 34 males, 0 females.
Comparison:	Four 90 minute sessions of narrative exposure therapy over 3 weeks (N = 17) vs waitlist control (N = 17)
Follow-up:	Follow up at baseline, 3 and 6 weeks, and 3 and 6 months.

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Results:	Mean initial treatment outcome difference PTSD measure for NET group was 6.65 vs .58 for waitlist (p<0.001). Mean difference depression measure for NET group was 1.47 vs -0.06 for waitlist (p<0.001) Mean difference anxiety measure for NET group was 2.00 vs .12 for waitlist (p<0.001). P-values all rose above 0.05 by 3-month follow-up and stayed above for 6-month follow-up
Conclusion:	"In conclusion, NET is an effective treatment for traumatized firefighters displaying psychological symptoms"
Comments:	Waitlist control bias. Data suggest NET is effective for decreasing PTSD symptoms initially post treatment but is not sustained at 3 and 6 months.

Author Year (Score):	**Boden 2011 (score=4.5)**
Category:	Seeking Safety Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by VA Health Services Research and Development Service, granted to Drs Trafton and Kimerling. No COI.
Sample size:	N =98 male military veterans with a SUD and PTSD
Source of Trauma:	History of multiple traumas, Childhood trauma, military-related trauma
Age/Sex:	Mean age: 54 years; 98 males, 0 females
Comparison:	SS Group: (n=49) attended 24 group sessions (3 months of twice-weekly groups) of seeking safety, plus weekly individual case management sessions vs TAU Group: (n=49) received treatment as usual of at least 3 group sessions
Follow-up:	3, 6 months
Results:	SS group showed greater improvement than TAU group over time (p<.05). Reduction in drug use days was 2 days for SS group and a 0.5-day increase was observed in the TAU group. PTSD scores changed over time for the entire group (p<.01), but not between groups (p=.56). Alcohol use and PTSD severity decreased for both groups (p<.01).
Conclusion:	"The manualized treatment approach for substance use disorder, Seeking Safety, is well received and associated with better drug use outcomes than 'treatment as usual' in male veterans with posttraumatic stress disorder. However, the mechanism of its effect is unclear."
Comments:	Usual care bias. Data suggest seeking safety was associated with improved drug outcomes compared to TAU.

Author Year (Score):	**Hien 2004 (score=4.0)**
Category:	Seeking Safety therapy
Study type:	RCT
Conflict of Interest:	Sponsored by National Institute on Drug Abuse grant as a part of the National Institute of Justice Violence Against Women and Families Consortium. No mention of COI.
Sample size:	N=107 females with substance use disorder and comorbid PTSD
Source of Trauma:	Lifetime traumatic event, histories of trauma,
Age/Sex:	Mean age: 37.3 years; 0 males, 107 females
Comparison:	SS Group: (n=41) vs Relapse Prevention: (n=34) vs Community Care: (n=32)
Follow-up:	3, 6, 9 months

Results:	SS group and relapse prevention showed better results than community care. SS group showed main effect for substance use severity of F=8.49 (p<0.001). PTSD severity showed main effect of t=-2.5 for SS group (p<0.01) and t=-2.8 for relapse prevention group (p<.01). Community care group worsened over time in all primary outcome measures.
Conclusion:	"Seeking safety and relapse prevention are efficacious short-term treatments for low-income urban women with PTSD, substance use disorder, and other psychiatric symptoms."
Comments:	Data suggest at 9 months there was more improvement in substance abuse and PTSD symptoms in CBT group.

Author Year (Score):	**Boden 2014 (score=3.0)**
Comments:	Usual care bias. Data suggest focusing on coping skills may benefit those with both PTSD and SUD.

Author Year (Score):	**Cohen 2013 (score=3.0)**
Comments:	Usual care bias. Data suggest an integrated treatment for PTSD and SUD was associated with better IPV outcomes.

Author Year (Score):	**Mills 2017 (score=NA)**
Comments:	Secondary analysis. Data suggest improvement in PTSD symptoms substance use and depression improved during treatment but the length of imaginal exposures did not influence outcomes.

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Mind/body interventions have been used for PTSD patients to attempt to relieve stress and encompass a variety of techniques designed to use the mind to impact physical functioning and improve health [217, 218]. These include relaxation, meditation, deep breathing, emotional freedom techniques, hypnotherapeutic techniques, art therapy, music therapy, spiritual-based interventions, guided imagery, neurofeedback techniques, and mindfulness [218-224].

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**

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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;

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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.

Evidence for the Use of Mind/Body Interventions

Author Year (Score):	**Kelly 2016 (score=6.5)**
Category:	Mind-Body Interventions
Study type:	RCT
Conflict of Interest:	Sponsored by a 1440 grant from Mind Life Institute awarded to AK and ELG and by NIDA Grant. No mention of COI.
Sample size:	N=45 self-identified female survivors of interpersonal violence
Source of Trauma:	Physical or sexual abuse
Age/Sex:	Mean age: 41.5±14.6 years; 0 males, 45 females
Comparison:	TI-MBSR intervention: (n=23) received 2-2.5 hour weekly sessions of guided mediation, gentle movement exercise, didactic lecture, and group discussion as well as practice mindfulness for 30-45 min per day vs Waitlist Control Group: (n=22)
Follow-up:	8 weeks, 6 months, 12 months
Results:	TI-MBSR group showed decrease in both PTSD (p=.004) and depressive (p=.006) symptoms. Mindfulness practice showed reduction in PTSD symptoms (p=.004).
Conclusion:	"TI-MBSR appears to be a promising and feasible phase I intervention for female survivors of interpersonal trauma."
Comments:	Waitlist control bias. Data suggest reduction in PTSD and depressive symptoms in TI-MBSR group and a correlation between minutes of practice and predictions for symptom reduction.

Author Year (Score):	**Polusny 2015 (score=6.5)**
Category:	Mind-Body Interventions
Study type:	RCT
Conflict of Interest:	Sponsored by VA grant to Dr. Lim. No COI.
Sample size:	N=116 veterans with PTSD

Source of Trauma:	Combat exposure, sexual trauma, physical assault, disaster exposure, serious injury event, life-threatening illness or injury, Sudden unexpected death, other traumatic event
Age/Sex:	Mean age: 58.5±9.8 years; 98 males, 18 females
Comparison:	Mindfulness Based Therapy: (n=58) received 8 weekly 2.5 hour group sessions followed by 7weekly 2.5-hour group sessions and a 6.5-hour retreat, for a total of 9 sessions of mindfulness therapy, yoga, and meditation vs Present-Centered Group Therapy: (n=58) received 9 weekly 1.5 hour group sessions focused on current life problems as manifestations of PTSD
Follow-up:	3, 6, 9, 17 weeks
Results:	PCL scores improved for both MBT (from 63.6 to 54.4) and PCT (from 58.8 to 56.0). MBT group showed greater improvement than PCT group (6.44; 95% CI 3.34-9.53, p<0.001). Although self-reported improvement in PTSD symptoms was better for MBT group, no statistical difference was observed between groups (p=.03, p=.55; respectively).
Conclusion:	"Among veterans with PTSD, mindfulness-based stress reduction therapy, compared with present-centered group therapy, resulted in a greater decrease in PTSD symptom severity. However, the magnitude of the average improvement suggests a modest effect."
Comments:	Data suggest mindfulness stress reduction better than present-centered group therapy for clinically improved PTSD symptoms, quality of life, depression and mindfulness. However, both treatment groups improved and results at 2 months are similar for both groups.

Author Year (Score):	**Nakamura 2011 (score=6.0)**
Category:	Mind-Body Interventions
Study type:	RCT
Conflict of Interest:	Sponsored by National Institutes of Health (NIH) to the first author. No mention of COI.
Sample size:	N=63 veterans with sleep disturbance due to PTSD
Source of Trauma:	Combat-related trauma
Age/Sex:	Mean age: 52.1 years; 60 males, 3 females
Comparison:	MBB Group: (n=33) vs received 2 1.5 hour sessions over 3 weeks of mind-body bridging program that taught experiential tools to improve sleep SH Group: (n=25) received 2 1-hour sessions over 3 weeks of active education control called sleep hygiene program (education on exercise, diet, alcohol and caffeine intake before bed, regular practice, etc.)
Follow-up:	3 weeks
Results:	MBB group showed fewer participants with no improvement compared to SH group (3% vs 24% respectively). Median improvement score for MBB group was 20-30 compared to SH group with 0-10. Mean sleep disturbance score was lower in MBB group at follow-up than SH group (p=.002). PTSD symptoms PCL-M scores lessened for MBB group by 8.1 compared to SH group by 2.6.
Conclusion:	"This study provides preliminary evidence that a brief sleep-focused MBB could be a promising intervention for sleep and potentially other comorbid symptoms (e.g., PTSD). MBB could help patients develop awareness skills to deal with sleep-related symptoms. Integration of MBB into primary care settings may enhance care of patients with sleep disturbance and co-morbid symptoms."

Comments:	Data provide preliminary evidence that brief MBB may assist in improving sleep and PTSD symptoms. However there were no improvement in quality of life or depression in either group.
Author Year (Score):	**Bormann 2014 (score=6.0)**
Category:	Mind-body interventions
Study type:	RCT
Conflict of Interest:	Sponsored by US Department of Veterans Affairs, Office of Research and Development, Health Services Research & Development, Nursing Research Initiative. No COI.
Sample size:	N=146 veterans with PTSD
Source of Trauma:	Military-related trauma
Age/Sex:	Mean age: 57±10.1 years; 142 males, 4 females
Comparison:	MRP +TAU: (n=71) received 6 90-min weekly group sessions of mantram repetition program (3 tools for training attention and regulating emotion) and treatment as usual vs TAU: (n=75) received treatment as usual which consisted of case management
Follow-up:	6 weeks
Results:	Treatment effect was 6.46 MAAS scale (p=.0006). Average mantram practice sets were 7.97 for MRP group which showed effect of MRP on mindful attention of p=.04.
Conclusion:	"The MRP intervention and specifically, mantram practice, improved mindful attention in veterans with PTSD, yielding improved overall psychological well-being. MRP may be a beneficial adjunct to usual care in veterans with PTSD."
Comments:	Data suggest mantram practice improved attention thus yielding improved psychological well-being in PTSD veterans.
Author Year (Score):	**Oman 2015 (score=NA)**
Category:	Mind-body interventions
Study type:	Secondary Analysis of Bormann 2014
Conflict of Interest:	Sponsored by the U.S. Department of Veterans Affairs, Office of Research and Development, Health Services Research & Development, Nursing Research Initiative. No mention of COI.
Sample size:	N=146 veterans with PTSD
Source of Trauma:	Military-related trauma
Age/Sex:	Mean age: 58±9 years; 129 males, 3 females
Comparison:	MRP+CM: (n=71) received 6 90-min weekly sessions mantram repetition program and case management vs CM: (n=75) received case management alone
Follow-up:	6 weeks
Results:	MRP+CM group showed efficacy at 6 weeks (p=.003) with a main effect of 0.75 (95% CI 0.26-1.24). Control group achieved 0.87 self-efficacy points units compared to MRP+CM group with 0.75 units. PTSD symptoms were reduced using CAPS (Cohen's d=0.39; p<04). Improvement in mental health, depression, spiritual well-being, and physical-health satisfaction were observed (p<.05).
Conclusion:	"We concluded that MRP fosters self-efficacy for managing PTSD symptoms, favorably affecting diverse facets of well-being, and that physical health effects merit investigation."
Comments:	Data suggest a significant improvement in PTSD symptoms by fostering self-efficacy from MRP group.

Author Year (Score):	**Kip 2013 (score=6.0)**
Category:	Mind-body interventions
Study type:	RCT
Conflict of Interest:	Sponsored by the Army Medical Research and Materiel Command, and Telemedicine and Advanced Technology Research Center. COI: One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N= 57 U.S. service members/veterans
Source of Trauma:	Combat-related psychological trauma, witnessing death, execution, major injuries
Age/Sex:	Mean age: 41 ± 13 years; 46 males, 11 females
Comparison:	ART Group: (n=29) received 2-5 sessions for 60-75-min each session of accelerated resolution therapy (ART) including imaginal exposure, bilateral eye movements, and imagery rescripting vs AC Group: (n=28) received 2 1-hour sessions of fitness and career assessment and planning
Follow-up:	3 months
Results:	Mean PCL-M score change for ART group was -17.2±13.4 and the AC group was -2.5±6 (p<.0001). ART group showed greater reduction in depression, anxiety, and trauma-related guilt, and aggression compared to AC group (p<0.0001).
Conclusion:	"ART appears to be a safe and effective treatment for symptoms of combat-related PTSD, including refractory PTSD, and is delivered in significantly less time than therapies endorsed by the Department of Defense and Veterans Administration. "
Comments:	Data suggest strong and sustained treatment results in ART group for PTSD, depression, and anxiety at 3 months which were statistically significant and involves less time.

Author Year (Score):	**Kearney 2016 (score=5.5)**
Category:	Mind-body interventions
Study type:	RCT
Conflict of Interest:	Sponsored a grant from the VA Office of Research and Development. No COI.
Sample size:	N=55 veterans with gulf war illness
Source of Trauma:	Combat-related trauma
Age/Sex:	Mean age: 49.96 years; 47 males, 8 females
Comparison:	MBSR Group: (n=26) received mindfulness based stress reduction class weekly 2.5 hour sessions for 8 weeks plus 1 extra 7-hour session between weeks 6-7 vs TAU: (n=29)
Follow-up:	2, 6 months
Results:	MBSR group showed greater reduction in pain at 6 months than TAU group (f=0.33, p=.049) and also for cognitive failures (f=.4, p<.001). This was not observed for fatigue in MBSR group (f=0.32, p=.027). Greater reduction in PTSD symptoms were observed in MBSR group compared to TAU group (f=0.31, p=.082).
Conclusion:	"Mindfulness-based stress reduction in addition to treatment as usual is associated with significant improvements in self-reported symptoms of Gulf War illness, including pain, fatigue, cognitive failures, and depression."

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Comments:	Usual care bias. Data suggest significant reductions in pain, depression, fatigue, and cognitive failures in the intervention group but gains were not maintained at 6 months.

Author Year (Score):	**Jain 2012 (score=5.0)**
Category:	Mind-body interventions
Study type:	RCT
Conflict of Interest:	Sponsored by Donald and Ruth Taylor as well as Samueli Institute. No mention of COI.
Sample size:	N=123 active-duty military with PTSD
Source of Trauma:	No mention of specific trauma
Age/Sex:	Mean age: 27.5 years; 112 males, 11 females
Comparison:	HT+GI+TAU: (n=68) received 6 sessions of healing touch over a 3-week period (two sessions per week) with guided imagery and treatment as usual care vs TAU: (n=55) received treatment as usual
Follow-up:	No follow-up.
Results:	PTSD symptoms decreased for the HT+GT group (Cohen's d=0.85) and a decrease in PCL scores showed significance of p<0.0005. HT+GI group showed greater improvements in quality of life (p=0.002) and cynicism (p=0.001) compared to TAU group.
Conclusion:	"Participation in a complementary medicine intervention resulted in a clinically significant reduction in PTSD and related symptoms in a returning, combat-exposed active duty military population. Further investigation of GT and biofield therapy approaches for mitigating PTSD in military populations is warranted."
Comments:	Usual care bias. Data suggest HT+GT resulted in a significant number of PTSD symptom reduction as well as increased quality of life and decreased depression.

Author Year (Score):	**Bormann 2013 (score=4.5)**
Category:	Mind-Body Interventions
Study type:	RCT
Conflict of Interest:	Sponsored by US Department of Veterans Affairs, Office of Research and Development, Health Services Research & Development, Nursing Research Initiative. No COI.
Sample size:	N=146 veterans with PTSD
Source of Trauma:	Military-related trauma
Age/Sex:	Mean age: 57±10.1 years; 142 males, 4 females
Comparison:	MRP +TAU: (n=66) received 6 90-min weekly group sessions of mantram repetition program (3 tools for training attention and regulating emotion) and treatment as usual vs TAU: (n=70) received treatment as usual which consisted of case management
Follow-up:	6 weeks
Results:	PCL scores dropped 5.62 for the MRP+TAU group compared to 2.47 for TAU group (p<.05). CAPS symptom severity improved by a mean of 21.26 points for the MRP+TAU group. MRP+TAU group showed reduced depression and improved mental health quality compared to TAU group, but not for anxiety.
Conclusion:	"In summary, the 6-week MRP was well received and tolerated, and demonstrated some improvement in PSTD symptoms, depression, and mental-health-related quality of life in veterans, when delivered as an adjunct to TAU (medication and case management)."

Comments:	Usual care bias. Data suggest a meditational mantram intervention may be of benefit as an adjunct to TAU to decrease PTSD symptoms in veterans with PTSD.

Author Year (Score):	**Possemato 2015 (score=4.5)**
Category:	Mind-body interventions
Study type:	RCT
Conflict of Interest:	Sponsored by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, and Office of Mental Health Services. No mention of COI.
Sample size:	N=62 patients with PTSD
Source of Trauma:	Military-related trauma
Age/Sex:	Mean age: 44.6±16.3 years; 54 males, 8 females
Comparison:	PCBMT: (n=36) received weekly in-person 1.5-hour PCBMT group sessions for 4 weeks vs PCTAU: (n=26) received primary care mental health with treatment as usual
Follow-up:	8 weeks
Results:	PCBMT group and PCTAU grouped showed similar improvements in PTSD severity in CAPS score (p=.03; p=.001, respectively) and PCL score (p=.16; p=.04, respectively). PCBMT group showed a greater decrease in depression compared to PCTAU group (p=.03).
Conclusion:	"Our data support preliminary efficacy of BMT for Veterans with PTSD. Whether PCBMT facilitates engagement into, or improves outcomes of, full length empirically supported treatment for PTSD remains to be evaluated."
Comments:	Treatment group with only 50% completion. Usual care bias. Data suggest severity of PTSD symptoms decreased in both groups but at 8 weeks depression was lower and PTSD gains were maintained in BMT group.

Author Year (Score):	**Wang 2015 (score=4.5)**
Category:	Mind-body interventions
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. No COI.
Sample size:	N=52 motor vehicle accident survivors with PTSD
Source of Trauma:	Motor-vehicle accident related trauma
Age/Sex:	Mean age: 40.3 years; 19 males, 27 females
Comparison:	HA Group: (n=26) received 8 weekly sessions of 40 minutes in small groups of 4-6 participants of creative arts therapy vs Waitlist Group: (n=26)
Follow-up:	2, 6, 12 months
Results:	No significant differences between groups in effect time in CAPS (p=.74) or IES-R (p<0.01). No group differences were observed for depression as well (p>.05).
Conclusion:	"Our results fail to support the hypothesis that the creative arts program is effect in avoiding MVA-related PTSD symptoms. But it only seems to be a short-term, rather than a long-term effect."
Comments:	Data suggest lack of efficacy.

Author Year (Score):	**Watson 1997 (score=2.5)**
Comments:	Data suggest lack of efficacy.

Evidence for the Use of Relaxation

Author Year (Score):	**Taylor 2003 (score=5.0)**
Category:	Relaxation
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by the British Columbia Health Research Foundation.
Sample size:	N = 60 who met the DSM-IV-TR criteria for PTSD
Source of Trauma:	No specified source of trauma mentioned.
Age/Sex:	Mean age: 37 years; 15 males, 45 females.
Comparison:	Each randomized to eight 90-minute individual sessions of exposure therapy (n=22) vs. eye movement desensitization and reprocessing (EMDR) (n=19) vs. relaxation therapy (n=19)
Follow-up:	Follow up at 3 months.
Results:	Outcome measured via CAPS scores. For each of the four dimensions evaluated (re-experiencing, avoidance, numbing, hyperarousal) reductions in CAPS scores were significant: relaxation group – $t(14) > 3.55$ ($p < 0.005$, $n^2 > 0.47$), EMDR – $t(14) > 3.66$ ($p < 0.005$, $n^2 > 0.49$), exposure therapy – $t(14) > 4.52$ ($p < 0.001$, $n^2 > 0.59$)
Conclusion:	"Compared with EMDR and relaxation training, exposure therapy (a) produced significantly larger reductions in avoidance and reexperiencing symptoms, (b) tended to be faster at reducing avoidance, and (c) tended to yield a greater proportion of participants who no longer met criteria for PTSD after treatment. EMDR and relaxation did not differ from one another in speed or efficacy."
Comments:	Data suggest lack of efficacy as exposure therapy superior to both EMRR and relaxation training in reducing avoidance or recurring symptoms, but there was similar efficacy on all other measures.

Author Year (Score):	**Thrasher 2010 (score=4.5)**
Category:	Relaxation
Study type:	RCT
Conflict of Interest:	Sponsored by the Wellcome Trust (035091), London, and by the UK Medical Research Council. No COI.
Sample size:	N = 77 participants with chronic PTSD.
Source of Trauma:	Trauma, personal, use of weapon, injury, disability, disfigurement, bereavement.
Age/Sex:	Mean age: 38 years; 24 males, 53 females.
Comparison:	Active treatment (n=57) – patients received either cognitive restructuring and/or exposure therapy. Vs. Relaxation only (n=20) –

Follow-up:	No mention of follow up.
Results:	Active treatment, compared with relaxation, CAPS change scores (mean, SD) were: 34.8, 22.8, compared with 13.2, 23.1. Overall, higher Significant others scale (SOS) scores (better social support) were significantly associated with greater improvement in CAPS, r = 0.36, df = 75, P <0.001. The SOS did not predict outcome with relaxation, r = 0.14, df = 18, P = 0.57. For active treatment, however, higher SOS strongly predicted better outcome, r = 0.46, df = 55, P<0.001.
Conclusion:	"Better social support is associated with significantly greater gain following cognitive restructuring and (or) exposure therapy for PTSD. Future interventions should consider augmenting social support as an adjunct to treatment."
Comments:	Data suggest lack of efficacy and suggests increased social support is predictive for better gain post exposure therapy or cognitive restructuring in the treatment of PTSD.

Author Year (Score):	**Freyth 2010 (score=3.5)**
Comments:	Data suggest at 4 years post treatment more patients sought additional treatment in the supportive counseling group.

Deep breathing exercises have been used to treat PTSD patients [167, 181, 228].

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.

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Evidence for the Use of Deep Breathing Exercises

Author Year (Score):	**Seppala 2014 (score=5.0)**
Category:	Deep Breathing Exercises
Study type:	RCT
Conflict of Interest:	Sponsored by Disabled Veterans of America Charitable Service Trust. No mention of COI.
Sample size:	N = 21 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 28. 6 years; 21 males, 0 females.
Comparison:	Active Group (n=11) patients attended Sudarshan Kriya yoga daily for a week for 3-hour sessions. vs Wait-List control group: (n= 10) patients were allocated to the wait-list group
Follow-up:	1 week before (time 1), 1 week after (time 2) the 7-day intervention. 1 month (time 3) and 1 year (time 4) post intervention.
Results:	Regarding PTSD symptoms, a Group × Time interaction was observed for the PCL–M, $F(3, 44.92) = 4.52$, $p = .007$. The active group showed fewer symptoms at Time 2, $t(45.08) = 4.39$, $p < .001$, Time 3, $t(45.22) = 3.17$, $p = .003$, and Time 4, $t(45.15) = 4.54$, $p < .001$, compared to Time 1.
Conclusion:	"This study found that a breathing-based meditation intervention resulted in improvements on psychophysiological and symptom measures. Sudarshan Kriya yoga, a week-long intervention with longitudinal benefits, shows promise as a viable alternative or adjunct intervention for addressing PTSD and suicide in returning veterans."
Comments:	Waitlist control bias. Data suggest the breathing-based meditation group lowered PTSD scores over control as well as decreasing anxiety and respiration rate.

Author Year (Score):	**Kim 2013 (score=4.5)**
Category:	Deep Breathing Exercises
Study type:	RCT
Conflict of Interest:	Sponsored by DHHS/NIH/NCATS UL1RR031977-01 and 5KL2RR031976-02, UNM Clinical and Translational Science Center. No COI.
Sample size:	N = 29 nurses with PTSD.
Source of Trauma:	Not specified.
Age/Sex:	Mean age: 47.55 years; 1 males, 28 females.
Comparison:	Mind Body intervention (MBX): (n=11) – patients participated in 16 standardized, semiweekly 60 min MBX sessions. Vs. Control group (CON): (n=11) these participants did have PTSD symptoms, but were not given the treatment. Vs. BASE group: (n=7) participants who were not positive for PTSD were assigned to this group to collect normative data for cortisol levels
Follow-up:	Baseline weeks 4, 8, and 16.
Results:	Eight-week outcomes for the MBX group were superior to those for the CON group (mean difference for PCL-C scores, - 13.6; 95% confidence interval [CI], -25.6, - 1.6; P = 0.01; mean difference for serum cortisol concentration, 5.8; 95% CI, 0.83, 10.8; P = .01). In the within-group analysis using t-testing, participation in the 8-week MBX significantly reduced PTSD symptom severity in the MBX group as measured by PCL-C (43.1±11.2 vs 24.3±3.3; 95%CI,

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	11.7, 25.9; P < .001). The changes in the MBX group were maintained for the 16-week follow up (mean differences for PCL-C scores, 0.3; 95% CI, -2.9, 3.4; p=0.85).
Conclusion:	"The results suggest that MBX appears to reduce the prevalence of PTSD-like symptoms in individuals exhibiting subclinical features of PTSD."
Comments:	Predominately-female subjects. Small sample size. Data suggest MBX may decrease subclinical PTSD features.

Meditation has been used to treat PTSD patients [181, 229-232].

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.

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Evidence for the Use of Meditation

Author Year (Score):	**Seppala 2014 (score=5.0)**
Category:	Meditation
Study type:	RCT
Conflict of Interest:	Sponsored by Disabled Veterans of America Charitable Service Trust. No mention of COI.
Sample size:	N = 21 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 28. 6 years; 21 males, 0 females.
Comparison:	Active Group (n=11) patients attended Sudarshan Kriya yoga daily for a week for 3-hour sessions. vs Wait-List control group: (n= 10) patients were allocated to the wait-list group
Follow-up:	1 week before (time 1), 1 week after (time 2) the 7-day intervention. 1 month (time 3) and 1 year (time 4) post intervention.
Results:	Regarding PTSD symptoms, a Group × Time interaction was observed for the PCL–M, $F(3, 44.92) = 4.52$, $p = .007$. The active group showed fewer symptoms at Time 2, $t(45.08) = 4.39$, $p < .001$, Time 3, $t(45.22) = 3.17$, $p = .003$, and Time 4, $t(45.15) = 4.54$, $p < .001$, compared to Time 1.
Conclusion:	"This study found that a breathing-based meditation intervention resulted in improvements on psychophysiological and symptom measures. Sudarshan Kriya yoga, a week-long intervention with longitudinal benefits, shows promise as a viable alternative or adjunct intervention for addressing PTSD and suicide in returning veterans."
Comments:	Waitlist control bias. Data suggest the breathing-based meditation group lowered PTSD scores over control as well as decreasing anxiety and respiration rate.

Exposure therapy involves the use of a variety of exercises which make a patient confront a traumatic memory and reorganize it [233]. Exposure therapies are often combined with CBT. This may be done through virtual reality exposure, imaginal exposure, narrative exposure,in vivo exposure to a traumatic event [234, 235], and/or virtual reality exposure (reviewed separately). Prolonged Exposure Therapy (PE) is a treatment that involves forced visual confrontation of trauma-related stimuli [236-242].

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.

Evidence for the Use of Exposure Therapy and Prolonged Exposure Therapy

Author Year (Score):	**Litz 2012 (score=7.0)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by VA as part of a joint VA/NIMH solicitation for R-34 type PTSD trials. COI: one or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=26 veterans with PTSD
Source of Trauma:	Military-related trauma
Age/Sex:	Mean age: 32.2±9.3 years; 26 males, 0 females
Comparison:	DCS: (n=13) received 6 60-90-min sessions of exposure therapy (20 min after session starts) and 50 mg D-cycloserine (DCS) prior to sessions 2-5 vs Placebo: (n=13) received 6 60-90-min sessions of exposure therapy (20 min after session starts) and placebo pill prior to sessions 2-5
Follow-up:	3, 6 months
Results:	Veterans in the DCS group showed less symptom reduction than those in placebo group. CAPS scores decreased at 6 month follow-up (p=.061). PCL scores also decreased (p<.001), while BDI-II did not decrease (p=.17).
Conclusion:	"In contrast to previous trials using DCS to enhance exposure therapy, results indicated that veterans in the exposure therapy plus DCS condition experienced significantly less symptom reduction than those in the exposure therapy plus placebo condition over the course of the treatment."
Comments:	Both groups received prolonged therapy. Data are difficult to interpret as many secondary diagnoses co-exist with the PTSD diagnosis which could bias results. Data suggest D-cycloserine not effective as adjunct to PE.

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Author Year (Score):	**Schnurr 2007 (score=6.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by VA cooperative Studies Program and Department of Defense. COI: One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=283 females veterans/active duty personnel.
Source of Trauma:	Military service.
Age/Sex:	Mean age: 44.7 years; 0 males, 284 females
Comparison:	Group 1: received prolonged exposure therapy for 10 weeks. (N=141) vs Group 2: received present-centered therapy for ten sessions (N=143).
Follow-up:	Baseline, post treatment, 3 and 6 months.
Results:	Group 1, PTSD CAPS sale, posttreatment vs 6 month follow-up: 52.9 (47.7-58.0) vs 50.4 (45.0 – 55.8). Group 2, PTSD CAPS sale, posttreatment vs 6 month follow-up: 60.1 (55.3 – 64.8) vs 54.5 (49.3 – 59.7). Between group 1 and group 2 effect for PTSD CAPS scale $p<0.05$.
Conclusion:	"Prolonged exposure is an effective treatment for PTSD in female veterans and active-duty military personnel. It is feasible to implement prolonged exposure across a range of clinical settings."
Comments:	Data suggest prolonged exposure was better than present-centered therapy for reducing PTSD symptoms showing statistical sig. p=0.03.

Author Year (Score):	**Yehuda 2015 (Score=6.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Lightfighters Trust Foundation. The authors declared no COI.
Sample size:	N = 24 military veterans with PTSD.
Source of Trauma:	War.
Age/Sex:	Mean age: 49.6 years; 24 males, 0 female.
Comparison:	Hydrocortisone & PE group: received 30mg oral hydrocortisone intervention prior to 10 sessions of prolonged exposure psychotherapy (n=12) vs placebo & PE group: received placebo prior to 10 sessions of prolonged exposure psychotherapy (n=12).
Follow-up:	Follow-up at 6 weeks.
Results:	Veterans in hydrocortisone group showed significant change in CAPS total score (Cohen's d=0.43; 95%CI 0.78 to 0.05).
Conclusion:	"[H]ydrocortisone augmentation of PE may result in greater retention in treatment and thereby promote PTSD symptom improvement."
Comments:	High dropout rate in placebo group. Negative feedback sensitivity maintained by the glucocorticoid receptor. Both groups got PE.

Author Year (Score):	**Bryant 2008, a (score=6.5)**
Category:	Exposure Therapy
Study type:	RCT

Conflict of Interest:	Supported by National Health and Medical Research Council Program. No COI.
Sample size:	N=90 consecutive civilian trauma survivors referred to a traumatic stress clinic.
Source of Trauma:	Nonsexual assault and motor vehicle accident.
Age/Sex:	Mean age: 39.13±10 .87 years; 48 males, 52 females
Comparison:	Group 1: received imaginal exposure (N=31) vs Group 2: received in vivo exposure (N=28) vs Group 3: received both Imaginal exposure and in vivo exposure. (N=31) vs Group 4: received imaginal exposure, in vivo exposure, and cognitive restructuring. (N=28)
Follow-up:	Follow up at baseline, 3 months and 6 months.
Results:	Group 1 vs group 2 vs group 3 vs group 4, 6 month follow up participants with PTSD: 75% vs 69% vs 63% vs 31% ($p<0.01$). Group 4 showed significantly superior reductions in CAPS score compared to all other groups using ANOVA analyses ($p<0.05$).
Conclusion:	"[t]he current results suggest that therapists should consider implementing cognitive restructuring techniques in conjunction with exposure-based therapies."
Comments:	At 6 months, combination therapy resulted in fewer PTSD individuals. Data suggest a combination of CR with exposure therapy may be the best treatment for treating PTSD.

Author Year (Score):	**Markowitz 2015 (Score=6.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the New York State Psychiatric Institute, and National Institute of Mental Health grant. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=110 patients with chronic PTSD meet DSM-IV diagnosis standard.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 40.10±11.57 years; 33 males, 77 females.
Comparison:	PE group: received 10 weeks Prolonged exposure therapy with 90 minutes per weekly session (n=38) vs. psychotherapy group: received 14 weeks interpersonal psychotherapy with 50 minutes per weekly session (n=40) vs. relaxation group: received 9 weeks relaxation therapy with 90 minutes per weekly session (n=32).
Follow-up:	No mention of follow-up.
Results:	Three groups indicated improvement for CAPS: Prolonged exposure group d=1.88, interpersonal psychotherapy group d=1.69, and relaxation therapy group d=1.32. Among the three groups, prolonged exposure group indicated significant improvement ($p=0.010$), no significance was found in other two groups ($p=0.097$).
Conclusion:	"IPT had (non-significantly) lower attrition and higher response rates than prolonged exposure. Contrary to widespread Clinical belief, PTSD treatment may not require cognitive behavioral exposure to trauma reminders."
Comments:	Data suggest comparable efficacy between IPT and PE and IPT had an associated higher response rate (63% vs. 47% for PE and 38% for Relaxation Therapy) This data suggest cognitive behavioral exposures may not be required for PTSD treatment.

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Author Year (Score):	**Langkaas 2017 (Score=6.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Ministry of Education and Research, and the Ministry of Health and Care Services. The authors declared no COI.
Sample size:	N=65 patients with PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 45.2±9.7 years; 27 males, 38 females.
Comparison:	PE group: received 10 weeks prolonged exposure with 10 sessions and 90 to 120 minutes per session (n=31) vs. IE group: received 10 weeks rescripting-based imagery exposure with 10 sessions and 90 to 120 minutes per session (n=34).
Follow-up:	Follow-up at 12 months.
Results:	Two treatment groups indicated higher effects on PSS-I than control group (imagery rescripting group: p=0.03; prolonged exposure group: p=0.002).
Conclusion:	"[E]xposure mainly being effective for fear-based PTSD and strengthen the notion that exposure-based treatment is a generally effective treatment for all types of PTSD."
Comments:	Data suggest comparable efficacy. Patients nor treaters not blinded but paper said they were.

Author Year (Score):	**Asukai 2010 (Score=6.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by Japan's Ministry of Education, Culture, Sports, Science and Technology. No mention of COI.
Sample size:	N=24 civilian trauma survivors with PTSD.
Source of Trauma:	Civilian trauma.
Age/Sex:	Mean age: 29.3 years; 3 males, 21 females.
Comparison:	TAU group: received 10 weeks prolonged exposure with concurrent treatment as usual (n=12) vs. TAU & PE group: received 10 weeks treatment as usual and prolonged exposure later on (n=12).
Follow-up:	Follow-up at 3, 6, and 12 months.
Results:	CAPS differed significantly in pre and posttest in prolonged therapy group ($p<0.001$). Completers in both groups indicated significantly decreased CAPS scores ($p<0.001$).
Conclusion:	"The study's findings will promote the future dissemination and implementation of evidence-based treatment for PTSD in non-Western settings."
Comments:	Mostly female study participants with most also having depression. Waitlist control bias. Data suggest PE improved PTSD and sustained gains for up to 12 months post treatment.

Author Year (Score):	**Bryant 2008, b (score=6.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT

Conflict of Interest:	Supported by grant 300304 from the National Health and Medical Research. No COI.
Sample size:	N=90 consecutive civilian trauma survivors referred to a traumatic stress clinic.
Source of Trauma:	Motor vehicle accident and non-sexual assault.
Age/Sex:	Mean age: 35.4 years; 38 males, 52 females
Comparison:	Group 1: received prolong exposure therapy for 5 weeks (N=30) vs Group 2: received cognitive therapy for 5 weeks (N=30) vs Group 3: was a waitlisted control group (n=30)
Follow-up:	Baseline, 6 weeks, 3 and 6 months.
Results:	Group 1 vs Group 2, PTSD CAPS effect size comparison (0.80 considered significant) at 3 months: 0.42 (95% CI -0.09 to 0.92). Group 1 vs Group 3 PTSD CAPS effect size comparison at 3 months: 0.95 (95% CI 0.42-1.49). Group 2 vs group 3, PTSD CAPS effect size comparison at 3 months: 0.50 (95% CI -0.01 to 1.10).
Conclusion:	"Exposure-based therapy leads to greater reduction in subsequent PTSD symptoms in patients with ASD when compared with cognitive restructuring. Exposure should be used in early intervention for people who are at high risk for developing PTSD."
Comments:	Data suggest an early intervention of exposure based therapy is superior to cognitive restructuring for preventing PTSD in high risk individuals.

Author Year (Score):	**Tarrier 2000 (score=6.0)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by grant from The Wellcome Trust awarded to first author. No mention of COI.
Sample size:	N=62 patients with PTSD.
Source of Trauma:	Crime, accident, Other
Age/Sex:	Mean age: 38.6±11.6 years; 36 males, 26 females
Comparison:	Cognitive Therapy: (n=33) received 16 treatment sessions of cognitive therapy aimed to be emotion-focused and elicit patient's beliefs about meaning of event vs Imaginal Exposure: (n=29) received 16 treatment sessions of imaginal exposure therapy that was trauma focused and aimed to produce habituation of emotional responses by describing event
Follow-up:	6, 12 months
Results:	SSC change in treatment condition was 4.26 for CT (p=.004) and 5.61 for IE (p=.001). Therapy effect for means of symptoms for CT group was 38.5 and 27.96 for IE (F (1, 44) =3.06, p=.09). Results indicate a greater reduction in symptoms for patients receiving IE (p=.024).
Conclusion:	"It was cautiously concluded that although some PTSD patients could not tolerate exposure, those who could may receive greater subjective benefit than those who received cognitive therapy."
Comments:	Both treatments showed comparable efficacy but patients who receive imaginal exposure show improved PTSD symptoms upon subjective ratings. However, some patients are unable to withstand imaginal exposure due to feelings of guilt and lot emotions related to the incident.

Author Year (Score):	**McLay 2017 (score=6.0)**
Category:	Exposure Therapy

Study type:	RCT
Conflict of Interest:	Sponsored by U.S. Army Medical Research and Material Command, Fort Detrick, MD. No COI.
Sample size:	N=81 individuals with combat-related PTSD
Source of Trauma:	Combat
Age/Sex:	Mean age: 32.5 years; 78 males, 3 females
Comparison:	CET Group: (n=38) received 90-min sessions twice a week for 9 weeks of a trauma interview, education, exposure introduced, except virtual reality vs VRET: (n=43) received 90-min sessions twice a week for 9 weeks of a trauma interview, education, exposure introduced, virtual reality, etc.
Follow-up:	3 months
Results:	No differences were observed for group or time and group interaction, but an effect was observed for time ($p<0.001$) for CAPS scores. PTSD symptoms improved for both treatments, but no difference was observed between groups.
Conclusion:	"This study supported the utility of exposure therapy for PTSD, but did not support additional benefit by the inclusion of virtual reality."
Comments:	Data suggest exposure therapy (CET) and virtual reality exposure therapy (VRET) have comparable results, but virtual reality did not provide additional benefit.

Author Year (Score):	**Wells 2014 (Score=6.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. The authors declared no COI.
Sample size:	N=32 outpatients with PTSD diagnosis
Source of Trauma:	No mention of trauma source.
Age/Sex:	Mean age: 41±13.6 years; 20 males, 12 females.
Comparison:	MCT group: received 8 sessions of Metacognitive therapy with 60 minutes per session (n=11) vs. PE group: received 8 sessions prolonged exposure condition with 60 minutes per session (n=11) vs. control group: received 8 weeks wait list control (n=10).
Follow-up:	Follow-up at 3 months.
Results:	IES in treatment group indicated significant change ($p<0.0005$); MCT group showed lower IES scores than PE group (Mean $_{diff}$=14.9; $p=0.04$).
Conclusion:	"In conclusion; both treatments were effective but MCT had a clear advantage."
Comments:	Waitlist control bias. Data suggest both MCT and PE are effective in chronic PTSD patients with MCT resulting in better clinical gains.

Author Year (Score):	**Marks 1998 (Score=6.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Well-come Trust in London, England. No mention of COI.
Sample size:	N=87 patients with PTSD.
Source of Trauma:	No mention of trauma source.
Age/Sex:	Mean age: 38±10 years; 56 males, 31 females.

Comparison:	PE group: received 10 sessions of prolonged exposure therapy with 90 minutes per session (n=23) vs. cognitive group: received 10 sessions of cognitive therapy with 90 minutes per session (n=19) vs. PE & cognitive group: received 10 sessions of exposure and cognitive therapies with 105 minutes per session (n=24) vs. Relaxation group: received 10 sessions Relaxation therapy with 90 minutes per session (n=21).
Follow-up:	Follow-up at 1, 3, and 6 months.
Results:	Effect size of IES score in exposure group=2.6; cognitive group=0.08; exposure and cognitive group=1.9; relaxation group=1.1. CAPS score effect size in exposure group=1.4; cognitive group=2.2; exposure and cognitive group=1.9; relaxation group=0.8.
Conclusion:	"Both prolonged exposure and cognitive restructuring were each therapeutic on their own, were not mutually enhancing when combined, and were each superior to relaxation."
Comments:	Data suggest prolonged exposure and cognitive restructuring were effective but not synergistic when combined and each were better than relaxation.

Author Year (Score):	**Mills 2012 (score=5.5)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the Australian National Health and Medical Research Council. No mention of COI.
Sample size:	N = 103 participants with a DSM-IV-TR diagnoses of PTSD and substance dependence.
Source of Trauma:	Physical assault, threatened or held captive, witnessed injury or death, sexual assault, accident or disaster, torture and combat exposure.
Age/Sex:	Mean age: 33.7 years; 39 males, 64 females.
Comparison:	COPE plus usual treatment (N=55) vs only usual treatment (N=48)
Follow-up:	Follow up at baseline 6 weeks, 3 and 9-months
Results:	Mean difference CAPS score for COPE + usual care was -38.24 (95% CI -47.93,-28.54) vs -22.14 (95% CI -30.33,-13.95) for only usual treatment.
Conclusion:	"Among patients with PTSD and substance dependence, the combined use of COPE plus usual treatment, compared with usual treatment alone, resulted in improvement in PTSD symptom severity without an increase in severity of substance dependence."
Comments:	Data suggest COPE and usual care resulted in improved PTSD symptoms without a concomitant substance dependence increase.

Author Year (Score):	**Sloan 2012 (score=5.5)**
Category:	Exposure therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a National Institute of Mental Health grant awarded to Denise M. Sloan. No mention of COI.
Sample size:	N=46 individuals with motor-vehicle accident related PTSD
Source of Trauma:	Motor vehicle accident, physical assault, sexual assault
Age/Sex:	Mean age: 40.7±13.1 years; 16 males, 30 females

Comparison:	WET: (n=22) received 5 weekly sessions of 40 min-1 hour of written exposure therapy sessions vs WL: (n=24) received waitlist
Follow-up:	6 months
Results:	Standardized mean gain (ESsg) for WET was 3.18 (95% CI 2.2-4.16) indicating decreasing PTSD symptom severity and -14 for WL (95% CI -.39-.12).
Conclusion:	"These Findings suggest that a brief, written exposure treatment may efficaciously treat PTSD."
Comments:	Waitlist control bias. Few dropouts with good compliance. Data suggest WET improved PTSD symptoms with treatment gains lasting 30 weeks post intervention.

Author Year (Score):	**Wisco 2016 (score=5.5)**
Category:	Exposure Therapy
Study type:	Sub-analysis of Sloan 2012.
Conflict of Interest:	Sponsored by National Institute of Mental Health grants awarded to Terence M. Keane and Denise M. Sloan. No COI.
Sample size:	N=46 individuals with motor-vehicle accident related PTSD
Source of Trauma:	Motor vehicle accident, physical assault, sexual assault
Age/Sex:	Mean age: 39.5 years; 30 males, 16 females
Comparison:	Exposure-based therapy: (n=22) received 5 weekly sessions to write about index trauma in detail (30 min writing, then check with therapist) vs Waitlist Control: (n=24)
Follow-up:	6 months
Results:	A decrease in PTSD symptom severity was observed for treatment group with an effect size of 3.49 (6 weeks) and 2.18 (18 weeks). Standardized mean gain for treatment was ESsg=3.18 (95% CI 2.2-4.16) and ESsg=-14 (95% CI -.39-.12) for waitlist group indicating decrease in PTSD symptom severity. Also observed that there were reductions in self-reported negative affect (p<.001) and arousal (p<.001).
Conclusion:	"These findings highlight the importance of multimethod arousal assessment and add to a growing literature suggesting refinements of EPT."
Comments:	Waitlist control bias. Data suggest the interventional group exhibited larger treatment gains than the control group. Also, study found treatment gains were correlated with initial physiological activation.

Author Year (Score):	**Nacasch 2015 (Score=5.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. The authors declared no COI.
Sample size:	N=40 patients with PTSD.
Source of Trauma:	Combat, terrorist attack, accident, sexual or non-sexual assault.
Age/Sex:	Mean age: 36.87±13.4 years; 24 males, 16 females.
Comparison:	PE & IE group 1: received 10 to 15 sessions of 90-minutes prolonged exposure with 40-minute imaginal exposure intervention (n=20) vs. PE & IE group2: received 10 to 15 sessions of 60 minutes prolonged exposure with 20-minute imaginal exposure intervention (n=20).
Follow-up:	Follow-up at 6 months.

Results:	Short duration group indicated no inferior PSS-I scores, compared with long duration group (p=0.02). Time indicated main effect on PSS-I (p<0.001). Post intervention PSS-I showed no significant improvement in both groups (p=0.8).
Conclusion:	"[T]he outcomes of 60-minute sessions of PE do not differ from those of 90-minute sessions."
Comments:	Data suggest comparable efficacy for both treatment session types for PTSD outcomes.

Author Year (Score):	**Schneier 2012 (Score=5.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by National Institute of Mental Health Grant, and GlaxoSmithKline. The authors declared no COI.
Sample size:	N=37 adult survivors of WTC attacks.
Source of Trauma:	World Trade Center attacks of September 11 in 2011.
Age/Sex:	Mean age: 50.3 years; 17 males, 20 females.
Comparison:	PE & paroxetine group: received 10 weeks of combined prolonged exposure sessions with 12.5 mg/day paroxetine intervention (n=19) vs. PE & placebo group: received 10 weeks of prolonged exposure with 25 -50 mg/day placebo intervention (n=18).
Follow-up:	Follow-up at 6 months.
Results:	In week 10, both groups' CAPS scores improved significantly (p<0.001). Combined treatment group showed greater improvement than placebo group (p=0.01). More frequent remission showed in combined treatment group than placebo group (p=0.03).
Conclusion:	"Initial treatment with combined paroxetine plus prolonged exposure was more efficacious than prolonged exposure plus placebo for PTSD related to the World Trade Center attacks."
Comments:	Data suggest PE plus paroxetine better than PE plus placebo for PTSD from ETC attack.

Author Year (Score):	**Nacasch, 2011 (Score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=30 patients with combat related or terror related PTSD.
Source of Trauma:	Combat, or terror.
Age/Sex:	Mean age: 34.3 years; 30 males, 0 females.
Comparison:	PE group: received 9 to 15 sessions of prolonged exposure therapy with 90 to 120 minutes weekly session (n=15) vs. TAU group: received 9 to 15 sessions of treatment as usual with 1 hour weekly session (n=15).
Follow-up:	Follow-up at 12 months.
Results:	Treatment-by –time intervention indicated significant PSS-I score (p<0.001), it also indicated significant STAI-T score (p=0.016). Group-by-time intervention indicated significant PSS-I scores (p<0.001).
Conclusion:	"[P]rolonged exposure therapy is beneficial in the amelioration of combat-and terror-related PTSD symptoms."
Comments:	Usual care bias. Data suggest PE reduces symptoms of combat and terror-related PTSD vs. usual care.

Author Year (Score):	**Jun 2013 (score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the National Institute of Mental Health. No mention of COI.
Sample size:	N=200 patients with chronic PTSD.
Source of Trauma:	Sexual or nonsexual assault, vehicle accident, domestic violence, or combat.
Age/Sex:	Mean age: 37.41±11.30 years; 49 males, 151 females.
Comparison:	PE group: received 10 sessions of prolonged exposure lasted 90 to 120 minutes weekly (n=116) vs. Sertraline group: received 10 weeks of pharmacotherapy with 115 mg/day sertraline (n=84).
Follow-up:	No mention of follow-up
Results:	PTSD symptom severity (PSS-I) with sudden gains increased prediction of PTSD severity (p<0.001). Association between sudden gains and better outcome was found (p<0.001).
Conclusion:	"Individuals in both PE and sertraline experienced gains, though sertraline was associated with earlier large but reversible gains, and PE was associated with later gains."
Comments:	Data suggest both groups showed improvement in PTSD symptoms but Sertraline group showed improvement gains earlier which were reversible.

Author Year (Score):	**Simon 2008 (score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by GlaxoSmithKline. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=68 patients with primary diagnosis of PTSD.
Source of Trauma:	No mention of source of trauma
Age/Sex:	Mean age: 41.75±13.32 years; 24 males, 44 females.
Comparison:	PE group: received 8 sessions of open prolonged exposure therapy over 4 to 6 weeks (n=44) vs. Paroxetine &PE group: received 45.8 ±16.5 mg/day paroxetine CR augmentation of 5 sessions of prolonged exposure therapy every 2 weeks (n=11) vs. Placebo & PE group: received 44.8 ± 15.5 mg/day placebo augmentation of 5 sessions of prolonged exposure therapy every 2 weeks (n=14).
Follow-up:	Follow-up at 3 months.
Results:	Patients who completed Phase I indicated significant reduction on SPRINT score with mean points of 9.86±8.40 (p<0.0001). By the end of Phase II, SPRINT score indicated no association between the intervention group and placebo (p>0.05).
Conclusion:	"[O]ur data do not support the addition of paroxetine CR compared with placebo to continued PE for individuals with PTSD who remain symptomatic after initial PE, suggesting that the development of novel treatment approaches for PTSD refractory to PE is needed."
Comments:	Data suggest lack of efficacy of Paroxetine CR.

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Author Year (Score):	**Yuen 2015 (Score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by VA Clincial Sciences Research and Development and VA health Services Research and Development. The authors declared no COI.
Sample size:	N=52 veterans with PTSD.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 43.98±15.18 years; 51 males, 1 female.
Comparison:	In-person PE group: received 8 to 12 weeks of in-person prolonged exposure (n=29) vs. Tele PE group: received 8 to 12 weeks of home-based telehealth prolonged exposure (n=23).
Follow-up:	No mention of follow-up.
Results:	CAPS scores indicated no differences between the two intervention groups before treatment (p=0.04), in the in-person PE intervention, CAPS score decreased significantly after treatment (p<0.01); and CAPS score in the home-based PE group also decreased significantly after treatment (p<0.01) .
Conclusion:	"[P]E can be delivered via home-based telehealth with outcomes and satisfaction ratings comparable to in-person practices for certain symptoms, however additional research is needed."
Comments:	Data suggest comparable efficacy between in-person PE and home-based televideo PE.

Author Year (Score):	**Zoellner 2017 (Score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=42 chronic PTSD patients
Source of Trauma:	Sexual or non-sexual assault, car accident, combat, natural disaster.
Age/Sex:	Mean age: 37.5±12.4 years; 12 males, 30 females.
Comparison:	PE group: received 10 sessions pf waitlist/standard prolonged exposure twice per week (n=11) vs. MB & IE group: received 260 mg/day methylene blue and 5 daily imaginal exposure with 50 minutes per session (n=15) vs. IE group: received 260 mg/day placebo and 5 daily imaginal exposure group with 50 minutes per session (n=16).
Follow-up:	Follow- up at 1 and 3 months.
Results:	Treatment and time interaction indicated significant influence on primary outcome-evaluator-rated PTSD severity (p<0.0001). IE & MB and IE & placebo groups indicated significant difference with waitlist PE group (p=0.04).
Conclusion:	"The findings provide preliminary efficacy for a brief IE treatment for PTSD and point to the potential utility of MB for enhancing outcome."
Comments:	Waitlist control bias. Data suggest improved outcomes in both treatment groups with a trend towards MB being a little better than placebo.

Author Year (Score):	**De Bont 2013 (Score=5.0)**
Category:	Prolonged Exposure Therapy

Study type:	RCT
Conflict of Interest:	No mention of sponsorship. The authors declared no COI.
Sample size:	N=10 patients with psychotic disorder.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 43.6 years; 2 males, 8 females.
Comparison:	PE group: received 12 sessions of prolonged exposure with maximum 90 minutes per session (n=5) vs. EMDR group: received 12 sessions of eye movement desensitization and reprocessing group with maximum 90 minutes per session (n=5).
Follow-up:	Follow-up at 3 months.
Results:	PSS-SR scores indicated that PTSD symptom severity decreased in intervention (p<0.001). CAPS total scores also decreased in treatment (p=0.012).
Conclusion:	"PTSD patients with comorbid psychotic disorders benefit from trauma-focused treatment approaches such as PE and EMDR."
Comments:	Small sample. Patients had primary diagnosis of psychosis in addition to PTSD. Data suggest patients with PTSD and other psychotic illnesses benefit from treatment such as PE and EMDR.

Author Year (Score):	**Rauch 2015 (Score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the VA Office of Research and Development Clinical Sciences Research and Development. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=36 veterans with PTSD.
Source of Trauma:	Combat
Age/Sex:	Mean age: 31.9±7.6 years; 33 makes, 3 females.
Comparison:	PE group: received 10 to 12 sessions of prolonged exposure therapy with 80 minutes per session (n=18) vs. PCT group: received 10 to 12 sessions of present-centered therapy with 80 minutes per session (n=18).
Follow-up:	No mention of specific follow-up time length.
Results:	91% of the PE group indicated significant reductions in their CAPS score (from 79.2±12.1 pretest to 30.0±18.4 posttest), and 60% of the PCT group also indicated reduction (from 77.4±12.1 pretest to 53.6±28.7). No significant difference was found between time and treatment for the CAPS scores change (p=0.08).
Conclusion:	"Both increased cortisol response to personal trauma script prior to PTSD therapy and reductions in cognitive symptoms of PTSD were significantly and uniquely related to reductions in the core symptoms of PTSD in PE."
Comments:	PE was associated with a significantly higher number of PTSD symptom reduction than PCT (p=0.008). Data also suggest that cortisol measures likely are not related to changes in cognition.

Author Year (Score):	**Taylor 2003 (Score=5.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the British Columbia Health Research Foundation. No mention of COI.

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Sample size:	N=60 patients with diagnosis of PTSD.
Source of Trauma:	Sexual or physical assault, traffic accidents, or witness homicide.
Age/Sex:	Mean age: 37±10 years; 15 males, 45 females.
Comparison:	PE group: received 8 sessions of prolonged exposure therapy included four sessions of imaginal exposure and then 4 sessions of in vivo exposure with 60-90 minutes per session (n=22) vs. Relaxation group: received 8 sessions of relaxation training included 3 different exercises with 60-90 minutes per session (n=19) vs. EMDR group: received 8 sessions of eye movement desensitization and reprocessing with 90 minutes per session (n=19).
Follow-up:	No mention of specific follow-up time length.
Results:	CAPS scores in each treatment declined significantly: relaxation training (t-14>3.55; p<0.005); prolonged exposure therapy (t-14>4.52; p<0.001); eye movement desensitization and reprocessing (t-14>3.66; p<0.005). In the four dimensions of PTSD, numbing was significantly affected by time (p<0.01), but other three dimensions (re-experiencing, hyper-arousal, and avoidance) indicated no change (p>0.1).
Conclusion:	"[E]xposure therapy (a) produced significantly larger reductions in avoidance and reexperiencing symptoms, (b) tended to be faster at reducing avoidance, and (c) tended to yield a greater proportion of participants who no longer met criteria for PTSD after treatment. EMDR and relaxation did not differ from one another in speed or efficacy."
Comments:	Data suggest exposure therapy superior to both EMDR and Relaxation Training in reducing avoidance or reducing symptoms of PTSD but there was similar efficacy on all other measures.

Author Year (Score):	**Olden 2017 (score=5.0)**
Category:	Exposure Therapy
Study type:	Sub-analysis of Sloan 2012.
Conflict of Interest:	No mention of sponsorship. No COI.
Sample size:	N=11 adults with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 42.82 years; 9 males, 2 females.
Comparison:	Completers (n=7) – patients received 100 mg of DCS or the placebo 90 minutes before their weekly exposure session. Treatment lasted 12-15 weeks. Vs. Dropouts (n=4) – patients did not complete the study.
Follow-up:	No follow up.
Results:	Total CAPS scores dropped by more than half from M = 87.45, SD = 18.93 to M = 34.57, SD = 17.71 ($p < 0.001$, $d = 2.79$), with cluster D symptoms (hyperarousal) showing the most significant decline in symptoms ($p < 0.001$, $d = 2.70$), followed by cluster B (re-experiencing) symptoms ($p < 0.001$, $d = 2.58$) and cluster C (avoidance/numbing) symptoms ($p < 0.001$, $d = 2.21$).
Conclusion:	"The results suggest that it may be feasible to conduct clinical research using telehealth for PTSD and to use telehealth to increase access to care."
Comments:	Small sample. Data suggest an approximate 50% reduction in PTSD symptoms post telehealth-delivered medication augmented exposure therapy vs placebo.

Author Year (Score):	**Osuch 2009 (score=5.0)**

Category:	Exposure Therapy
Study type:	Cross-over.
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 9 subjects with chronic, treatment-refractory PTSD.
Source of Trauma:	Not specified.
Age/Sex:	Mean age: 41.4 years; 1 male, 8 females.
Comparison:	Active Group: (n=9) patients received 20 30-minute sessions imaginal exposure therapy with 1 Hz of rTMS. VS. Sham: (n=8) patients received 20 30 minute sessions imaginal exposure therapy with the sham rTMS.
Follow-up:	No follow up.
Results:	The CAPS B (instrusion) mean difference in the active group was -0.22, p=.48, d=-0.30 and in the sham group was -0.19, p=0.56, d=-0.25. Cohen's d was 0.45 between the active and sham group. The CAPS C (avoidance) mean difference in the active group was -0.33, p=.60, d=-0.23 and in the sham group was -0.72, p=0.28, d=-0.47. Cohen's d was 0.00 between the active and sham group. The CAPS D (hyperarousal) mean difference in the active group was -1.00, p=.08, d=-0.76 and in the sham group was -0.09, p=0.87, d=-0.07. Cohen's d was -0.42 between the active and sham group.
Conclusion:	"Active rTMS with exposure may have symptomatic and physiological effects. Larger studies are needed to confirm these preliminary findings and verify whether rTMS plus exposure therapy has a role in the treatment of PTSD."
Comments:	Small sample crossover design RCT with sham. Patients had refractory to treatment PTSD. Data suggest treatment group showed larger improvement compared to sham.

Author Year (Score):	**Beidel 2017 (score=5.0)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the U.S. Army Medical Research & Materiel Command-Military Operational Medicine Research Program. No mention of COI.
Sample size:	N = 92 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 35.6 years; 86 males, 6 females.
Comparison:	Trauma Management Therapy (TMT) (n=49) – Patients received 29 sessions: one education, 14 VRET, 14-group treatment. Vs. Virtual Reality Exposure Therapy (VRET) (n=43) Patients received 29 sessions: one education, 14 VRET, 14-group treatment and 7 sessions of psychoeducation.
Follow-up:	3 and 6 months.
Results:	CAPS score to TMT: Pre outcomes: M=85.5 sd (12.7), Post outcomes M=42.3 sd (22.0). CAPS score for EXP: Pre M=82.7 sd (17.2), Post M=34.9 sd (18.0). PCL-M score for CAPS: Pre M=63.4 sd(11.7) Mid M=38.9 sd(14.7),Post M=40.4 sd (14.8) CAPS PCL-M score for EXP: Pre M=59.4 sd(12.6), Mid M=34.6 sd(10.0), Post M=33.0 sd (9.7)
Conclusion:	"The results support the use of VRET as an efficacious treatment for combat-related PTSD, but suggest that VRET alone does not result in optimal treatment outcomes across domains associated with PTSD."
Comments:	Mean age differences between groups (37.86 vs 33.26). Dropout rate=39%. Data suggest both groups improved depression and

	anger, but sleep was not improved in either group. VRET helped some PTSD symptoms, but not all.
Author Year (Score):	**Lee 2002 (Score=4.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=24 participants with PTSD.
Source of Trauma:	Sexual or physical assault, traffic accidents, murder encounter, or combat.
Age/Sex:	Mean age: 35.3 years; 13 males, 11 females.
Comparison:	SITPE group: received 7 sessions of Stress inoculation training with prolonged exposure with 90 minute per weekly session (n=12) vs. EMDR group: received 7 sessions of eye movement desensitization and reprocessing with 90 minute per weekly session (n=12).
Follow-up:	Follow-up at 3 months.
Results:	Both groups indicated effective outcome in reduction of PTSD diagnostic status. In EMDR group, 83% participants showed no symptoms of PTSD; and in SITPE group, 75% participants also showed no PTSD symptoms. The two groups indicated significantly difference in improvement ($p<0.05$).
Conclusion:	"EMDR did significantly better than SITPE. At follow-up EMDR was found to lead to greater gains on all measures."
Comments:	Wait control bias. Data suggest comparable efficacy on global PTSD measures but on subscale measures, EMDR was better than SITPE like for the degree of intrusion. All measures showed EMDR better than SITPE at 3 month follow-up.
Author Year (Score):	**Acierno 2017 (Score=4.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the South Carolina Clinical & Translational Research Institute, Department of Veterans Affairs Health Services Research, and the National Institute of Mental Health. Several authors have received or will receive benefits for personal or professional use.
Sample size:	N=132 veterans with PTSD.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 41.8±14.5 years; 127 males, 5 females.
Comparison:	In-person PE group: received 6 sessions of in-person prolonged exposure in 10 weeks (n=69) vs. Tele-based PE group: received 6 sessions of home-based telehealth prolonged exposure in 10 weeks (n=63).
Follow-up:	Follow-up at 3 and 6 months.
Results:	No significance was found in time-by visit 9interaction for PCL and BDI scores: PCL score in in-person PE group=-1.9; PCL score in home-based PE group=-1.8.
Conclusion:	"[T]elehealth treatment delivered directly into patients' homes may dramatically increase the reach of this evidence-based therapy for PTSD without diminishing effectiveness."
Comments:	Data suggest comparable efficacy for both HBT and IP PE at both 3 and 6 months.

Author Year (Score):	**Ruglass 2017 (score=4.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the National Institute on Drug Abuse. Drs. T. Killeen and S. Back report they receive royalties from Oxford University Press for a treatment manual they wrote on utilizing COPE.
Sample size:	N = 110 patients with PTSD.
Source of Trauma:	Physical assault, sexual assault, accident or disaster, or sudden injury or death of other.
Age/Sex:	Mean age: 44.56 years; 70 males, 40 females.
Comparison:	COPE (n=39) – patients received an integrated program of PE for PTSD and RPT for SUD for 90-min weekly sessions for 12 weeks. Vs. RPT (n=43) – patients received a cognitive-behavioral SUD intervention focusing on coping strategies to manage situations that increase the risk of substance use relapse for 90-mins weekly for 12 weeks vs. AMCG (n=28) – patients met with research assistant weekly for 12 weeks to complete self-report measures, urine toxicology, alcohol breathalyzer, and to confirm general health/safety.
Follow-up:	1, 2, and 3 month.
Results:	Results for PTSD outcome: MPSS-SR total scores by the end-of-treatment session for COPE = -42.99, 95% CI -56.30 to -29.68, p<0.001 and for RPT = -31.51, 95% CI -40.64 to -22.38, p<0.001. Symptom reduction between groups: COPE-AMCG = –34.06, 95% CI –51.36 to –16.75, p < 0.001; RPT-AMCG = –22.58, 95% CI –36.92 to –8.24, p = 0.002; COPE-RPT = –11.48, 95% CI –27.62 to 4.67, p = 0.16. CAPS total severity score at 1 month follow up: COPE = -27.12, 95% CI –35.84 to –18.40, p<0.001; RPT = –25.38, 95% CI –33.12 to –17.64, p<0.001. CAPS total severity score at 3 month follow up: COPE = –28.31, 95% CI –36.01 to –20.60, p < 0.001; RPT = –26.71, 95% CI –34.28 to –19.14, p<0.001).
Conclusion:	"COPE and RPT reduced PTSD and SUD severity in participants with PTSD + SUD. Findings suggest that among those with full PTSD, COPE improves PTSD symptoms more than a SUD-only treatment. The use of PE for PTSD was associated with significant decreases in PTSD symptoms without worsening of substance use."
Comments:	Data suggest COPE better than SUD-only treatment as if decreases PTSD symptoms without escalating substance abuse and treatment gains for both groups were stable at 3 months.

Author Year (Score):	**Thrasher 2010 (score=4.5)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Wellcome Trust (035091), London, and by the UK Medical Research Council. No COI.
Sample size:	N = 77 participants with chronic PTSD.
Source of Trauma:	Trauma, personal, use of weapon, injury, disability, disfigurement, bereavement.
Age/Sex:	Mean age: 38 years; 24 males, 53 females.
Comparison:	Active treatment (n=57) – patients received either cognitive restructuring and/or exposure therapy. Vs. Relaxation only (n=20) –
Follow-up:	No mention of follow up.

Results:	Active treatment, compared with relaxation, CAPS change scores (mean, SD) were: 34.8, 22.8, compared with 13.2, 23.1. Overall, higher Significant others scale (SOS) scores (better social support) were significantly associated with greater improvement in CAPS, r = 0.36, df = 75, P <0.001. The SOS did not predict outcome with relaxation, r = 0.14, df = 18, P = 0.57. For active treatment, however, higher SOS strongly predicted better outcome, r = 0.46, df = 55, P<0.001.
Conclusion:	"Better social support is associated with significantly greater gain following cognitive restructuring and (or) exposure therapy for PTSD. Future interventions should consider augmenting social support as an adjunct to treatment."
Comments:	Data suggest increased social support is predictive for better gain post exposure therapy or cognitive restructuring in the treatment of PTSD.

Author Year (Score):	**Davis 2011 (score=4.0)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the University of Tulsa Office of Research and Sponsored Programs. No COI.
Sample size:	N=47 Patients with PTSD and nightmare disturbance.
Source of Trauma:	Sexual contact, serious accidents and physical assault with a weapon.
Age/Sex:	Mean age=38.49 years; 11 males. 36 females.
Comparison:	Treatment condition group (n=24): initial psychological interview that assessed for details of nightmare. Exposure, relaxation and rescripting therapy (ERRT) is conducted for 2 hours once a week for 3 consecutive weeks. Vs. Treatment control condition (n=23): initial psychological interview that assessed for details of nightmare. ERRT is conducted for 2 hours once a week for 3 consecutive weeks.
Follow-up:	Follow up at baseline, 3 months, and six months.
Results:	Treatment group (M=3.29, SD=0.62) baseline scores on severity of nightmare is reported greater than the control group (M = 2.91, SD = 0.65), $F_{1,47}$ = 4.13, p < 0.05,
Conclusion:	"Findings provide additional support for the use of ERRT in treating nightmares and related difficulties and improving sleep."
Comments:	Data suggest EERT improves sleep quality and reduces nightmares in PTSD patients.

Author Year (Score):	**Beidel, 2011 (score=4.0)**
Category:	Exposure Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health (NIMH). No mention of COI.
Sample size:	N = 35 veterans.
Source of Trauma:	Combat related.
Age/Sex:	Mean age: 59.3 years; 35 males, 0 females.
Comparison:	Trauma Management Therapy (TMT) (n=14) – patients received TMT, a multicomponent behavioral treatment that consisted of intensive EXP, programmed practice, and social and emotional

	rehabilitation. Treatment consisted of 14 90-minute sessions. Vs. Exposure Therapy Only (EXP) (n=16) – patients received 1 session of psychoeducation/treatment orientation and 14 sessions of EXP.
Follow-up:	No follow up.
Results:	The CAPS total score for PTSD symptoms in the TMT group was 84.9 pre-tx and 69.0 in post-tx; in the EXP group was 90.6 pre-tx and 65.5 post-tx; p=0.001. The PCL-M score for PTSD symptoms in the TMT group was 67.0 pre-tx and 60.9 post-tx; in the EXP group was 68.2 pre-tx and 63.6 post-tx; p=0.01. There were significant main effects for time for the CAPS Total Score (F (df = 1, 28) = 34.08, p < .001) and the PCLM (F (df = 1, 28) = 6.72, p < .01).
Conclusion:	"This study demonstrates efficacy of exposure therapy for treating the core symptoms of PTSD among combat veterans with a severe and chronic form of this disorder. Moreover, multi-component CBT shows promise for improving social functioning beyond that provided by exposure therapy alone, particularly by increasing social engagement/interpersonal functioning in a cohort of veterans with severe and chronic PTSD."
Comments:	Participants all male combat veterans. Data suggest comparable efficacy between both groups for statistically significant improvement in PTSD symptoms.

Author Year (Score):	**Arntz 2007 (Score=4.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=67 patients with PTSD who met DSM criteria.
Source of Trauma:	Physical abuse, weapon assault, sexual assault, traffic accident, trauma witnessing.
Age/Sex:	Mean age: 35±12 years; 23 males, 44 females.
Comparison:	IE group: received 9 weekly sessions of imaginal exposure with 90 minutes per session in 10 weeks (n=39) vs. IE & IR group: received 9 weekly sessions of combined imaginal exposure with imagery rescripting with 90 minutes per session in 10 weeks (n=29).
Follow-up:	Follow-up at 1 and 6 months.
Results:	Time has strong effect on PSS scores in the intervention (p<0.001). Linear and quadratic trends effect on PSS scores are also significant (p<0.001).
Conclusion:	"[T]he addition of rescripting to IE makes the treatment more acceptable for both patients and therapists, and leads to better effects on non-fear problems like anger and guilt."
Comments:	Imagery rescripting. Data suggest comparable efficacy in both groups for reduction of PTSD severity. Rgere was a trend towards favoring IE+IR for decreasing anger and guilt.

Author Year (Score):	**Øktedalen 2014 (Score=4.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=65 patients with trauma-related shame and guilt of PTSD symptoms.
Source of Trauma:	No mention of source of trauma.

Age/Sex:	Mean age: 45.18±9.73; 28 males, 37 females.
Comparison:	IE group: received 10 weekly sessions of imagery exposure with 40 to 60 minutes per session (n=34) vs. IR group: received 10 weekly sessions of imagery rescripting with 40 to 60 minutes per session (n=33).
Follow-up:	No mention of follow-up.
Results:	Hypothesis 1 testing indicated higher level of shame significantly correlated to greater PTSD symptoms (p<0.001). Hypothesis 3 testing indicated no correlation between within-person effect and shame and guilt (p=0.129).
Conclusion:	"[W]ithin-person change in shame and guilt predicts change in PTSD symptoms from session to session during treatment."
Comments:	Imagery rescripting. Data suggest shame and guilt are positively correlated with PTSD and change in guilt and shame and highly predictable for PTSD symptoms.

Author Year (Score):	**Horesh 2017 (Score=4.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Jerry Lee Foundation in Philadelphia and the Jewish Federation of New York, National Institute of Mental Health, and Lundbeck Pharmaceuticals Ltd. No mention of COI.
Sample size:	N=89 patients with PTSD.
Source of Trauma:	Vehicle accidents, or terrorist attacks.
Age/Sex:	Mean age: 40.28 years; 37 males.52 females.
Comparison:	PE group: received 12 weekly sessions of prolonged exposure-based therapy with 1.5 hour per session (n=56) vs. CT group: received 12 weekly sessions of cognitive therapy with 1.5 hour per session (n=33).
Follow-up:	No mention of specific follow-up time length.
Results:	Total scores in two groups main effect and group & time interactions indicated no significant effect (p=0.917; p=0.659). No significant change was found for total CAPS scores (p=0.55).
Conclusion:	"[P]E and CT are specifically, and differentially, useful in treating one particular PTSD symptom cluster."
Comments:	Waitlist control bias. Data suggest comparable efficacy for both treatment groups.

Author Year (Score):	**Castillo 2016 (Score=4.0)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the Department of Defense Grant. No mention of COI.
Sample size:	N=86 female veterans with PTSD
Source of Trauma:	Service duty after 911 attacks in 2001.
Age/Sex:	Mean age: 35.9 years;
Comparison:	Tx group: received 16 weeks of treatment included 5 imaginal exposure, 5 cognitive, and 4 behavioral sessions with 90 minutes per session (n=44) vs. WL group: received 16 weeks of minimal attention waitlist condition with 60 minutes per bimonthly unstructured session (n=42).
Follow-up:	Follow-up at 3 and 6 months.

Results:	Significant interaction indicated in the CAPS scores between treatment group and waitlist group comparison ($p<0.001$). Treatment group indicated significant decrease on CAPS score after intervention ($p<0.001$); waitlist group showed no change on CAPS score ($p=0.37$).
Conclusion:	"This study supports the use of group format for PTSD with 3 modules using improved methodology, with a novel, 3-member group which allows repeated in-session weekly imaginal exposures."
Comments:	Waitlist control bias. Data suggest group-delivered cognitive exposure therapy improved PTSD symptoms.

Author Year (Score):	**Rothbaum 2006 (score=3.5)**
Category:	Prolonged Exposure Therapy
Comments:	Data suggest Sertraline augmentation with prolonged exposure led to a significant decrease in the severity of PTSD symptoms.

Author Year (Score):	**Frommberger 2004 (score=3.5)**
Category:	Prolonged Exposure Therapy
Comments:	Data suggest Paroxetine inferior to CBT at 6 months.

Author Year (Score):	**Strachan 2011 (Score=3.5)**
Category:	Prolonged Exposure Therapy
Comments:	Data suggest a home based integrated tele health approach of exposure based treatment (BA and exposure components) may reduce PTSD, depression and anxiety.

Author Year (Score):	**Gros 2017 (Score=3.5)**
Category:	Prolonged Exposure Therapy
Comments:	Variable numbers of treatment sessions based on a case by case basis. Disability status and telehealth appeared predictive for treatment discontinuation.

Author Year (Score):	**Freyth 2010 (Score=3.5)**
Category:	Prolonged Exposure Therapy
Comments:	Data suggest at 4 years post treatment more patients sought additional treatment in the supportive counseling group.

Author Year (Score):	**Nosen 2014 (score=3.0)**
Category:	Exposure Therapy
Comments:	Baseline differences for current substance use. Data suggest EXP, a trauma focused therapy may be beneficial for substance use treatment for reducing PTSD associated with trauma cues.

Author Year (Score):	**Gros 2013 (score=2.5)**
Category:	Exposure Therapy

Comments:	Sparse methods. Data suggest disability is a predictor for treatment discontinuation.

Author Year (Score):	**Zalta 2014 (Score=2.0)**
Category:	Prolonged Exposure Therapy
Comments:	Sparse methods and limited details. Data suggest PTSD improvement may occur via modification of negative cognitions via PE.

Author Year (Score):	**Moser 2010 (Score=2.0)**
Category:	Prolonged Exposure Therapy
Comments:	Sparse methods with limited information. Data suggest a slight trend of better results from only PE therapy.

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Virtual reality exposure therapy (VRET) has been used to treat phobias and change behavior [246-248]. VRET also has been suggested as an effective treatment for PTSD [234, 235, 249, 250].

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.

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Evidence for the Use of Virtual Reality

Author Year (Score):	**Rothbaum 2014 (score=6.0)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health. COI, Dr. Rothbaum is a consultant to and owns equity in Virtually Better, Inc., Drs. Ressler and Davis are founding members of Extinction Pharmaceuticals / Therapade Technologies
Sample size:	N = 156 medically stable Iraq/Afghanistan veterans who met DSM-IV criteria for PTSD due to military trauma verified via the participant's discharge papers
Source of Trauma:	Military service.
Age/Sex:	Mean age: 35.1 years; 148 males, 8 females.
Comparison:	5 weekly 90- Minute virtual reality exposure sessions (VRE) + D-cycloserine 50 mg VS 5 weekly 90-minute VRE sessions + 0.25 mg alprazolam VS 5 weekly 90-minute VRE sessions + pill placebo
Follow-up:	Baseline screening assessment, follow-up assessments at 3, 6, and 12 months post-treatment.
Results:	Across all conditions, over course of trial, effect on Clinical Administered PTSD Scale (CAPS) (b = −12.19, CI: −16.04 to −8.33, (p < .001), d = 1.56) and effect on PTSD Symptom Scale (PSS) (b = −4.68, CI: −6.56 to −2.80, (p < .001), d = 1.16). Effect on CAPS after 12-months (b = −1.19, CI: −1.86 to −0.53, (p < .001)), effect on PSS after 12 months (b = −0.22, CI: −0.54 to 0.11, (p = .191)). learning x D-cycloserine interaction for the CAPS (b = −2.19, CI: −3.44 to −0.94, (p = .001)) and PSS (b = −0.82, CI: −1.19 to −0.45, (p = .001)).
Conclusion:	"A small number of VRE sessions were associated with reduced PTSD diagnosis and symptoms in Iraq/Afghanistan veterans, although there was no control condition for the VRE. Overall, there was no advantage of D-cycloserine on PTSD symptoms in primary analyses. In secondary analyses, benzodiazepine use during treatment may impair recovery, and D-cycloserine may enhance VRE in patients who demonstrate within-session learning. D-cycloserine augmentation treatment in PTSD patients may reduce cortisol and startle reactivity compared to the alprazolam and placebo treatment, consistent with the animal literature."
Comments:	High dropout rate. Analysis of data between clinical and biological measures dissimilar. Data suggest VRE improves PTSD symptoms. However, data suggest D-cycloserine showed lack of efficacy with an apparent long term attenuated response with use of alprazolam.

Author Year (Score):	**Tarrier 2000 (score=6.0)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by grant from The Wellcome Trust awarded to first author. No mention of COI.
Sample size:	N=62 patients with PTSD.
Source of Trauma:	Crime, accident, Other
Age/Sex:	Mean age: 38.6±11.6 years; 36 males, 26 females
Comparison:	Cognitive Therapy: (n=33) received 16 treatment sessions of cognitive therapy aimed to be emotion-focused and elicit patient's beliefs about meaning of event vs Imaginal Exposure: (n=29) received 16 treatment sessions of imaginal exposure therapy that

	was trauma focused and aimed to produce habituation of emotional responses by describing event
Follow-up:	6, 12 months
Results:	SSC change in treatment condition was 4.26 for CT (p=.004) and 5.61 for IE (p=.001). Therapy effect for means of symptoms for CT group was 38.5 and 27.96 for IE (F (1, 44) =3.06, p=.09). Results indicate a greater reduction in symptoms for patients receiving IE (p=.024).
Conclusion:	"It was cautiously concluded that although some PTSD patients could not tolerate exposure, those who could may receive greater subjective benefit than those who received cognitive therapy."
Comments:	Both treatments showed comparable efficacy but patients who receive imaginal exposure show improved PTSD symptoms upon subjective ratings. However, some patients are unable to withstand imaginal exposure due to feelings of guilt and lot emotions related to the incident.

Author Year (Score):	**McLay 2017 (score=6.0)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by U.S. Army Medical Research and Material Command, Fort Detrick, MD. No COI.
Sample size:	N=81 individuals with combat-related PTSD
Source of Trauma:	Combat
Age/Sex:	Mean age: 32.5 years; 78 males, 3 females
Comparison:	CET Group: (n=38) received 90-min sessions twice a week for 9 weeks of a trauma interview, education, exposure introduced, except virtual reality vs VRET: (n=43) received 90-min sessions twice a week for 9 weeks of a trauma interview, education, exposure introduced, virtual reality, etc.
Follow-up:	3 months
Results:	No differences were observed for group or time and group interaction, but an effect was observed for time (p<0.001) for CAPS scores. PTSD symptoms improved for both treatments, but no difference was observed between groups.
Conclusion:	"This study supported the utility of exposure therapy for PTSD, but did not support additional benefit by the inclusion of virtual reality."
Comments:	Data suggest exposure therapy (CET) and virtual reality exposure therapy (VRET) have comparable results, but virtual reality did not provide additional benefit.

Author Year (Score):	**Difede 2014 (score=5.5)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by DeWitt-Wallace Fund of the New York Community Trust. No COI.
Sample size:	N=25 patients with chronic PTSD
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 45.9 years; 19 males, 6 females
Comparison:	VRE-DCS: (n=13) received 12 weekly 90-min sessions of virtual reality therapy vs VRE-placebo: (n=12) received placebo
Follow-up:	6 months

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Results:	CAPS scores showed group differences at follow-up of F=7.85 (p=.01). Remission rates were higher in VRE-DCS group at follow-up than placebo (69% vs 17%). Treatment group also showed less sleep disturbance than placebo (p=.014).
Conclusion:	"Patients in the VRE-DCS group showed earlier and greater improvement in PTSD symptoms compared with the VRE-placebo group. These results suggest a promising new treatment for PTSD."
Comments:	Data suggest the VRE-DCE group showed both earlier and greater improvement of PTSD symptoms.

Author Year (Score):	**Beidel 2017 (score=5.0)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Supported by the U.S. Army Medical Research & Materiel Command-Military Operational Medicine Research Program. No mention of COI.
Sample size:	N = 92 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 35.6 years; 86 males, 6 females.
Comparison:	Trauma Management Therapy (TMT) (n=49) – Patients received 29 sessions: one education, 14 VRET, 14-group treatment. Vs. Virtual Reality Exposure Therapy (VRET) (n=43) Patients received 29 sessions: one education, 14 VRET, 14-group treatment and 7 sessions of psychoeducation.
Follow-up:	3 and 6 months.
Results:	CAPS score to TMT: Pre outcomes: M=85.5 sd (12.7), Post outcomes M=42.3 sd (22.0). CAPS score for EXP: Pre M=82.7 sd (17.2), Post M=34.9 sd (18.0). PCL-M score for CAPS: Pre M=63.4 sd(11.7) Mid M=38.9 sd(14.7),Post M=40.4 sd (14.8) CAPS PCL-M score for EXP: Pre M=59.4 sd(12.6), Mid M=34.6 sd(10.0), Post M=33.0 sd (9.7)
Conclusion:	"The results support the use of VRET as an efficacious treatment for combat-related PTSD, but suggest that VRET alone does not result in optimal treatment outcomes across domains associated with PTSD."
Comments:	Mean age differences between groups (37.86 vs 33.26). Dropout rate=39%. Data suggest both groups improved depression and anger, but sleep was not improved in either group. VRET helped some PTSD symptoms, but not all.

Author Year (Score):	**Smith 2015 (score=4.5)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health. COI, Dr. Olsen and Laura Boteler-Humm are employed by and own shares in SIMmersion LLC. Dr. Bell was a paid consultant by SIMmersion LLC to assist with the development of VR-JIT.
Sample size:	N = 33 veterans with PTSD
Source of Trauma:	Military service.
Age/Sex:	Mean age: 51.1 years; 32 males, 1 female.
Comparison:	Virtual Reality Job Interview Training (N=23) VS waitlist treatment-as-usual (TAU) controls (N=10)
Follow-up:	Baseline assessment, two-weeks after baseline

Results:	Role-Play Performance Total score results: The group-by-time interaction was significant (F = 3.4, (p = 0.04)). Large effect size improvement between pre-test and post-test (d=0.76) for the VR-JIT group, and a small difference for the TAU group (d = 0.04). Job Interview self-confidence rating results: the group-by-time interaction did not reach significance (F=2.0, (p = 0.09)) Medium effect size improvement in the VR-JIT group (d = 0.58), and a small difference for the TAU group (d = 0.20).
Conclusion:	"Results provide preliminary support that VR-JIT is acceptable to trainees and may be efficacious for improving job interview skills and self-confidence in veterans with PTSD."
Comments:	Waitlist control bias. Small sample. Data suggest VR-JIT may be beneficial for enhancing job interviewing skills and confidence in veterans with PTSD.

Author Year (Score):	**Reger 2016 (score=4.5)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by the U.S. Army Medical Research and Materiel Command Military Operational Medicine Research program. COI, Dr. Barbara Rothbaum is a consultant for and owns equity in Virtually Better, Inc.
Sample size:	N = 156 active-duty soldiers who had a deployment-related trauma that occurred in Iraq or Afghanistan that met Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition-Text Revision criteria for PTSD based on the Clinician-Administered PTSD Scale
Source of Trauma:	Military service.
Age/Sex:	Mean Age: 30.26; 150 males, 6 females.
Comparison:	10 sessions of Prolonged Exposure Therapy (N=51) vs 10 sessions Virtual Reality Exposure Therapy (N=52) vs Waitlist (N=53)
Follow-up:	Before randomization, after 5 sessions, at posttreatment, and 3 and 6 months posttreatment.
Results:	CAPS difference Prolonged Exposure vs Waitlist: b = -21.90 (p=.001); CAPS difference Virtual Reality Exposure vs Waitlist: -13.23 (p= .005)
Conclusion:	"PE is an efficacious treatment for active-duty Army soldiers with PTSD from deployments to Iraq or Afghanistan. Results extend previous evidence supporting the efficacy of PE to active-duty military personnel and raise important questions for future research on VRE."
Comments:	Waitlist control bias. High dropout rate in both PE and VRE groups. Data suggest both PE and VRE groups had improved PTSD symptoms.

Author Year (Score):	**Mclay 2011 (score=4.0)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. COI, Drs. Mark and Brenda Wiederhold are part owners of, and Drs. Wood, Webb-Murphy, and Spira have previously been employed by, Virtual Reality Medical Center which develops and sells the Virtual Reality system described in this work.

Sample size:	N = 20 Active Duty Service Members who had been diagnosed by a military mental health professional as having PTSD related to service in Iraq or Afghanistan.
Source of Trauma:	Military service.
Age/Sex:	Mean age: 28.4 years; 19 males, 1 female.
Comparison:	VR-graded exposure therapy (N = 10) vs treatment as usual (N = 10)
Follow-up:	Initial assessment, assessment at 10 weeks
Results:	Mean CPS change score over the course of treatment VR-GET vs TAU 35.4 vs 9.4 ($p < .05$)
Conclusion:	"The findings here indicated that Service Members with PTSD related to service in Iraq or Afghanistan were more likely to improve if they received VR-GET than if they received TAU. Like most aspects of mental health, a one-size fits-all approach is unlikely to emerge. Future work should determine which approaches work best for which patients. In the meantime, VR-GET may present one avenue by which some Service Members with PTSD may be offered relief."
Comments:	Small sample. Usual care bias. Data suggest significant improvement in PTSD in VR group.

Author Year (Score):	**Gahm 2014 (score=4.0)**
Category:	Virtual Reality
Study type:	RCT
Conflict of Interest:	Sponsored by the U.S. Army Medical Research and Materiel Command. No mention of COI.
Sample size:	N = 162 Soldiers with PTSD from deployments to Iraq or Afghanistan
Source of Trauma:	Military service.
Age/Sex:	Mean age: not provided; Gender not provided.
Comparison:	10 sessions of Prolonged Exposure Therapy (N=54) vs 10 sessions Virtual Reality Exposure Therapy (N=54) vs Waitlist (N=54)
Follow-up:	Before randomization, after 5 sessions, at posttreatment, and 3 and 6 months posttreatment.
Results:	CAPS change: PE vs WL: b = -22.34, ($p < .001$), VRET vs WL: b = -13.3, ($p = .003$)
Conclusion:	"This study represents the first assessor blinded, randomized study of PE with active duty military members in addition to being the first randomized, controlled trial comparing PE and VRET. As such, its findings documenting the efficacy of these treatments represent a significant contribution to our understanding of effective treatments for PTSD. In addition, this study demonstrated that PE without VR was superior to PE with VR (VRET). This finding was in contrast to the hypothesized outcome that VRET would be superior to PE alone. While multiple potential explanations for this finding exist, including the potential for VR to be effective with some subgroups of patients, the finding stands.
Comments:	Early study termination. Waitlist control bias. Significant dropouts in 2 of 3 groups. Issues with participant recruitment and subsequent retention.

Author Year (Score):	**Miyahira, 2012 (score=2.5)**
Category:	Virtual Reality
Comments:	Sparse methods. High dropout rate (47.6%) in VR groups. Data suggest a combination of CBT and VR may improve symptoms of PTSD.

Individual debriefing is psychological treatment intended to reduce the psychological morbidity that arises after exposure to trauma and has been used for PTSD [92, 111].

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.

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Evidence for the Use of Individual Debriefing

Author Year (Score):	**Sijbrandij 2006 (score=5.5)**
Category:	Individual Debriefing
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by The Netherlands Organisation for Health Research and Development.
Sample size:	N = 236 experiencing a traumatic event satisfying DSM-IV A1 PTSD diagnosis
Source of Trauma:	Civilian trauma. No specific trauma source described
Age/Sex:	Mean age: 40.39 years; 121 males, 115 females.
Comparison:	Emotional debriefing (n=76) vs Educational debriefing (n=79) vs No debriefing (n=81). Emotional and educational debriefings based on Critical Incidents Stress Debriefing protocol
Follow-up:	Follow up at 2 and 6 weeks and 6 months.
Results:	Mixed-model analysis on Structured Interview for PTSD (SI–PTSD): severity of PTSD decreased over time in all groups ($p<0.001$). No significant difference in SI–PTSD total score between groups ($F=1.17$, d.f.=174, $P=0.33$)
Conclusion:	"Our study did not provide evidence for the usefulness of individual psychological debriefing in reducing symptoms of PTSD, anxiety and depression after psychological trauma."
Comments:	Mixed population of trauma types with low numbers of PTSD diagnosis. Data suggest lack of efficacy.

Author Year (Score):	**Bisson 2004 (score=5.5)**
Category:	Individual Debriefing
Study type:	RCT
Conflict of Interest:	Sponsored by the Welsh Office of Research and Development for Health and Social Care. No mention of COI.
Sample size:	N = 152 with DSM-IV PTSD diagnosis
Source of Trauma:	Physical injured – motor vehicle accident, assault, industrial accident
Age/Sex:	Mean age not specified; 65 males, 87 females.
Comparison:	Four 1-hour cognitive behavioral weekly sessions for 5 to 10 week (n=76) vs No intervention (n=76)
Follow-up:	Follow up at 3 and 13 months.
Results:	Impact of Event Scale (IES): Initial score for intervention group and control group, respectively – 47.0, 45.0. IES 3 month scores – 10.0, 5.4 (Adjusted mean difference=4.1, $F=1.5$, $p=0.1$). IES 13 month scores – 20.7, 11.2 (Adjusted mean difference=8.4, $F=9.0$, $p=0.006$)
Conclusion:	"A brief cognitive-behavioural intervention reduces symptoms of posttraumatic stress disorder in individuals with physical injury who display initial distress."
Comments:	Standard Care Bias. Data suggest intervention group maintained sustained results (less PTSD symptoms) at 13 months.

Author Year (Score):	**Marchand 2006 (score=4.0)**
Category:	Individual Debriefing
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by the Institut de Recherche en Santé et Sécurité du Travail du Québec (awarded to Marchand).

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Sample size:	N = 75 with PTSD symptoms satisfying the DSM-IV criterion A2 PTSD diagnosis
Source of Trauma:	Victims of armed robbery that included acts of violence (threat of death or injury to physical assault and threat with weapon)
Age/Sex:	Mean age: 21.82 years; 36 males, 39 females.
Comparison:	Individual debriefing, two 1-hour session every week (n=33) vs no intervention (n=42)
Follow-up:	Follow up at 1 and 3 months.
Results:	24% participants dropped out. For study completers there was a main effect of time ($F=12.7$, $p<0.001$). No significant group or time x group effects found ($F(1,54)=0.99$, $p>.32$)
Conclusion:	"Results revealed no differences between the CISD-A and the control group in preventing PTSD or attenuating posttraumatic symptoms 1 and 3 months later."
Comments:	PTSD from armed robbery. Data suggest lack of efficacy.

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Group debriefing is a type of psychological debriefing involving crisis intervention models with the aim of mitigating trauma related to PTSD [260, 261].

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.

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Evidence for the Use of Group Debriefing

Author Year (Score):	**Devilly 2008, a (score=4.0)**
Category:	Group Debriefing
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=64 healthy students all shown a stressful video depicting paramedics responding to a graphic motor vehicle accident.
Source of Trauma:	No mention of source of trauma
Age/Sex:	Mean age: 23.4 years; 21 males, 43 females
Comparison:	Debrief Group (n=59) received 40-50 min session of perceived distress (PD) on 7 stage critical incident stress debriefing (CISD) model of group debriefing vs Control (n=13)
Follow-up:	4 weeks
Results:	MANOVA test showed significant effect for passage of time (wilk's lamba (3,54)=.86, p<.04). Tukey's HSD test showed significant main effect for anxiety (p<.03). All other tests did not show significant effect. PDS measures did not show significant differences in PTSD symptomatology total scores.
Conclusion:	"Those who were debriefed later recalled having wanted to talk more to someone about the video than those who were not debriefed. It is suggested that cognitive dissonance may explain this result."
Comments:	Short term follow-up (1 month). Data suggest lack of efficacy of debriefing group on psychological health. However, the debriefing group were more likely to discuss the video compared to the non-debriefed group.

Author Year (Score):	**Devilly 2008, b (score=3.5)**
Category:	Group Debriefing
Comments:	Sparse methods. Data suggest lack of efficacy.

Author Year (Score):	**Tuckey 2014 (score=3.5)**
Category:	Group Debriefing
Comments:	Data suggest CISD was associated with a significant reduction of post-intervention alcohol use compared to screening group and greater quality of life.

Author Year (Score):	**Adler 2008 (score=2.0)**
Category:	Group Debriefing
Comments:	High attrition rate. Data suggest a minimal trend of lower PTSD symptoms with CISD.

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Critical incident stress debriefing has been used to treat PTSD [92, 260, 262-266].

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.

Evidence for the Use of Critical Incident Stress Debriefing

Author Year (Score):	**Bisson 2004 (score=5.5)**
Category:	Critical Incident Stress Debriefing
Study type:	RCT
Conflict of Interest:	Sponsored by the Welsh Office of Research and Development for Health and Social Care. No mention of COI.
Sample size:	N = 152 with DSM-IV PTSD diagnosis

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Source of Trauma:	Physical injured – motor vehicle accident, assault, industrial accident
Age/Sex:	Mean age not specified; 65 males, 87 females.
Comparison:	Four 1-hour cognitive behavioral weekly sessions for 5 to 10 week (n=76) vs No intervention (n=76)
Follow-up:	Follow up at 3 and 13 months.
Results:	Impact of Event Scale (IES): Initial score for intervention group and control group, respectively – 47.0, 45.0. IES 3 month scores – 10.0, 5.4 (Adjusted mean difference=4.1, F=1.5, p=0.1). IES 13 month scores – 20.7, 11.2 (Adjusted mean difference=8.4, F=9.0, p=0.006)
Conclusion:	"A brief cognitive-behavioural intervention reduces symptoms of posttraumatic stress disorder in individuals with physical injury who display initial distress."
Comments:	Standard Care Bias. Data suggest intervention group maintained sustained results (less PTSD symptoms) at 13 months.

Author Year (Score):	**Marchand 2006 (score=4.0)**
Category:	Critical Incident Stress Debriefing
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by the Institut de Recherche en Santé et Sécurité du Travail du Québec (awarded to Marchand).
Sample size:	N = 75 with PTSD symptoms satisfying the DSM-IV criterion A2 PTSD diagnosis
Source of Trauma:	Victims of armed robbery that included acts of violence (threat of death or injury to physical assault and threat with weapon)
Age/Sex:	Mean age: 21.82 years; 36 males, 39 females.
Comparison:	Individual debriefing, two 1-hour session every week (n=33) vs no intervention (n=42)
Follow-up:	Follow up at 1 and 3 months.
Results:	24% participants dropped out. For study completers there was a main effect of time ($F=12.7$, $p<0.001$). No significant group or time x group effects found ($F(1,54)=0.99$, $p>.32$)
Conclusion:	"Results revealed no differences between the CISD-A and the control group in preventing PTSD or attenuating posttraumatic symptoms 1 and 3 months later."
Comments:	PTSD from armed robbery. Data suggest lack of efficacy.

Author Year (Score):	**Devilly 2008, a (score=4.0)**
Category:	Critical Incident Stress Debriefing
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=64 healthy students all shown a stressful video depicting paramedics responding to a graphic motor vehicle accident.
Source of Trauma:	No mention of source of trauma
Age/Sex:	Mean age: 23.4 years; 21 males, 43 females
Comparison:	Debrief Group (n=59) received 40-50 min session of perceived distress (PD) on 7 stage critical incident stress debriefing (CISD) model of group debriefing vs Control (n=13)
Follow-up:	4 weeks

Results:	MANOVA test showed significant effect for passage of time (wilk's lamba (3,54)=.86, p<.04). Tukey's HSD test showed significant main effect for anxiety (p<.03). All other tests did not show significant effect. PDS measures did not show significant differences in PTSD symptomatology total scores.
Conclusion:	"Those who were debriefed later recalled having wanted to talk more to someone about the video than those who were not debriefed. It is suggested that cognitive dissonance may explain this result."
Comments:	Short term follow-up (1 month). Data suggest lack of efficacy of debriefing group on psychological health. However, the debriefing group were more likely to discuss the video compared to the non-debriefed group.

Author Year (Score):	**Devilly 2008, b (score=3.5)**
Category:	Critical Incident Stress Debriefing
Comments:	Sparse methods. Data suggest lack of efficacy.

Author Year (Score):	**Tuckey 2014 (score=3.5)**
Category:	Critical Incident Stress Debriefing
Comments:	Data suggest CISD was associated with a significant reduction of post-intervention alcohol use compared to screening group and greater quality of life.

Author Year (Score):	**Tarquinio 2016 (score=2.5)**
Category:	Critical Incident Stress Debriefing
Comments:	No comparison with the control group, only between interventions, which suggest EMDR may be better than CISD. Meaningful differences between treatment arms and control arms at baseline.

Author Year (Score):	**Adler 2008 (score=2.0)**
Category:	Critical Incident Stress Debriefing
Comments:	High attrition rate. Data suggest a minimal trend of lower PTSD symptoms with CISD.

Author Year (Score):	**Campfield 2001 (score=1.5)**
Category:	Critical Incident Stress Debriefing
Comments:	Meaningful differences between treatment groups at baseline.

Author Year (Score):	**Macnab 2003 (score=1.0)**
Category:	Critical Incident Stress Debriefing
Comments:	Methodological details sparse. Randomization questionable.

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Psychodynamic psychotherapy involves therapists encouraging patients with PTSD to address and process through thoughts and emotions that have been suppressed surrounding the traumatic event in their life [267-271].

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.

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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.

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Evidence for the Use of Interpersonal Therapy

Author Year (Score):	**Markowitz 2015 (Score=6.5)**
Category:	Prolonged Exposure Therapy
Study type:	RCT
Conflict of Interest:	Supported by the New York State Psychiatric Institute, and National Institute of Mental Health grant. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=110 patients with chronic PTSD meet DSM-IV diagnosis standard.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 40.10±11.57 years; 33 males, 77 females.
Comparison:	PE group: received 10 weeks Prolonged exposure therapy with 90 minutes per weekly session (n=38) vs. psychotherapy group: received 14 weeks interpersonal psychotherapy with 50 minutes per weekly session (n=40) vs. relaxation group: received 9 weeks relaxation therapy with 90 minutes per weekly session (n=32).
Follow-up:	No mention of follow-up.
Results:	Three groups indicated improvement for CAPS: Prolonged exposure group d=1.88, interpersonal psychotherapy group d=1.69, and relaxation therapy group d=1.32. Among the three groups, prolonged exposure group indicated significant improvement (p=0.010), no significance was found in other two groups (p=0.097).
Conclusion:	"IPT had (non-significantly) lower attrition and higher response rates than prolonged exposure. Contrary to widespread Clinical belief, PTSD treatment may not require cognitive behavioral exposure to trauma reminders."
Comments:	Data suggest comparable efficacy between IPT and PE and IPT had an associated higher response rate (63% vs. 47% for PE and 38% for Relaxation Therapy) These data suggest cognitive behavioral exposures may not be required for PTSD treatment.

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Hypnosis has been used to treat PTSD [272-274].

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.

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Evidence for the Use of Hypnotherapy

Author Year (Score):	**Bryant 2005 (score=4.0)**
Category:	Hypnotherapy
Study type:	RCT
Conflict of Interest:	Sponsored by National Health and Medical Research Council. No mention of COI.
Sample size:	N=87 trauma survivors
Source of Trauma:	Non sexual assault and motor vehicle accidents.
Age/Sex:	Mean age: 33.58 years; 34 males, 53 females
Comparison:	Group 1: (n=33) received 6 sessions of CBT only vs Group 2: (n=30) received CBT and hypnosis treatment vs Group 3: (n=24) received supportive counseling
Follow-up:	6 months
Results:	MANCOVA on post-treatment showed an effect of F (14, 154)=5.8, p<.005. Post hoc Tukey Group 2 participants scored lower than Group 3 participants did for IES-Intrusion (p<.005). Similarly, Group 1 scored lower than Group 3 for IES-Intrusion (p<.05).
Conclusion:	"These findings suggest that hypnosis may have use in facilitating the treatment effects of CBT for posttraumatic stress."
Comments:	Standard care bias. Data suggest CBT plus hypnotherapy results in less PTSD related symptoms.

Author Year (Score):	**Bryant 2006 (score=4.0)**
Category:	Hypnotherapy
Study type:	RCT
Conflict of Interest:	Sponsored by National Health and Medical Research Council. No mention of COI.
Sample size:	N=87 trauma survivors
Source of Trauma:	Non sexual assault and motor vehicle accidents.
Age/Sex:	Mean age: 33.58 years; 34 males, 53 females
Comparison:	Group 1: (n=33) received 6 sessions of CBT only vs Group 2: (n=30) received CBT and hypnosis treatment vs Group 3: (n=24) received supportive counseling
Follow-up:	Baseline, post treatment, and 6 month, and 3 year follow up.
Results:	Intent to treat analysis (chi squared), group 1 vs 2 vs 3 in prevalence of PTSD diagnosis at 3 year follow up (n (%)): 13 (36%) vs 14 (46%) vs 16 (67%) (X^2 ((N=87) =5.16, p<0.08). Without intent to treat group 1 vs 2 vs 3 (n (%)): 2 (11%) vs 4 (22%) vs 10 (62%) (X^2 ((N=53) =11.95, p<0.005).
Conclusion:	"The major finding of this 3-year follow-up was that patients who received CBT or CBT/hypnosis in the initial month after their trauma presented with less PTSD symptoms, and particularly re-experiencing and hyperarousal symptoms, than those who received SC."
Comments:	Standard care bias. Data suggest CBT plus hypnotherapy results in less PTSD related symptoms through 3 years. Follow-up of Bryant 2005.

Author Year (Score):	**Abramowitz 2008 (score=4.0)**
Category:	Hypnotherapy
Study type:	RCT
Conflict of Interest:	No mention of COI or sponsorship

Sample size:	N=32 patients with PTSD with insomnia
Source of Trauma:	Military service.
Age/Sex:	Mean age: 31.7 years, 32 males, 0 females
Comparison:	Group 1: (n=16) received zolpidem 10 mg 2 times a week 1.5 hour sessions for 2 weeks vs Group 2: (n=17) received symptom-oriented hypnotherapy 2 times a week 1.5 hour sessions for 2 weeks
Follow-up:	1 month
Results:	Group 1 show an effect of F(1,30)=4.96 compared to Group 2 (p=.034). PTSD symptoms reduced from 36.7±9.4 to 31.7±9.8.
Conclusion:	"(W)e found that symptomatic hypnotherapy is an effective adjunct to psycho- and pharmacotherapy for chronic insomnia and sleep disorders in a group of patients suffering from chronic combat-related PTSD."
Comments:	Small sample. Data suggest improved PTSD symptoms in hypnotherapy versus zolpidem group for 1 month post-treatment.

Author Year (Score):	**Galovski 2016 (score=4.0)**
Category:	Hypnotherapy
Study type:	RCT
Conflict of Interest:	COI: Tara Galvoski was recipient of a grant, and Thomas Fletcher was the paid statistical consultant on the project. No mention of sponsorship.
Sample size:	N=108 interpersonal assault survivors
Source of Trauma:	Sexual and/or physical assault.
Age/Sex:	Mean age: 36.87±11.8 years;
Comparison:	Group 1: (n=56) received sleep and symptom monitoring for 3 weeks vs Group 2: (n=52) received 3 weekly, 60 minute sessions of hypnosis. All participants received CPT for 12 weeks, 60 minute sessions.
Follow-up:	3 months
Results:	Hypnosis group showed improved sleep measure (CAPS), sleep latency (PSQI), global sleep (PSQI), and insomnia (ISI) (ps<.05). Hypnosis group also showed reduction in depression (BDI-II) over sleep intervention phase (p<.05). Sleep monitoring group showed a 25% decrease in PSQI compared to 47% of hypnosis group.
Conclusion:	"Hypnosis was effective in improving sleep impairment, but those improvements did not augment gains in PTSD recovery during the trauma-focused intervention."
Comments:	Standard care bias. High dropout rate. Data suggest hypnosis improved sleep and depression in PTSD individuals.

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Eye movement desensitization and reprocessing (EMDR) is an eight-phase psychotherapy that consists of multiple cointerventions including exposing clients to selected traumatic images and cognitions, while inducing saccadic eye movements [279-286].

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.

Evidence for the Use of Eye Movement Desensitization Reprocessing

Author Year (Score):	**Sack 2016 (score=6.5)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. COI: M. Sack is an EMDR supervisor and has received money by contributing to articles on EMDR.
Sample size:	N = 139 patients diagnosed with PTSD according to the Clinician Administered PTSD Scale.
Source of Trauma:	Natural disaster, severe disease, accident, physical assault, sexual trauma.
Age/Sex:	Mean age: 39.6 ± 12.4 years; 54 males, 85 females
Comparison:	Up to eight sessions of either exposure with eyes moving while fixating on the moving hand of the therapist(EM) (N=47) vs exposure with fixating on the nonmoving hand of the therapist (EF)(N=47) vs exposure without the explicit task of fixating on an external focus of attention (EC)(N=45)
Follow-up:	Follow up pretreatment and post treatment.
Results:	Number of participants that showed remission was 80.9% for EM, 78.7% EF, and 80.0% EC (χ^2= 0.070, p=0.97). Linear model CAPS score for EM (d=2.06,p<0.001), EF(d=2.58,p<0.001), and EC(d=1.44,p<0.001)
Conclusion:	"Exposure in combination with an explicit external focus of attention leads to larger PTSD symptom reduction than exposure alone. Eye movements have no advantage compared to visually fixating on a nonmoving hand."
Comments:	Data suggest there was no advantage with eye movement induction during EMDR over fixation on a non-moving hand.

Author Year (Score):	**Nijdam 2012 (score=6.0)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by the Academic Medical Centre, Amsterdam, The Netherlands.
Sample size:	N = 140 with PTSD diagnosis via DSM-IV
Source of Trauma:	Assault, sexual assault, accident, disaster, war-related
Age/Sex:	Mean age: 37.8 years; 61 males, 79 females.

Comparison:	Eye movement desensitization and reprocessing – weekly 90 minutes sessions for 17 weeks (n = 70) vs. Brief eclectic psychotherapy – weekly 45-60 minute sessions for 17 weeks (n = 70)
Follow-up:	No follow-up reported
Results:	Mixed-model analysis showed significant main effect of time ($F = 17.99$, $dF = 1065$, $p < 0.001$), treatment condition ($F = 12.20$, $dF = 169$, $p < 0.005$), and significant interaction between time and treatment condition ($F = 4.0$, $dF = 1065$, $p < 0.001$). Response difference between groups ($t = 3.49$, $dF = 169$, $p < 0.005$). Mean difference on Impact of Event Scale-Revised score = 13.1 (95% CI 5.69-20.5).
Conclusion:	"Although both treatments are effective, EMDR results in a faster recovery compared with the more gradual improvement with brief eclectic psychotherapy."
Comments:	Data suggest comparable (in)efficacy.

Author Year (Score):	**Hogberg 2006 (score=5.5)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	Sponsored by the Stockholm Public Transport Authority, Connex Sverige AB, Swedish State Railways, Stockholm County Council, The Vardal Foundation, LJ Boethius' Konigska Foundation. No mention of COI.
Sample size:	N = 24 employees of the Stockholm public transportation system who had either experienced a person-under-train accident or assault at work.
Source of Trauma:	Experiencing a person-under-train accident or assault.
Age/Sex:	Mean age: 43 years; 19 males, 5 females
Comparison:	Five 90 minute sessions of EMDR (N=13) vs waitlist control (N=11)
Follow-up:	Follow up at baseline, between week 3 and 5, between week 12 and 16 and between week 15 and 17.
Results:	After treatment, 67% of the treatment group no longer fulfilled the criteria for PTSD vs 11% of the waitlist control (p=0.02)
Conclusion:	"Our study supports the use of EMDR to treat subjects who developed PTSD at work. More research is needed to evaluate long-term effects as well as mediators of change in the method. It would also be of value to study the potential usefulness of EMDR with other diagnostic categories."
Comments:	Small sample. Waitlist control bias. Data suggest EMDR improved PTSD symptoms.

Author Year (Score):	**Van den Berg 2015 (score=5.5)**
Category:	Eye Movement Desensitization and Prolonged Exposure
Conclusion:	"Standard PE and EMDR protocols were effective, safe, and feasible in patients with PTSD and severe psychotic disorders."
Comments:	Baseline differences of unclear significance. High dropouts/non-compliance after randomization, but subsequently good compliance. All groups improved, but 2 active treatments were both better and equivalent.

Author Year (Score):	**Karatzias 2011 (score=5.5)**

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Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 46 participants from the waiting list of a National Health Service Psychotherapy Service in Scotland satisfying DSM-IV PTSD criteria.
Source of Trauma:	Accident, assault, murder.
Age/Sex:	Mean age: years; males, females
Comparison:	EMDR group (N=23) vs emotional freedom training (EFT) group (N=23)
Follow-up:	Follow up at baseline, pretreatment, posttreatment and 3 months.
Results:	Significant time outcomes for CAPS $F(2,43) = 36.3$, $p \leq 0.001$, $\eta^2=0.452$ and PCL-C $F(2,43)=38.2$, $p \leq 0.001$, $\eta^2=0.465$. No significant group effects. CAPS total effect sizes pretreatment vs posttreatment were d=1.1 for EMDR and d=1.0 for EFT.
Conclusion:	"Overall, the results indicated that both interventions produced significant therapeutic gains at posttreatment and follow-up in an equal number of sessions. Similar treatment effect sizes were observed in both treatment groups. Regarding clinical significant changes, a slightly higher proportion of patients in the EMDR group produced substantial clinical changes compared with the EFT group."
Comments:	Significant dropout rate. Data suggest both EFT and EMDR resulted in significant clinical improvement in PTSD symptoms with only a slightly higher degree of improvement in EMDR at 3 month follow-up.

Author Year (Score):	**van der Kolk 2007 (score=5.5)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health. Dr. Korn has served on the speakers or advisory boards for and received honoraria from the EMDR International Association and the EMDR Institute, Inc. Drs. van der Kolk, Spinazzola, Blaustein, J. Hopper, E. Hopper, and Simpson report no additional financial affiliations or other relationships relevant to the subject of this article.
Sample size:	N = 88 patients with PTSD.
Source of Trauma:	Child sexual and/or physical abuse, adult sexual and/or physical assault, domestic violence, traumatic loss, war/terrorism/violence, and injury/accident.
Age/Sex:	Mean age: 36.1 years; 15 males, 73 females.
Comparison:	Eye movement desensitization and reprocessing (EMDR) (n=29) patients underwent 90 minute individual session. Sessions for 8 weeks Vs Fluoxetine (n=30) treatment consisted of 20-30 minute individual sessions for 8 weeks. Starting Fluoxetine dosage was 10 mg/day and was increased 10 mg to max of 60 mg/day for 8 weeks. Vs. Placebo (N = 29) – treatment consisted of 20-30 minute individual sessions. Starting placebo dosage was 10 mg/day and was increased 10 mg to max of 60 mg/day for 8 weeks.
Follow-up:	6 months
Results:	The CAPS total score, mean (SD) for the EMDR group is 28.37 (19.66), Fluoxetine 38.69 (20.30), and placebo 39.81 (18.76), p=0.09. The 2-group comparisons are as follows: EMDR vs. fluoxetine: p=0.27; EMDR vs. placebo: p=0.03; fluoxetine vs. placebo: p=0.67. At 6-month follow-up, 75.0% of adult-onset versus 33.3% of child-onset trauma subjects receiving EMDR

	achieved asymptomatic end-state functioning compared with none in the fluoxetine group.
Conclusion:	"This study supports the efficacy of brief EMDR treatment to produce substantial and sustained reduction of PTSD and depression in most victims of adult-onset trauma. It suggests a role for SSRIs as a reliable first-line intervention to achieve moderate symptom relief for adult victims of childhood-onset trauma. "
Comments:	Data suggest psychotherapy (EMDR) more effective in providing sustained improvement in PTSD symptoms compared to fluoxetine and placebo.

Author Year (Score):	**Taylor 2003 (score=5.0)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	No mention of COI. Sponsored by the British Columbia Health Research Foundation.
Sample size:	N = 60 who met the DSM-IV-TR criteria for PTSD
Source of Trauma:	No specified source of trauma mentioned.
Age/Sex:	Mean age: 37 years; 15 males, 45 females.
Comparison:	Each randomized to eight 90 minute individual sessions of exposure therapy (n=22) vs. eye movement desensitization and reprocessing (EMDR) (n=19) vs. relaxation therapy (n=19)
Follow-up:	Follow up at 3 months.
Results:	Outcome measured via CAPS scores. For each of the four dimensions evaluated (re-experiencing, avoidance, numbing, hyperarousal) reductions in CAPS scores were significant: relaxation group – $t(14) > 3.55$ ($p < 0.005$, $n^2 > 0.47$), EMDR – $t(14) > 3.66$ ($p < 0.005$, $n^2 > 0.49$), exposure therapy – $t(14) > 4.52$ ($p < 0.001$, $n^2 > 0.59$)
Conclusion:	"Compared with EMDR and relaxation training, exposure therapy (a) produced significantly larger reductions in avoidance and reexperiencing symptoms, (b) tended to be faster at reducing avoidance, and (c) tended to yield a greater proportion of participants who no longer met criteria for PTSD after treatment. EMDR and relaxation did not differ from one another in speed or efficacy."
Comments:	Data suggest exposure therapy superior to both EMDR and relaxation training in reducing avoidance or recurring symptoms, but there was similar efficacy on all other measures.

Author Year (Score):	**De Bont 2013 (Score=5.0)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. The authors declared no COI.
Sample size:	N=10 patients with psychotic disorder.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 43.6 years; 2 males, 8 females.
Comparison:	PE group: received 12 sessions of prolonged exposure with maximum 90 minutes per session (n=5) vs. EMDR group: received 12 sessions of eye movement desensitization and reprocessing group with maximum 90 minutes per session (n=5).
Follow-up:	Follow-up at 3 months.

Results:	PSS-SR scores indicated that PTSD symptom severity decreased in intervention (p<0.001). CAPS total scores also decreased in treatment (p=0.012).
Conclusion:	"PTSD patients with comorbid psychotic disorders benefit from trauma-focused treatment approaches such as PE and EMDR."
Comments:	Small sample. Patients had primary diagnosis of psychosis in addition to PTSD. Data suggest patients with PTSD and other psychotic illnesses benefit from treatment such as PE and EMDR.

Author Year (Score):	**Lee 2002 (Score=4.5)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=24 participants with PTSD.
Source of Trauma:	Sexual or physical assault, traffic accidents, murder encounter, or combat.
Age/Sex:	Mean age: 35.3 years; 13 males, 11 females.
Comparison:	SITPE group: received 7 sessions of Stress inoculation training with prolonged exposure with 90 minute per weekly session (n=12) vs. EMDR group: received 7 sessions of eye movement desensitization and reprocessing with 90 minute per weekly session (n=12).
Follow-up:	Follow-up at 3 months.
Results:	Both groups indicated effective outcome in reduction of PTSD diagnostic status. In EMDR group, 83% participants showed no symptoms of PTSD; and in SITPE group, 75% participants also showed no PTSD symptoms. The two groups indicated significantly difference in improvement (p<0.05).
Conclusion:	"EMDR did significantly better than SITPE. At follow-up EMDR was found to lead to greater gains on all measures."
Comments:	Wait control bias. Data suggest comparable efficacy on global PTSD measures but on subscale measures, EMDR was better than SITPE like for the degree of intrusion. All measures showed EMDR better than SITPE at 3 month follow-up.

Author Year (Score):	**Power 2002 (score=4.5)**
Category:	Eye Movement Desensitization and Reprocessing
Study type:	RCT
Conflict of Interest:	Sponsored by the Scottish Home and Health Department. No mention of COI.
Sample size:	N = 72 participants who satisfied the DSM-IV PTSD criteria.
Source of Trauma:	Vehicular passenger, pedestrian, occupational accident, physical assault, traumatic death, real/implied physical threat.
Age/Sex:	Mean age: 39.2 years; 42 males, 30 females
Comparison:	EMDR group (N=27) vs exposure plus cognitive restructuring(E+CR) (N=21) vs waitlist control (N=24)
Follow-up:	Follow up at baseline, 10 weeks and an average of 15 months.
Results:	IOE total had significant time (F(1,71)=101.3,p<0.001), time x group (F(2,71)=21.2, p<0.001) and group (F(2,71)=8.8, p<0.001). IOE total of 11.8 for EMDR vs 29.6 for WL posttreatment (p<.001). IOE total of 19.2 for E+CR vs 29.6 for WL posttreatment (p<0.05). For the HADS depressions scale, 81% EMDR vs 43% E+CR had significant symptoms reduction (p<0.05).

Conclusion:	"In summary, at end of treatment and at follow-up, both EMDR and E + CR are effective in the treatment of PTSD with only a slight advantage in favour of EMDR."
Comments:	Waitlist control bias. Data suggest comparable (in)efficacy between both treatment groups (EMDR and E+CR) with a slight advantage of EMDR with respect to patient self-reported depression symptoms.

Author Year (Score):	**Carlson 1998 (score = 4.0)**
Category:	EMDR and Biofeedback
Study type:	RCT
Conclusion:	"Compared with the other conditions, significant treatment effects in the EMDR condition were obtained at posttreatment on a number of self-report, psychometric, and standardized interview measures."
Comments:	Many study weaknesses. Data suggest durable efficacy of EMDR.

Author Year (Score):	**Wilson 1995 (score=3.5)**
Category:	EMDR and Biofeedback
Comments:	Waitlist control bias. Data suggest EMDR decreased anxiety and increased cognition.

Author Year (Score):	**Ahmadi 2015 (score=3.0)**
Category:	EMDR and Biofeedback
Comments:	Data suggest REM desensitization may be useful for improvement in sleep and intrusive thoughts but not for depression in PTSD.

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Thought field therapy (TFT), also known as the Callahan technique, is a therapeutic tool used to attempt to relieve anxiety and other symptoms [293, 294]. TFT is an approach developed from a mix of three modalities and theories: acupuncture, chiropractic, and psychotherapy [295]. A typical TFT session will involve tapping on the face, hand, and body while the patient produces feelings, thoughts, or memories that are the target for treatment (e.g., anxiety, sadness, and restlessness) [293, 294]. Each TFT session will include a set of protocol or algorithm, which designates the specific acupoint to be tapped, as well as the order in which they are to be tapped. Symptoms of PTSD, such as hyperarousal, dissociation, and defensive avoidance, are targeted using a trauma treatment protocol [293-295].

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.

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Evidence for the Use of Thought Field Therapy

Author Year (Score):	**Irgens 2012 (score=4.0)**
Category:	Thought Field Therapy
Study type:	RCT
Conflict of Interest:	Sponsored by the Norwegian ExtraFoundation for Health and Rehabilitation through EXTRA Funds, and by the Josef and Haldis Andresens Legat. No mention of COI.
Sample size:	N = 45 patients with anxiety.
Source of Trauma:	Panic disorder, social phobia, PTSD, and generalized stress disorder
Age/Sex:	Mean age: 37 years; 12 males, 33 females.
Comparison:	Thought Field Therapy (TFT) (n= 23) patients received two sessions of individual therapy. Assessment was done five weeks before treatment, one to two weeks after treatment, three months after treatment, and 12 months after treatment. vs Waiting List (n=22) patients had a two and half month wait-list condition.
Follow-up:	12 mo
Results:	The comparison of TFT and the 2.5 Wait List mean scores were pretreatment (1.57, 1.31) and post treatment (1.06, 1.22), respectively. The F(1,43) for time was 20.6, $p<0.01$. The F(1,43) of time x group was 10.00, $p<0.01$. The Cohen's d value for difference in effect between the treatment group and the wait-list group was 0.96.
Conclusion:	"The results of this randomized study with wait-list controls and 12-month follow-up suggest that TFT is effective for reducing symptoms of anxiety in patients with anxiety disorders. However, lack of appropriate controls does not allow for any conclusion regarding the cause of this change."
Comments:	Waitlist control bias. Data suggest TFT improved some measures of anxiety and one measure of function and the improvements were maintained up to 12 months.

Author Year (Score):	**Connolly 2011 (score=3.5)**
Category:	Thought Field Therapy
Comments:	Waitlist control bias, participant's mostly female, sparse methods. Data suggest positive effects of TFT on Rwandan genocide survivors, which were maintained for up to 2 years.

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Emotional freedom techniques are a form of counseling that incorporates the physical tapping of the body on acupuncture points while simultaneously having the patient focus on traumatic events as a form of self-acceptance therapy [296, 297]. It is similar to Thought Field Therapy and is typically used as adjunct therapy. With EFT, the client verbalizes the problem with a statement such as, "Even though I have this phobia, I totally and utterly love and accept myself." This is purportedly a potential way for patients who are struggling to manage symptoms of PTSD [298].

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.

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Evidence for the Use of Emotional Freedom Techniques

Author Year (Score):	**Church 2013 (score=4.0)**
Category:	Emotional Freedom Techniques (EFT)
Study type:	RCT
Conflict of Interest:	Supported by private donations to the nonprofit Veterans Stress Project. No COI.
Sample size:	N=59 veterans meeting clinical criterion for PTSD
Source of Trauma:	Military Service
Age/Sex:	Mean age: 51.7±14.05 years; 3 males, 6 females.
Comparison:	Group 1: received sessions of EFT training (N=30) vs. Group 2: received the stand of care/ waitlist treatment (SOC/WL) (N=29)
Follow-up:	Baseline, 3, and 6 months.
Results:	Group 1 vs group 2 post intervention PTSD Checklist-Military score, SA-45 Global severity index, positive symptom total: 39.41±2.7 vs 63.23±2.0 ($p<0.0001$), 58.51±1.9 vs 69.98±1.4 ($p<0.0001$), 57.61±1.9 vs 70.42±1.3 ($p<0.001$). All SA-45 domains were significantly significant except for interpersonal sensitivity favoring EFT.
Conclusion:	"[T]aken together with previous research showing EFT's efficacy in treating PTSD symptoms, the results of this study indicate that a six-session protocol of EFT can be a useful adjunctive intervention for veterans."
Comments:	Waitlist control bias. Data suggest EFT decreased PTSD symptoms and some subjects no longer met PTSD criteria after EFT; if the bias does not account for the results.

Author Year (Score):	**Church 2016 (score=4.0)**
Category:	Emotional Freedom Techniques(EFT)
Study type:	RCT
Conflict of Interest:	Supported by private individual donations to the nonprofit National Institute for Integrative Healthcare. First author receives income from publication and presentations relative to the approach under examination.
Sample size:	N=21 veterans who did not meet clinical criterion for PTSD.
Source of Trauma:	Military Service
Age/Sex:	Mean age: 56±11.1 years; 14 males, 7 females.
Comparison:	Group 1: received sessions of EFT training (N=12) vs. Group 2: received treatment as usual (TAU) (N=9)
Follow-up:	Baseline, after the 3 and the 6th session, 3, and 6 months after intervention.
Results:	Group 1 vs group 2 post intervention PTSD Checklist-Military score, SA-45 Global severity index, positive symptom total: 25±2.4 vs 36±3.0 ($p=0.0004$), 50±2.4 vs 61±2.7 ($p=0.021$), 50±2.6 vs 61±2.6 ($p=0.038$).). All SA-45 domains were significantly significant favoring EFT except for interpersonal sensitivity, Somatization, Phobic anxiety, and Psychoticism.
Conclusion:	"Symptom improvements were similar to those assessed in studies of PTSD positive veterans. EFT may thus be protective against an increase in symptoms and a later PTSD diagnosis. As a simple and quickly learned self-help method, EFT may be a clinically useful element of a resiliency program for veterans and active-duty warriors."
Comments:	Small sample. Waitlist control bias. EFT potentially useful for decreasing PTSD in at risk veterans if the bias does not account for the results.

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Neurofeedback (also called EEG biofeedback or neurotherapy) has been used to treat anxiety, affective disorders, and PTSD [222, 300-305].

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.

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Evidence for the Use of Neurofeedback (Brain Computer Device and Interface)

Author Year (Score):	**Van der Kolk 2016 (score=4.5)**
Category:	Brain Computer Devices
Study type:	RCT
Conflict of Interest:	No mention of sponsorship. No COI.
Sample size:	N= 52 individuals with chronic PTSD
Source of Trauma:	Military sexual trauma, witness death or executions or major injuries, explosion, homicide of civilian, multiple traumas, domestic violence, sexual abuse, childhood emotional abuse
Age/Sex:	Mean age: 44.4±13.2 years; 7 males, 42 females
Comparison:	Neurofeedback group: (n=28) received 24 sessions twice weekly for 30-min sessions of neurofeedback intervention procedure vs Waitlist (n= 24) received waitlist control therapy and was offered NF after 3 week follow-up
Follow-up:	1 month, 6 weeks, 12 weeks, 16 weeks
Results:	More patients met PTSD inclusion criteria at 12 weeks from the waitlist group than from NF group (p=0.007) as well as at 16 weeks (p=.002). Treatment condition with time interaction showed an effect of b=-10.45, t=-5.1 (p<.001). NF group showed greater improvement in PTSD symptoms than waitlist group.
Conclusion:	"Compared with the control group NF produced significant PTSD symptom improvement in individuals with chronic PTSD, as well as in affect regulation capacities. NF deserves further investigation for its potential to ameliorate PTSD and to improve affect regulation, and to clarify its mechanisms of action."
Comments:	Waitlist control bias. Chronic PTSD patients. Data suggest NF resulted in PTSD symptom improvement.

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Animal-assisted therapy is the inclusion of animals in psychiatric treatment, such as dogs and horses [306-309], and has been used in treatment of PTSD [308, 310, 311].

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.

Evidence for the Use of Animal-Assisted Therapy

Author Year (Score):	**Lass-Hennemann 2014 (score=3.5)**
Category:	Animal-Assisted Therapy
Comments:	All participants were female. Data suggest that dog presence may reduce subjective stress from viewing a traumatic film.

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.

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Evidence for the Use of Sertraline

Author Year (Score):	**Li 2017 (score=7.5)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by grants from the Science and Technology Talents Program of Harbin, Post Doctoral Fund, Harbin High Level Talent Fund, and Heilongjiang Natural Science Foundation. No COI.
Sample size:	N = 72 patients with PTSD for at least 6 months with a score of ≥4 on the Clinical Global Impression Scale-Severity.
Source of Trauma:	27 had military related trauma, no mention of remaining sources.
Age/Sex:	Mean age: 46.0 years; 63 males, 9 females.
Comparison:	135 mg daily Sertraline group (N = 36) vs 135 mg daily placebo group (N = 36)
Follow-up:	Follow up at baseline, 6 and 12 weeks.
Results:	IES_R score change after six weeks was -24.3 for Sertraline and -18.1 for Placebo (p<0.01). CGI-S score change was -1.0 for Sertraline and -0.6 for Placebo (p<0.01). Symptoms of all 36 patients in the sertraline group were reduced vs for 25 patients in the placebo group.
Conclusion:	"In summary, we demonstrated that 12 weeks of sertraline was efficacious and well tolerated in Chinese patients with PTSD."
Comments:	Data suggest sertraline is better than placebo for PTSD

Author Year (Score):	**Davidson 2001 (score=7.0)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by Pfizer Inc. No mention of COI.
Sample size:	N = 208 patients diagnosed with PTSD by the DSM-III-R criteria from the Clinician Administered PTSD Scale. Minimum of 6 months of PTSD.
Source of Trauma:	Physical or sexual assault, seeing someone hurt or die, serious accident/fire/injury, being in a war or combat
Age/Sex:	Mean age: 37.1 years; 46 males, 162 females
Comparison:	50 to 200 mg daily Sertraline group (N = 100) vs placebo group (N = 108)
Follow-up:	Follow up at baseline, 1, 2, 3, 4, 6, 8, 10, and 12 weeks.
Results:	CAPS-2 improvement slope better in sertraline vs placebo (p=0.003), CGI-I sertraline vs placebo (p<0.001), and CGI-S sertraline vs placebo (p<0.001).
Conclusion:	"The results of the current study suggest that sertraline is a safe, well-tolerated, and significantly effective treatment for PTSD."
Comments:	Predominantly female subjects in both groups. Data suggest that sertraline is effective for treating PTSD symptoms compared to placebo at 10 weeks.

Author Year (Score):	**Davidson 2001 (score=7.0)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from Pfizer Inc. No mention of COI.
Sample size:	N = 96 patients who completed the previous 24 week open-label study and had a Clinical Global Impression improvement score of

	≤2 and ≥30% improvement in total severity score in part 2 of the Clinician Administered PTSD Scale.
Source of Trauma:	Serious accident, injury, or fire, physical or sexual assault, seeing someone hurt or die, being in a war or combat.
Age/Sex:	Mean age: 43.4 years; 19 males, 67 females
Comparison:	50 to 200 mg daily Sertraline group (N = 46) vs placebo group (N = 50)
Follow-up:	Follow up from open label baseline at weeks 14, 16, 18, 20, 22, 24, 26, and 28.
Results:	Relapse rates for sertraline group (5.3%) vs placebo (26.1%) (p<0.02)
Conclusion:	"The results provide evidence for the ability of sertraline both to sustain improvement in PTSD symptoms and to provide prophylactic protection against relapse."
Comments:	Data suggest sustained improvement in PTSD symptoms at 28 weeks with less relapse (5% vs 26%)

Author Year (Score):	**Panahi 2011 (score=6.5)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by the Baqiyatallah University Of Medical Sciences. No COI.
Sample size:	N = 70 male Iranian Iran-Iraq war veterans that met the DSM-IV-TR criteria for PTSD and had PTSD for at least 6 months.
Source of Trauma:	War
Age/Sex:	Mean age: 45.6 years; 70 males, 0 females
Comparison:	50 to 200 mg daily of Sertraline (N = 35) vs placebo (N = 35)
Follow-up:	Follow up at baseline and weeks 2, 4, 6, 8, and 10.
Results:	Sertraline group (-24.8) vs placebo group (-20.4) mean reductions in the IES-R total (p<0.001). Sertraline group (-1.0) vs placebo group (-0.5) mean reduction in CGI-S score (p=0.003). Sertraline group (2.7) vs placebo group (3.4) mean endpoint score for CGI-I (p=0.001).
Conclusion:	"In summary, the findings of the present study indicate that sertraline therapy is associated with improved control and decreased severity of symptoms in Iranian Iran–Iraq war veterans with combat-related PTSD. Furthermore, sertraline was found to be safe and well tolerated in this group of subjects. However, regarding psychosocial and traumatic differences, individual and/or multicenter trials are warranted to confirm the efficacy of sertraline in other populations with combat-related PTSD."
Comments:	Data suggest sertraline may be effective in treating combat related PTSD

Author Year (Score):	**Davidson 2006 (score=6.0)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by Wyeth Pharmaceuticals. No mention of COI.
Sample size:	N=538 outpatients with a primary diagnosis of posttraumatic stress disorder
Source of Trauma:	Nonsexual abuse, sexual abuse, unexpected death, accidental injury, and combat
Age/Sex:	No mention of age or sex specifics.

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Comparison:	Venlafaxine ER: (n=179) received 75–300 mg/d, with a lead-in dose at baseline of 37.5 mg/d vs Sertraline: (n=173) received 50–200 mg/d, with a lead-in dose at baseline of 25 mg/d vs Placebo (n=179) All patients received an increased dose after 5 days of respective medications
Follow-up:	1, 2, 4, 6, 8, and 12 weeks
Results:	Venlafaxine ER showed greater improvement than placebo in CAPS-SX_{17} total score (p=0.0147), for avoidance/numbing cluster C (p=0.0208), and for hyper arousal cluster D (p=0.0348). Venlafaxine ER group also showed greater improvement than placebo for CGI-S (p=0.0068) but not for GAF.
Conclusion:	"Study results suggest that venlafaxine ER is effective and well-tolerated in the short-term treatment of PTSD."
Comments:	Data suggest venlafaxine better than placebo and similar to sertraline.

Author Year (Score):	**Friedman 2007 (score=5.5)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by funding from Pfizer Inc. COI: Dr. Baker is a stock shareholder of Pfizer, Dr. Sikes is an employee and Dr. Farfel is a former employee of Pfizer Inc.
Sample size:	N = 169 subjects diagnosed with PTSD using the DSM-III-R with a minimum of six months with PTSD. Score of 50 or higher on part 2 of the Clinician-Administered PTSD scale at the end of a 1-week placebo was required.
Source of Trauma:	Sexual or physical assault, motor vehicle accidents, and childhood abuse.
Age/Sex:	Mean age: 45.3 years; 135 males, 34 females
Comparison:	25 mg/day for first week with doses titrated weekly up to a max of 200 mg/day of Sertraline group (N = 86) vs placebo group (N = 83)
Follow-up:	Follow up at baseline, weeks 1, 2, 3, 4, 6, 8, 10, and 12.
Results:	Adjusted mean change on the CAPS-2 total severity score was -13.1 for the Sertraline group and -15.4 for placebo (F = 1.28, p = 0.26). Adjusted mean change for the IES total score was -8.7 for the sertraline group and -8.1 for placebo (F = 1.20, p = 0.28). CGI-I rate of change was not statistically significant (F = 0.69, p = 0.41)
Conclusion:	"In conclusion, the current study failed to find evidence for the efficacy of sertraline efficacy in the civilian population. The lack of efficacy did not appear to be due to the influence of gender, type of trauma, duration of illness, or history of alcohol/drug abuse."
Comments:	Data suggest lack of efficacy.

Author Year (Score):	**Tucker 2003 (score=5.5)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by Forest Pharmaceuticals, Inc. No mention of COI.
Sample size:	N = 59 subjects with PTSD according to the DSM-IV Structured Clinical Interview and the Clinician Administered PTSD Scale-I.
Source of Trauma:	Sexual abuse or rape, physical abuse or assault, witness to violent death, tornado, combat, motor vehicle accident, terrorist bomb, nuclear bomb exposure and life threatening event.
Age/Sex:	Mean age: 38.7 years; 15 males, 43 females

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Comparison:	20-50 mg/day Citalopram group (N = 25) vs 50-200 mg/day Sertraline group (N = 23) vs placebo (N = 10)
Follow-up:	Follow up at baseline, 1, 2, 3, 4, 6, 8, and 10 weeks.
Results:	ANOVA found no significant difference between the 3 groups for total or cluster B and D CAPS scores. The Sertraline group decreased more in cluster C than the other 2 groups.
Conclusion:	"The current double-blind study demonstrated significant reduction of PTSD symptoms for both citalopram and sertraline, which did not differ from each other in symptom reduction."
Comments:	Data suggest all groups improved but sertraline group improved in avoidance numbing symptoms while showing increased gastrointestinal complaints.

Author Year (Score):	**Rapaport 2002 (score=5.5)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by Pfizer, Inc. COI: Dr. Rapaport is a consultant for, has received grant/research support and honoraria from, and is on the speakers or advisory boards for Pfizer, Inc. Dr. Endicott is a consultant for Pfizer, Abbot, Eli Lilly, Boehringer Ingelheim, and GlaxoSmithKline and is on the speakers or advisory boards of Eli Lilly and Pfizer. Dr. Clary is employed by and is a major stock shareholder of Pfizer, Inc.
Sample size:	N = 359 patients with PTSD as determined by the Structured Clinical Interview for DSM-III-R for at least 6 months.
Source of Trauma:	Serious accident/injury/fire, physical or sexual assault, seeing someone hurt or die, and being in war or combat.
Age/Sex:	Mean age: 38.3 ± 10.6 years; 96 males, 263 females
Comparison:	Acute treatment studies: 50-200 mg/day Sertraline (N = 100) vs placebo (N = 108) others unknown. Same continued in 24 week continuation study. Relapse Prevention Study: 50-200 mg/day Sertraline (N = 40) vs placebo (N =46)
Follow-up:	Follow up at baseline, 12, 36, and 64 weeks.
Results:	Adjusted mean change in CAPS-2 sertraline 1.0 baseline to 1.4 endpoint vs placebo 1.3 baseline to 2.3 endpoint ($p<0.02$)
Conclusion:	"Sertraline treatment of chronic PTSD is associated with rapid improvement in quality of life that is progressive and sustained over the course of more than 1 year of treatment."
Comments:	Data suggest at 64 weeks, the benefits of sertraline treatment are sustained and quality of life improved.

Author Year (Score):	**Zohar 2002 (score=5.0)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 42 patients with PTSD according to the CAPS-I.
Source of Trauma:	Combat-related violence, motor vehicle accident, and captivity.
Age/Sex:	Mean age: 39.6 years; 37 males, 5 females
Comparison:	50-200 mg/day Sertraline group (N = 23) vs placebo group (N = 19)
Follow-up:	Follow up at baseline, 2, 4, 6, 8, and 10 weeks.
Results:	Mean adjusted CAPS-2 change was -18.7 for Sertraline vs -13.5 for placebo (p = 0.530) Mean adjusted CGI-S change score was -0.76 for sertraline vs -0.44 for placebo (p = 0.385). Mean CGI-I score at the endpoint was 2.9 for sertraline vs 3.3 for placebo (p =0.354).

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	Week 10 mean CGI-I score was 2.4 for sertraline vs 3.4 for placebo (p = 0.016)
Conclusion:	"In conclusion, the results of this pilot study suggest that sertraline may be an effective treatment for combat-related PTSD but that the degree of improvement from baseline is notably less than what has been reported previously in civilians treated for PTSD. Adequately powered studies are needed to confirm these results and to assess whether continued treatment maintains or further improves response."
Comments:	Pilot study suggesting sertraline may slightly improve PTSD vs placebo.

Author Year (Score):	**McRae 2004 (Score=5.0)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Supported by Bristol-Myers Squibb. No mention of COI.
Sample size:	N = 26 patients with PTSD who met DSM-IV criteria.
Source of Trauma:	No mention of specific trauma source.
Age/Sex:	Mean age: 40.27 years; 6 males, 20 females.
Comparison:	Patients in Nefazodone intervention group (n=13) vs. patients in Sertraline intervention group (n=13).
Follow-up:	No mention of follow-up.
Results:	CAPS score significantly decreased from 68.95 to 23.77 in nefazodone group (p<0.001). CGI-I score improved in both treatment groups (nefazodone: p=0.001; sertraline: p<0.001).
Conclusion:	"This study did not find significant differences in the effectiveness of nefazodone and sertraline for the treatment of PTSD."
Comments:	Data suggest comparable efficacy between both treatment groups at 12 weeks.

Author Year (Score):	**Brady 2000 (score=4.5)**
Category:	Sertraline
Study type:	RCT
Conflict of Interest:	Sponsored by Pfizer Inc. COI: Dr. Brady is a member of a Pfizer advisory board and has received support from Pfizer in the form of honoraria and grant support. Dr. Pearlstein is also a consultant to Pfizer and Drs. Sikes and Farfel own stock in and have stock options with Pfizer.
Sample size:	N = 187 patients who met DSM-III-R criteria for PTSD for a minimum of 6 months.
Source of Trauma:	.Serious unintentional injury or fire, physical or sexual assault, seeing someone hurt or die, being in war or combat, and natural disaster.
Age/Sex:	Mean age: 39.9 years; 50 males, 137 females
Comparison:	25 mg/day week one then 50-200 mg/day Sertraline (N = 94) vs placebo (N = 93)
Follow-up:	Follow up at baseline, 2, 4, 6, 8, 10, and 12 weeks.
Results:	Adjusted mean change in CAPS-2 was -33.0 for sertraline vs -23.2 for placebo (p=0.02). Adjusted mean change in CGI-S score was -1.2 for sertraline vs -0.8 for placebo (p=0.01). Mean CGI-I scores at endpoint was 2.5 for sertraline vs 3.0 for placebo (p = 0.02)
Conclusion:	"Conclusions: There may be subtypes of alcohol-dependent individuals who respond differently to serotonin reuptake inhibitor treatment. Further investigation of differential responders may

Comments:	lead to improvements in the pharmacological treatment of co-occurring alcohol dependence and PTSD." High dropout rate in both groups. Data suggest significant improvement in sertraline group on CAPS-2, IES, CGI-S and CGI-I compared with placebo.
Author Year (Score):	**Rothbaum 2006 (score=3.5)**
Category:	Sertraline
Comments:	Data suggest Sertraline augmentation with prolonged exposure led to a significant decrease in the severity of PTSD symptoms.
Author Year (Score):	**Chung 2004 (score=3.5)**
Category:	Sertraline
Comments:	6 week study only. Open label RCT. Data suggest mirtazapine may be effective in treating PTSD, although both medications showed improvement.
Author Year (Score):	**Le 2014 (score=2.0)**
Category:	Sertraline
Comments:	Data suggest prolonged exposure therapy is more cost effective than pharmacotherapy for treating PTSD.
Author Year (Score):	**Brady 2005 (score=3.5)**
Category:	Sertraline for Alcohol Dependence and PTSD
Comments:	Data suggest some alcohol dependent individuals who also have PTSD may exhibit a differential response to sertraline.

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Paroxetine (Paxil) is a selective serotonin reuptake inhibitor (SSRI) [327, 328] that has been used to treat symptoms of PTSD [327, 329-334].

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.

Evidence for the Use of Paroxetine

Author Year (Score):	**Tucker 2001 (Score=6.5)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Supported by SmithKline Beecham Pharmaceutical in Collegeville, Pennsylvania. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=307 patients with PTSD who met DSM-IV criteria.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 40.8 years; 106 males, 201 females.
Comparison:	Patients assigned to paroxetine group (n=151) vs. patients assigned to placebo group (n=156).
Follow-up:	No mention of specific follow-up time length.
Results:	Improvement for CAPS-2 in paroxetine group was significantly greater than that in placebo group ($p<0.001$). CGI-I in paroxetine group was significantly greater than that in placebo group ($p<0.001$).
Conclusion:	"Paroxetine in dose of 20 to 50 mg once daily is effective as a treatment for chronic PTSD."
Comments:	Data suggest at 12 weeks, the paroxetine group had significantly less PTSD symptoms.

Author Year (Score):	**Schneier 2012 (Score=5.5)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Supported by National Institute of Mental Health Grant, and GlaxoSmithKline. The authors declared no COI.
Sample size:	N=37 adult survivors of WTC attacks.
Source of Trauma:	World Trade Center attacks of September 11 in 2011.
Age/Sex:	Mean age: 50.3 years; 17 males, 20 females.
Comparison:	Survivors assigned to paroxetine intervention (n=19) vs. survivors assigned to placebo group (n=18).
Follow-up:	Follow-up at 6 months.
Results:	In week 10, both groups' CAPS scores improved significantly ($p<0.001$). Combined treatment group showed greater improvement than placebo group ($p=0.01$). More frequent remission showed in combined treatment group than placebo group ($p=0.03$).
Conclusion:	"Initial treatment with combined paroxetine plus prolonged exposure was more efficacious than prolonged exposure plus placebo for PTSD related to the World Trade Center attacks."
Comments:	Data suggest PE plus paroxetine better than PE plus placebo for PTSD from ETC attack.

Author Year (Score):	**Marshall 2007 (Score=4.5 small blind phase; 5.5 double blind phase)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Supported by National Institute of Mental Health. No mention of COI.
Sample size:	N=52 minority adults with chronic PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 39.8±11.2 years; 17 males, 35 females.
Comparison:	Patients assigned to paroxetine intervention group (n=25) vs. patients assigned to placebo group (n=27).
Follow-up:	Follow-up at 3 and 6 months.
Results:	Mean dosage for paroxetine in the study was 40.4±17.7mg, and 43.2±17.3 mg for placebo. For CGI-I scale, paroxetine group indicated 66.7% response rate, and placebo group for 27.3% (Odds ratio=5.33, p=0.0096). More paroxetine group patients were responders for 0 LOCF evaluation than placebo group (Odds ratio=4.45, p=0.0124).
Conclusion:	"Paroxetine was well tolerated and superior to placebo in ameliorating the symptoms of chronic PTSD, associated features of PTSD, dissociative symptoms, and interpersonal problems in the first trial conducted primarily in minority adults."
Comments:	Data suggest paroxetine superior to placebo in reducing symptoms of chronic PTSD. Also, in the additional 12 week double blind phase, confirmed improvement was observed in paroxetine group.

Author Year (Score):	**Fani 2009 (Score=5.0)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Supported by GlaxoSmithKline and NIH. No mention of COI.

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Sample size:	N=18 patients with PTSD.
Source of Trauma:	Life trauma, sexual abuse, physical abuse, or combat.
Age/Sex:	Mean age: 41±9.65 years; 8 males, 10 females.
Comparison:	Participants with paroxetine intervention (n=8) vs. patients with placebo (n=10).
Follow-up:	No mention of specific follow-up time length.
Results:	Measured by total CAPS score, paroxetine group indicated greater reduction (63.1%) than placebo group (58.7%) in PTSD symptoms (t=4.56; p=0.001). But the two groups did not indicate difference by direct comparison (p=0.09).
Conclusion:	"The current study did not show a statistically significant difference between the effects of paroxetine and placebo on memory function, which may in part be related to our small sample size."
Comments:	Small sample sizes. Data suggest improvement in memory function with paroxetine group vs. placebo which were non-significant.

Author Year (Score):	**Marshall 2001 (Score=5.0)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Supported by National Institute of Mental Health and GlaxoSmithKline. No mention of COI.
Sample size:	N=551 outpatients with chronic PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 41.8 ±11.6 years; 174 males, 377 females.
Comparison:	Patients received 20 mg/day paroxetine (n=183) vs. patients received 40 mg/day paroxetine (n=182) vs. patients received placebo (n=186).
Follow-up:	No mention of specific follow-up time length.
Results:	Improvement of Clinician-Administered PTSD Scale in paroxetine groups were greater than that in placebo group (p=0.001). CGI improvement rate indicated difference between paroxetine group (20 mg/day) and placebo group (x^2=24.39, p<0.001), and between paroxetine group (40 mg/day) and placebo group (x^2=14.26, p<0.001).
Conclusion:	"Doses of 20 and 40 mg/day of paroxetine are effective and well tolerated in the treatment of adults with chronic PTSD."
Comments:	Data suggest both paroxetine groups (20mg and 40 mg) significantly improved PTSD symptoms compared to placebo.

Author Year (Score):	**Popiel 2015 (Score=5.0)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Sponsored by and Polish Ministry of Science and Higher Education Grant and the Financial Mechanism Committee (Iceland, Liechtenstein, and Norway through EEA Mechanism). No mention of COI.
Sample size:	N=228 patients with PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 37.7 years; 174 males, 54 females.
Comparison:	Prolonged exposure group (n=114) vs. paroxetine group (n=57) vs. combination of prolonged exposure and paroxetine group (n=57).
Follow-up:	Follow-up at 1 year.

Results:	PE group indicated more frequent remission of PTSD symptoms than that in Ph group (X^2=4.83, P=0.027). Combination group and Ph group (x^2=0.42, p=0.51) or Combination group and PE group (x^2=2.44, p=0.11) showed non-significant different remission rates.
Conclusion:	"[P]aroxetine and combination treatment in PTSD PE was more effective than Ph in achieving remission of PTSD."
Comments:	TRAKT Study- Data suggest PE significantly better than paroxetine in reducing PTSD. There was no demonstrable additive benefit.

Author Year (Score):	**Simon 2008 (score=5.0)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Supported by GlaxoSmithKline Grant. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N= 91 patients with PTSD.
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 42.7 years; 34 males, 57 females.
Comparison:	Prolonged exposure therapy group (n=68) vs. paroxetine group (n=9) vs. placebo group (n=14).
Follow-up:	Follow-up at 3 months.
Results:	Phase I outcomes showed significant reduction for the SPRINT score (p<0.001). Phase II outcomes indicated non-significant correlation between paroxetine group and placebo group (p>0.05).
Conclusion:	"[O]ur data do not support the addition of paroxetine CR compared with placebo to continued PE for individuals with PTSD who remain symptomatic after initial PE, suggesting that the development of novel treatment approaches for PTSD refractory to PE is needed."
Comments:	Data suggest lack of efficacy of Paroxetine CR added to Prolonged Exposure.

Author Year (Score):	**Seo 2010 (score=5.0)**
Category:	Paroxetine
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the Korean Research Foundation. No mention of COI.
Sample size:	N = 40 patients diagnosed with PTSD based on the Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version.
Source of Trauma:	Multiple sources of trauma including: Traffic accidents, physical assault, sexual assault, witnessing a trauma, and other accidents.
Age/Sex:	Mean age: 37.25 years; 12 males, 28 females
Comparison:	Group receiving 15 mg/day of mirtazapine which (n=20) vs group receiving 10 mg/day of paroxetine (n=20). After 2 weeks, both could be titrated up to a max of 60 mg/day.
Follow-up:	Follow up at baseline, 2, 4, and 8 weeks.
Results:	Decrease in total CAPS-2 score baseline vs endpoint in mirtazapine (106.75 vs 68.70 p<.001) and paroxetine (104.20 vs 64.65 p<.001). Difference between groups for CAPS-2 (F = 0.16, p=0.691).
Conclusion:	"The results of this study support a possible role for mirtazapine in the treatment of PTSD symptoms. To reach a more definite conclusion, larger double-blind, placebo-controlled, head-to-head comparison studies are needed."
Comments:	Open label RCT. 8 week study. Data suggest comparable efficacy.

Author Year (Score):	**Frommberger 2004 (score=3.5)**
Category:	Paroxetine
Comments:	Data suggest Paroxetine inferior to CBT at 6 months.

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Fluoxetine (Prozac) is an SSRI that has been used to treat PTSD [342-349].

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.

Evidence for the Use of Fluoxetine

Author Year (Score):	**van der Kolk 2006 (score=5.5)**
Category:	Fluoxetine
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health. Dr. Korn has served on the speakers or advisory boards for and received honoraria from the EMDR International Association and the EMDR Institute, Inc. Drs. van der Kolk, Spinazzola, Blaustein, J. Hopper, E. Hopper, and Simpson report no additional financial affiliations or other relationships relevant to the subject of this article.
Sample size:	N = 88 patients with PTSD.
Source of Trauma:	Child sexual and/or physical abuse, adult sexual and/or physical assault, domestic violence, traumatic loss, war/terrorism/violence, and injury/accident.
Age/Sex:	Mean age: 36.1 years; 15 males, 73 females.
Comparison:	Eye movement desensitization and reprocessing (EMDR) (N = 29) – patients underwent 90 minute individual session vs. Fluoxetine (N = 30) – treatment consisted of 20-30 minute individual sessions. Starting Fluoxetine dosage was 10 mg/day and was increased 10 mg to max of 60 mg/day vs. Placebo (N = 29) – treatment consisted

	of 20-30 minute individual sessions. Starting placebo dosage was 10 mg/day and was increased 10 mg to max of 60 mg/day.
Follow-up:	6 months
Results:	The CAPS total score, mean (SD) for the EMDR group is 28.37 (19.66), Fluoxetine 38.69 (20.30), and placebo 39.81 (18.76), p=0.09. The 2-group comparisons are as follows: EMDR vs. fluoxetine: p=0.27; EMDR vs. placebo: p=0.03; fluoxetine vs. placebo: p=0.67. At 6-month follow-up, 75.0% of adult-onset versus 33.3% of child-onset trauma subjects receiving EMDR achieved asymptomatic end-state functioning compared with none in the fluoxetine group.
Conclusion:	"This study supports the efficacy of brief EMDR treatment to produce substantial and sustained reduction of PTSD and depression in most victims of adult-onset trauma. It suggests a role for SSRIs as a reliable first-line intervention to achieve moderate symptom relief for adult victims of childhood-onset trauma. "
Comments:	Data suggest psychotherapy (Eye Movement Desensitization and Reprocessing) more effective in providing sustained improvement in PTSD symptoms compared to fluoxetine and placebo. There is some evidence of efficacy for fluoxetine for child-onset but not adult-onset PTSD.

Author Year (Score):	**Martenyi 2007 (score=5.5)**
Category:	Fluoxetine
Study type:	RCT
Conflict of Interest:	Sponsored by Eli Lilly and Company. Drs Martenyi and Brown, as well as Ms Caldwell, are employees and shareholders of Eli Lilly and Company.
Sample size:	N = 411 patients with PTSD.
Source of Trauma:	Combat-related, sexual assault, domestic violence, accident, incest, and witnessed another person's death.
Age/Sex:	Mean age: 40.69 years; 117 males, 294 females.
Comparison:	Fluoxetine 20 mg/d (n=163) – patients received 20 mg/d fluoxetine for 12 weeks vs. Fluoxetine 40 mg/d (n=160) – patients initially received 20 mg/d fluoxetine, but were titrated to 40 mg/d fluoxetine after two weeks for a 12 week treatment period vs. Placebo (n=88) – patients received the placebo treatment for 12 weeks.
Follow-up:	No follow up. Baseline – 12 weeks.
Results:	The mean changes from baseline (SD) measured by the Clinician-Administered PTSD Scale scores were -42.9 (23.1), -42.8 (27.9), and -36.6 (25.7) in the 20-mg fluoxetine, 40-mg fluoxetine, and placebo arms, respectively. The least-square mean in the TOP-8 total measure were -10.59 (0.58), -10.25 (0.60), -10.59 (0.81), p=0.907, in the 20 mg fluoxetine, 40 mg fluoxetine, and placebo groups, respectively.
Conclusion:	"Placebo response rate was substantially higher in this study than in a previously published fluoxetine trial of posttraumatic stress disorder."
Comments:	Predominantly female participants. Data suggest lack of efficacy with a higher than previous reported placebo response rate.

Author Year (Score):	**Malik 1999 (score=5.5)**
Category:	Fluoxetine

Study type:	RCT
Conflict of Interest:	Sponsored by NIMH grant #ROl-MH43740-01 to Dr. Davidson. No mention of COI.
Sample size:	N = 16 patients with PTSD.
Source of Trauma:	Rape, physical assault, incest, marital abuse, life threatening illness, family violence, and traumatic bereavement.
Age/Sex:	Mean age: 40.6 years. 1 male, 15 females.
Comparison:	Fluoxetine (n=11) – patients received fluoxetine for 12 weeks vs. Placebo (n=5) – patients received the placebo for 12 weeks.
Follow-up:	Baseline to 12 weeks.
Results:	The significant variables in this study were: vitality in physical and mental health related measure: Fluoxetine (Baseline = 30, Endpoint = 65), Placebo (20, 10) $p<0.05$; primary mental health-related measure: Social functioning – Fluoxetine (50, 88), Placebo (50, 38), $p<0.05$; mental health – fluoxetine (36, 80), Placebo (40 20), $p<0.001$.
Conclusion:	"Overall, PTSD was associated with greatly reduced quality of life, but considerable improvement was achieved through treatment."
Comments:	Small sample. Data suggest improved quality of life after treatment with fluoxetine vs. placebo.

Author Year (Score):	**Connor 1999 (score=5.0)**
Category:	Fluoxetine
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the National Institute of Mental Health. Dr. Davidson was assisted by NIMH grant IR01-MH44740-01.
Sample size:	N=54 civilians with PTSD.
Source of Trauma:	Rape, incest, spousal sexual abuse, physical abuse, traumatic bereavement, violent crime, accident, assaultive violence, father in intensive care unit, ovarian cancer, witnessed emotional abuse, hurricane, tornado, life-threatening illness.
Age/Sex:	Mean age: 37 years; 5 males, 49 females.
Comparison:	Fluoxetine (n=27) – patients received up to 60 mg/day of fluoxetine for 12 weeks vs. Placebo (n=27) – patients received the placebo treatment for 12 weeks.
Follow-up:	Baseline to 12 weeks.
Results:	Highly significant differences were observed using the cut-off score of 1, for which week 12 response rates for fluoxetine and placebo were 59% and 19%, respectively ($x^2=8.87$, d.f.=1, $p<0.0005$; difference between rates 0.40, 95% CI 0.16-0.64). At week 12, 41% fluoxetine and 4% placebo patients met the CHEF criterion of response ($x^2=10.29$, d.f.=1, $p<0.001$; difference between rates 0.37. 95% CI 0.17-0.57).
Conclusion:	"Fluoxetine was superior for measure of PTSD severity, disability, stress vulnerability, and high end-state function. The placebo-group response was low when viewed as a broad outcome based on a portfolio of ratings, but was higher with a traditional global rating criterion."
Comments:	Data suggest fluoxetine effective for improved severity of PTSD symptoms disability, stress, and function.

Author Year (Score):	**Hertzberg 2000 (score=5.0)**
Category:	Fluoxetine
Study type:	RCT

Conflict of Interest:	Sponsored by an NIMH Grant MH44740-01. No mention of COI.
Sample size:	N = 12 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 46 years; 12 males, 0 females.
Comparison:	Fluoxetine (n=6) – patients received a fluoxetine for 12 weeks for a dose up to 60 mg/day vs. Placebo (n=6) – patients received the placebo for 12 weeks.
Follow-up:	Baseline to 12 weeks.
Results:	The Davidson Trauma scale reported score of (Baseline = 106±27, Week 12 = 103±23) and (111±12, 102±26) for fluoxetine and placebo groups, respectively. The Sheehan Disability Scale scores were (24±7, 23±6) and (27±4, 25±5) for fluoxetine and placebo groups, respectively. The structured interview for PTSD scores were (48±9, 47±8) and (43±10, 42±11) for fluoxetine and placebo groups, respectively.
Conclusion:	"Fluoxetine patients did not show a greater response than placebo patients in this small sample of male combat veterans with severe, chronic PTSD."
Comments:	Small sample with poor overall response rate. Data suggest lack of efficacy.

Author Year (Score):	**Davidson 2005 (score=4.5)**
Category:	Fluoxetine
Study type:	RCT
Conflict of Interest:	Sponsored by grant #R01 MH 56656 to the principal author. The authors thank Eli Lilly for providing medication and placebo. No mention of COI.
Sample size:	N = 62 patients with PTSD.
Source of Trauma:	Combat, sexual trauma, other violence, death (bereavement), and other.
Age/Sex:	Mean age: 44.05 years; 29 males, 28 females.
Comparison:	Placebo (PBO) (n=30) – patients received 10-60 mg/day of fluoxetine for 6 months vs. Fluoxetine (FLU) (n=27) – patients received 10 -60 mg/d of the placebo for 6 months.
Follow-up:	6 months.
Results:	Rates of relapse were 22% for FLU versus 50% for PBO (P = 0.029), and time to relapse on FLU was longer than for PBO (P = 0.02, log-rank statistic). The estimated relative risk for relapse was 1.55 (1.03, 2.35) on PBO, and 0.44 (0.20, 0.98) for FLU.
Conclusion:	"Thus, our study supports the ability of continuation and maintenance therapy with FLU to protect against relapse in PTSD, albeit not in a uniform manner on all ratings. The drug is well tolerated, and no pretreatment variables that we recorded predicted relapse. Although this is the largest single-center trial of relapse prevention in PTSD, the relatively small sample size limits statistical power."
Comments:	High dropout rate with small sample. Data suggest relapse rates were triple in Placebo group compared to fluoxetine.

Author Year (Score):	**Martenyi 2002 (score=4.5)**
Category:	Fluoxetine
Study type:	RCT
Conflict of Interest:	Sponsored by Eli Lilly and Co. No mention of COI.
Sample size:	N = 131 participants with PTSD

Source of Trauma:	Combat and noncombat related.
Age/Sex:	Mean age: 38.19 years; 106 males, 25 females.
Comparison:	Fluoxetine (n=69) – patients initially received 20 mg/day of fluoxetine, but it was titrated up to 80 mg/day over 12 weeks vs. Placebo (n=62) – patients received the placebo treatment for 12 weeks.
Follow-up:	Baseline to 12 weeks.
Results:	Fluoxetine/fluoxetine-treated patients had statistically significantly greater mean improvement in TOP–8 total score from baseline to end-point than did fluoxetine/ placebo-treated patients (fluoxetine/fluoxetine, -1.8; fluoxetine/placebo +0.05; $F=6.72_{1, 112}$, P=0.011). the CGI-S score showed improvement for fluoxetine/ fluoxetine-treated patients compared with fluoxetine/placebo-treated patients ($F=8.39_{1, 112}$, P=0.005).
Conclusion:	"Fluoxetine is effective and well tolerated in the prevention of PTSD relapse for up to 6months."
Comments:	Data suggest fluoxetine helps to prevent PTSD relapse for up to 6 months.

Author Year (Score):	**Barnett 2001 (score=4.5)**
Category:	Fluoxetine
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health grants R01-MH44740-01 and R01- MH56556-0l. Eli Lilly and Company supplied medication (fluoxetine and matching placebo). No mention of COI.
Sample size:	N = 65 patients with PTSD.
Source of Trauma:	Not specified in article.
Age/Sex:	Mean age: not mentioned; sex: not mentioned.
Comparison:	Fluoxetine (n=33) – patients received 10 mg/day dose of fluoxetine and was increased at a rate of 10 mg/week until max 60 mg/day was reached vs. Placebo (n=32) – patients received the same treatment and study group, but with the placebo medication.
Follow-up:	Baseline to 12 weeks.
Results:	Statistically significant TES: term "nausea" was statistically significant fluoxetine-associated TES as compared to placebo (x^2=6.52, df=1, p=0.01). ''Diarrhea'' (x^2=5.22, df=1, P=.02) and ''thirst'' (x^2=8.07, df=1, P=.005) SOSS items additionally emerged as statistically significant (fluoxetine > placebo). ''Rash'' item was a statistically more frequent TES in the placebo group than in the fluoxetine group (x^2=4.24, df=1, P=.04).
Conclusion:	"This systematic assessment of TES indicated that PTSD patients tolerated fluoxetine well without pronounced activating side effects."
Comments:	High discontinuation rate in all three groups prior to end of study, but fluoxetine appears to be well tolerated. Secondary analyses of Connor 99, Hertzberg 00)

Author Year (Score):	**Van der Kolk 1994 (score=2.5)**
Category:	Fluoxetine
Comments:	High dropouts and many methods details sparse. Data suggest efficacy.

Fluvoxamine is an SSRI antidepressant that has been used for obsessive-compulsive disorder (OCD) [354] and for agitation and insomnia in PTSD patients [355-358].

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.

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Evidence for the Use of Fluvoxamine

Author Year (Score):	**Spivak 2006 (score=5.0)**
Category:	Fluvoxamine
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the Medical Corps of the Israel Defense Force and the Agis Pharmaceutics Company (Ramat Gan, Israel). No mention of COI.
Sample size:	N = 40 patients with PTSD.
Source of Trauma:	Motor vehicle accidents
Age/Sex:	Mean age: 40.1 years; 21 males, 19 females.
Comparison:	Reboxetine (N = 20) – patients who received reboxetine commenced treatment at 8 mg/d (4 mg BID) and remained at this fixed dosage for the 8-week duration of the study vs. Fluvoxamine (N = 20) – Patients who received fluvoxamine commenced treatment at 150 mg/d (75 mg BID) and remained at this fixed dosage for the 8-week duration of the study.
Follow-up:	No mention of follow up.
Results:	There were no differences between the 2 subgroups in baseline CAPS-2 total scores (reboxetine-treated patients, 74.9 ± 14.9 vs. fluvoxamine-treated patients, 81.8 ± 11.0; t = 2.02, df = 38, P = 0.1), CAPS-2 reexperiencing cluster scores (22.2 ± 4.9 vs. 24.2 ± 3.9; t = 2.02, df = 38, P = 0.1), CAPS-2 avoidance cluster scores (30.3 ± 7.0 vs. 32.9 ± 5.8; t = 2.02, df = 38, P = 0.2), and CAPS-2 hyperarousal cluster scores (22.5 ± 4.7 vs. 24.7 ± 3.9; t = 2.02, df = 38, P = 0.1).
Conclusion:	"Study observations indicate comparable efficacy of reboxetine and fluvoxamine in the management of MVA-related PTSD despite reboxetine's selective noradrenergic activity. Reboxetine appears to be at least as effective as fluvoxamine and may offer an alternative management option in this often difficult-to-treat and disabling condition. A lower and flexible reboxetine dosing schedule will be recommended for future research to improve its tolerability in PTSD patients."
Comments:	Data suggest comparable (in)efficacy between reboxetine and fluvoxamine.

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Escitalopram (Lexapro) is an SSRI anti-depressant and is the S-enantiomer of citalopram that has been used to treat PTSD [330, 334, 361-364].

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.

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Evidence for the Use of Escitalopram

Author Year (Score):	**Suliman 2015 (Score=7.5)**
Category:	Escitalopram
Study type:	Pilot RCT
Conflict of Interest:	Supported by Lundbeck A/S. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N = 29 patients with acute stress disorder.
Source of Trauma:	Car collision, or physical assault or sexual assault.
Age/Sex:	Mean age: 29.52±8.17 years; 19 males, 10 females.
Comparison:	Patients assigned to escitalopram group (n =12) vs patients assigned to placebo group (n =17).
Follow-up:	Follow-up at 6 months.
Results:	Both escitalopram and placebo groups indicated reduction in CAPS score ($p<0.001$). Comparing with intervention group, the placebo group indicated greater reduction in its CAPS score (0.04).
Conclusion:	"SSRIs may not be efficacious in the prevention of PTSD. Nevertheless, the small sample size and baseline differences between groups limit the explanatory power of the study."
Comments:	Data suggest lack of efficacy.

Author Year (Score):	**Shalev 2012 (score=5.5)**
Category:	Escitalopram
Study type:	RCT
Conflict of Interest:	Sponsorship by contribution from Jerry Lee foundation and grant by Jewish Federation. COI.
Sample size:	N = 233 patients who survived a traumatic event with full PTSD
Source of Trauma:	Motor vehicle accident, terrorist attack, and "other".
Age/Sex:	Mean age 37.94 years; 107 males 126 females.
Comparison:	Twelve weekly sessions of prolonged exposure (PE; n=63), vs. cognitive therapy (CT; n=40) vs. double blind treatment with 2 daily tablets of either escitalopram (10 mg) or vs. Placebo (selective serotonin reuptake inhibitor/placebo (N=46), vs. 12 weeks in a waiting list group (n=93).
Follow-up:	2, 4, 6, 8, 10, 12 weeks.
Results:	At 5 month, 21.6% of participants who received vs 57.1% WL had PTSD. At 5 months, 20.0% of participants who received CT and 58.7% of comparable participants on the waiting list had PTSD. At 9 months, 20.8% of participants who received PE and 21.4% of participants on the waiting list had PTSD
Conclusion:	"Prolonged exposure, CT, and delayed PE effectively prevent chronic PTSD in recent survivors. The lack of improvement from treatment with escitalopram requires further evaluation. Trauma-focused clinical interventions have no added benefit to survivors with subthreshold PTSD symptoms."
Comments:	Data suggest lack of efficacy of escitalopram but prolonged exposure, CT and delayed PE improved PTSD symptoms.

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Citalopram (Celexa) is an SSRI that has been used to treat depression, anxiety, and PTSD [318, 330, 364, 366, 367].

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.

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† 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.

Evidence for the Use of Citalopram

Author Year (Score):	**Tucker 2003 (score=5.5)**
Category:	Citalopram
Study type:	RCT
Conflict of Interest:	Sponsored by Forest Pharmaceuticals, Inc. No mention of COI.
Sample size:	N = 59 subjects with PTSD according to the DSM-IV Structured Clinical Interview and the Clinician Administered PTSD Scale-I.
Source of Trauma:	Sexual abuse or rape, physical abuse or assault, witness to violent death, tornado, combat, motor vehicle accident, terrorist bomb, nuclear bomb exposure and life threatening event.
Age/Sex:	Mean age: 38.7 years; 15 males, 43 females
Comparison:	20-50 mg/day Citalopram group (N = 25) vs 50-200 mg/day Sertraline group (N = 23) vs placebo (N = 10)
Follow-up:	Follow up at baseline, 1, 2, 3, 4, 6, 8, and 10 weeks.
Results:	ANOVA found no significant difference between the 3 groups for total or cluster B and D CAPS scores. The Sertraline group decreased more in cluster C than the other 2 groups.
Conclusion:	"The current double-blind study demonstrated significant reduction of PTSD symptoms for both citalopram and sertraline, which did not differ from each other in symptom reduction."
Comments:	Data suggest all groups improved but sertraline group improved in avoidance numbing symptoms while showing increased gastrointestinal complaints.

Author Year (Score):	**Manteghi 2014 (Score=3.5)**
Category:	Citalopram
Comments:	High dropout rate. Sparse methods.

Vilazodone (Vibryd) has been used to treat depression [369-371] and has been infrequently used for the treatment of PTSD [372].

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.

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Evidence for the Use of Vilazodone

Author Year (Score):	**Ramaswamy 2017 (score=4.5)**
Category:	Vilazodone
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 59 participants with PTSD and comorbid depression
Source of Trauma:	No specific source of trauma described.
Age/Sex:	Mean age: 32.7 years; 57 males, 2 females.
Comparison:	Participants given vilazodone (n=29): Daily dose of 40 mg. Participants were tapered off vilazodone as follows: 20 mg/d week 13, 10 mg/d week 14, and no medication during week 15 vs. Participants given placebo (n=30)
Follow-up:	No follow up mention.
Results:	No significant differences seen between the two groups. Though the Vilazodone group showed a significant decrease in SDS work/school and social life scores ($P < .05$).
Conclusion:	"Treatment with vilazodone 40 mg/d did not improve symptoms of PTSD and comorbid depression. Further investigation of the biological mechanisms underlying PTSD may lead to identification of improved therapeutic targets."
Comments:	Data suggest lack of efficacy of vilazodone in improving PTSD symptoms.

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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

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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.

Evidence for the Use of Venlafaxine

Author Year (Score):	**Davidson 2006, B (score=6.0)**
Category:	Venlafaxine
Study type:	RCT
Conflict of Interest:	Sponsored by Wyeth Pharmaceuticals. No mention of COI.
Sample size:	N=538 outpatients with a primary diagnosis of posttraumatic stress disorder
Source of Trauma:	Nonsexual abuse, sexual abuse, unexpected death, accidental injury, and combat
Age/Sex:	No mention of age or sex specifics.
Comparison:	Venlafaxine ER: (n=179) received 75–300 mg/d, with a lead-in dose at baseline of 37.5 mg/d vs Sertraline: (n=173) received 50–200 mg/d, with a lead-in dose at baseline of 25 mg/d vs Placebo (n=179) All patients received an increased dose after 5 days of respective medications
Follow-up:	1, 2, 4, 6, 8, and 12 weeks
Results:	Venlafaxine ER showed greater improvement than placebo in CAPS-SX_{17} total score (p=0.0147), for avoidance/numbing cluster C (p=0.0208), and for hyper arousal cluster D (p=0.0348). Venlafaxine ER group also showed greater improvement than placebo for CGI-S (p=0.0068) but not for GAF.
Conclusion:	"Study results suggest that venlafaxine ER is effective and well-tolerated in the short-term treatment of PTSD."
Comments:	Data suggest venlafaxine better than placebo and similar to sertraline.

Author Year (Score):	**Davidson 2006, A (score=6.0)**
Category:	Venlafaxine
Study type:	RCT
Conflict of Interest:	Sponsored by Wyeth Pharmaceuticals. COI: One or more of the authors have received or will benefits for personal or professional use.
Sample size:	N=329 patients with primary diagnosis of posttraumatic stress disorder
Source of Trauma:	Combat, sexual abuse, sexual assault, nonsexual abuse, accidental injury, natural disaster, witnessing, unexpected death, other, unknown
Age/Sex:	Mean age: 41.3 years; 151 males, 178 females.
Comparison:	Venlafaxine ER: (n=161) received 75- 300 mg/d with a lead-in dose at baseline of 37.5 mg/d with increasing dose at days 5, 14, 28, and 42 vs Placebo: (n=168)
Follow-up:	2, 4, 6, 8, 12, 18, and 24 weeks

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Results:	Venlafaxine ER showed greater improvement than placebo in CAPS-SX_{17} total score (p=0.006). Improvement in treatment group compared to placebo was observed for re-experiencing cluster B (p=.008), avoidance/numbing cluster C (p=.006), Clinical Global Impression-Severity Illness scale Scores (p=.004), Hamilton rating scale for Depression (p=.007), and Global Assessment of functioning (p=.03), but not for hyperarousal cluster D (p=.06).
Conclusion:	"In this study, venlafaxine ER was effective and well tolerated in short-term and continuation treatment of patients with posttraumatic stress disorder."
Comments:	Data suggest a statistically significant improvement in PTSD symptoms with venlafaxine but dropout rates >30% in each group.

Author Year (Score):	**Stein 2009**
Category:	Venlafaxine
Study type:	Pooled Analysis
Conflict of Interest:	Sponsored by Wyeth Research, Collegeville, PA, USA. COI: One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=687 patients
Source of Trauma:	Accidental injury, combat, non-sexual assault, adult sexual assault, childhood sexual abuse, unexpected death, and other (unknown, witnessing, and natural disaster).
Age/Sex:	No mention of mean age; 271 males, 416 females
Comparison:	Venlafaxine ER (n=340) received dosing increased to a maximum dose of 75 mg/d at day 5, 150 mg/d at day 14, 225 mg/d at day 28, and 300 mg/d at day 42 vs Placebo (n=347)
Follow-up:	2, 4, 6, 8, 12 weeks
Results:	Improvement was greater for venlafaxine group compared to placebo for CAPS-SX17 scores in the following categories: intrusive recollections (p=.013), acting/feeling (p<.001), psychological distress at exposure (p=.011), physiological reactivity at exposure (p=.023), avoidance (p=.003), diminished interest (p=.01), detachment (p<.001), restricted range of affect (p=.001), sense of foreshortened future (p<.001), irritability (p<.001), concentration (p=.023), hypervigilance (p=.002), started response (p=.007). All other measures were did not observe greater improvement.
Conclusion:	"Venlafaxine ER demonstrated a broad spectrum effect in the treatment of PTSD. Symptoms of psychological distress and physiological reactivity in response to trauma cues, and irritability/anger outbursts, showed early and robust improvement with venlafaxine ER treatment, while symptoms of numbing and hyperarousal took longer to respond."
Comments:	Data suggest multiple effects of venlafaxine ER the earliest of which are anger and/or irritability but also appear to improve physiological reactivity, psychological distress in response to exposure cues and "intrusive recollections".

Author Year (Score):	**Rothbaum 2008**
Category:	Venlafaxine
Study type:	Pooled Analysis
Conflict of Interest:	Sponsored by grant from Corporate/Industry and Foundation. COI: One or more of the authors have received or will receive benefits for personal or professional use.

Sample size:	N=687 outpatients with primary diagnosis of PTSD
Source of Trauma:	Accidental injury, combat, nonsexual abuse, adult sexual abuse, childhood sexual abuse, unexpected death, and other unknown, witnessing, or natural disaster
Age/Sex:	No mention of mean age; 271 males, 416 females
Comparison:	Venlafaxine ER: (n=340) received 37.5 mg/day-300 mg/day vs Placebo (n=347)
Follow-up:	1, 2, 4, 6, 8 ,12, 24 weeks
Results:	Treatment for trauma-type showed a significance of p=.0278 for the CD-RISC and SDS, CAPS-SX_{17} total score, cluster C and D scores, CGI-S and $HAMD_{17}$ scores. Trauma type affected treatment responsiveness (SDS, p=.0057) and resilience (CD-RISC, p=.0012), with an effect on depression (HAM-D-17, p=.0625).
Conclusion:	"Overall, there does not appear to be a significant effect of gender on the efficacy of venlafaxine ER in the treatment of PTSD. Trauma type may affect treatment outcome but seems to affect domains such as disability and resilience more than core PTSD symptoms."
Comments:	Data suggest gender does not seem to affect the venlafaxine response while trauma type likely affects disabled and resilience more than PTSD symptoms

Author Year (Score):	**Davidson 2012**
Category:	Venlafaxine
Study type:	Post-hoc analysis
Conflict of Interest:	Sponsored by Wyeth Research, Collegeville, Pennsylvania, which was acquired by Pfizer Inc. in October 2009. Medical writing support for this manuscript was funded by Wyeth and was provided by Dennis Stancavish, MA, of Embryon, LLC, A Division of Advanced Health Media, LLC (formerly Medesta Publications Group, A Business of Advogent). No COI.
Sample size:	N=687 outpatients with primary diagnosis of PTSD
Source of Trauma:	Accidental injury, combat, nonsexual abuse, adult sexual abuse, childhood sexual abuse, unexpected death, and other unknown, witnessing, or natural disaster
Age/Sex:	No mention of mean age; 271 males, 416 females
Comparison:	Venlafaxine ER: (n=340) received 37.5 mg/day-300 mg/day vs Placebo (n=347)
Follow-up:	No follow-up.
Results:	The study found that CD-RISC and baseline CAPS-SX_{17} scores could predict remission ($p < 0.0001$). Patients with higher resilience and treated with venlafaxine ER were found to have greater chance at reaching remission. Combined treatment groups comparison ORs (95% CI) of achieving remission in relation to CD-RISC total, CD-RISC-10, and CD-RISC-2 were 1.026 (1.104, 1.038; $p<0.0001$), 1.058 (1.031, 1.086; $p < 0.0001$), and 1.279 (1.142, 1.434; $p < 0.0001$), respectively.
Conclusion:	"Our results suggest that higher pretreatment resilience is generally associated with a positive treatment response. Future research may be warranted to explore the relationship between response to active treatment and the spectrum of resiliency."
Comments:	Data suggest higher pretreatment resilience is usually correlated with a good treatment response.

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Author Year (Score):	**Stein 2013**
Category:	Venlafaxine
Study type:	Factor Analysis
Conflict of Interest:	Sponsored by Wyeth Research, Collegeville, Pennsylvania, which was acquired by Pfizer Inc. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=685 outpatients with a primary diagnosis of PTSD
Source of Trauma:	Accidental injury, combat, nonsexual abuse, adult sexual abuse, childhood sexual abuse, unexpected death, and other unknown, witnessing, or natural disaster
Age/Sex:	No mention of mean age; 271 males, 416 females
Comparison:	Venlafaxine ER: (n=339) vs Placebo (n=346)
Follow-up:	Baseline and 12 weeks
Results:	The EFA suggested 3 factors including: re-experiencing symptoms, mood and cognitive symptoms, and hyper arousal symptoms. Venlafaxine ER showed adjusted effect of -0.32 ($p<0.001$) compared to placebo. DSM-IV symptoms showed treatment effect of –0.25 ($P = 0.002$), –0.30 ($P < 0.001$), and –0.28 ($P = 0.001$), respectively for 3 factors.
Conclusion:	"Data are consistent with literature failing to confirm the three-factor structure of DSM-IV PTSD, and they support the DSM-5 inclusion of a symptom cluster addressing altered mood and cognition in PTSD. The efficacy of venlafaxine ER in reducing a range of symptom clusters in PTSD is consistent with its multiple mechanisms of action."
Comments:	Data suggest key PTSD symptoms include: avoidance, re-experiencing, arousal and negative mood and cognition changes which are improved with venlafaxine XR.

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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.

Evidence for the Use of Amitriptyline

Author Year (Score):	**Davidson 1990 (Score=3.5)**
Category:	Amitriptyline
Comments:	High dropout rate. Data suggest that at 8 weeks there is minimal efficacy compared to placebo.

Desipramine is a tricyclic antidepressant that is used to treat patients with PTSD [380-382].

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.

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Evidence for the Use of Desipramine

Author Year (Score):	**Reist 1989 (score=4.0)**
Category:	Desipramine
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N=18 patients with PTSD
Source of Trauma:	Military
Age/Sex:	Mean age: 38.4±6.0 years; 27 males, 0 females
Comparison:	All patients received desipramine 50mg/d up to 200 mg/d for 4 weeks and placebo
Follow-up:	4 weeks
Results:	Hamilton depression scale showed main effect on time (F=4.93, df=1, p=0.041) and Hamilton anxiety scale showed main effect for time (F=5.66, df=1, p=0.03). Depression improvement was better improved in desipramine compared to placebo (t=2.43, df=5, p=0.02).
Conclusion:	"Overall, the only apparent response to desipramine was in some symptoms of depression; there were no changes in anxiety and other PTSD symptoms."
Comments:	Crossover study showing lack of efficacy. Data suggest desipramine may be beneficial for depressive symptoms but not PTSD.

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Imipramine (Tofranil) is a TCA that is used for treatment of depression and has been used for treatment of PTSD [328, 383-387].

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.

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Evidence for the Use of Imipramine

Author Year (Score):	**Frank 1988 (Score=5.0)**
Category:	Imipramine
Study type:	RCT
Conflict of Interest:	Supported by the Alcohol, Drug Abuse, and Mental Health Administration. No mention of COI.
Sample size:	N = 34 veterans with PTSD.
Source of Trauma:	Combat exposure.
Age/Sex:	Mean age: 38±11.7 years; 34 males, 0 female.
Comparison:	Veterans assigned to imipramine intervention (n=12) vs veterans assigned to phenelzine group (n=11) vs. veterans assigned to placebo group (n=11).
Follow-up:	No mention of follow-up.
Results:	Impact of Event Scale in phenelzine group dropped significantly (total score from 41 to 20, p<0.003); the Scale in imipramine group dropped less significantly (total score from 40 to 30, p<0.003); the Scale in placebo group increased (total score from 35 to 36, p<0.003).
Conclusion:	"[T]he efficacy of imipramine and of phenelzine was compared with that of placebo in 34 male veterans with posttramatic stress disorder (PTSD). Both medications reduced PTSD symptoms.
Comments:	Data suggest phenelzine better than imipramine for reducing Impact of Event Scale Scores and both better than placebo.

Author Year (Score):	**Kosten 1991 (Score=4.0)**
Category:	Imipramine
Study type:	RCT
Conflict of Interest:	Supported by Research Scientist Award, and the Veterans Administration Research Funds.
Sample size:	N=60 veterans with PTSD.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 39±2.6 years; 60 males, 0 female.
Comparison:	Veterans in phenelzine group (n=19) vs. veterans in imipramine group (n=23) vs. veterans in placebo group (n=18).
Follow-up:	No mention of follow-up.
Results:	Impact of Event Scale score in Phenelzine group dropped 45% from 30.6 to 17.0; IES score in imipramine group dropped 25% from 36.5 to 27.4; IES score in placebo group dropped 5% from 33.0 to 31.3 (p<0.01).
Conclusion:	"[B]oth medications significantly reduced PTSD symptoms, as assessed by the Impact of Events Scale (IES), but the 44% improvement on phenelzine was greater than the 25% improvement on imipramine.
Comments:	High dropout rates in all 3 groups. Phenelzine group had less combat explosion than imipramine or placebo groups which may explain treatment response.

Author Year (Score):	**Kosten 1992 (Score=4.0)**
Category:	Imipramine
Study type:	RCT

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Conflict of Interest:	Supported by Research Scientist Award, and the Veteran's Administration Research Funds. No mention of COI.
Sample size:	N=57 veterans with PTSD.
Source of Trauma:	Vietnam combat.
Age/Sex:	Mean age: 39±2.3 years; 57 males, 0 female.
Comparison:	Veterans in imipramine group (n=23) vs. veterans in phenelzine group (n=18) vs. veterans in placebo group (n=16).
Follow-up:	Follow-up at 6 and 8 weeks.
Results:	Two scales of the Impact of Event Scale scores indicated significant improvement. The intrusion IES subscale improved 4.9 scores ($p<0.0001$). The avoidance IES subscale improved 4.6 scores ($p<0.0001$). The Alexithymia Provoked Response Questionnaire (APRQ) indicated significant correlation with IES terminal avoidance scale score ($r=0.3$, $p<0.05$).
Conclusion:	"Low alexithymia on the APRQ significantly predicted improvement on the avoidance items of the Impact of Events Scale (IES) particularly among patients treated with placebo, but was not associated with changes in the intrusion items of the scale."
Comments:	Data suggest low alexithymia on the APRQ scale may be correlated to predicting improvement on the avoidance items of the IES.

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Nortriptyline (Pamelor) is a TCA that has been used for treatment of PTSD [389-393].

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.

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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.

Evidence for the Use of Mirtazapine

Author Year (Score):	**Schneier 2015 (score=7.0)**
Category:	Mirtazapine
Study type:	RCT
Conflict of Interest:	Sponsored by grants from the National Institute of Mental Health and the Sycamore Fund. No COI.
Sample size:	N = 38 patients with at least moderate severity PTSD diagnosed by CAPS and the Structured Clinical Interview for DSM-IV Axis I disorders.
Source of Trauma:	Physical and interpersonal, non-combat related.
Age/Sex:	Mean age: 40.0 years; 13 males, 23 females
Comparison:	Patients receiving sertraline plus Mirtazapine (N = 18) vs patients receiving sertraline plus Placebo (N = 18)
Follow-up:	Follow up at 4, 8, 12, 16, 20, and 24 weeks.
Results:	Mirtazapine group vs placebo group did not differ significantly on CAPS total score (p=0.17). The Mirtazapine group had higher levels of improvement at all post baseline assessments with moderate between-group effect size (*d* = 0.51, 95% CI 1.23, −0.22). Remission rates increased in the Mirtazapine group vs the placebo group (num *df* = 1, den *df* = 115, *F* = 3.14, *P* = 0.08). Significant remission rate difference at week 24 (estimate = 1.56, *SE* = 0.73, *df* = 30, *t* = 2.12, *P* = 0.042, and OR = 4.7, 95% CI 1.1, 19.9). Depression severity improved in the Mirtazapine group vs the placebo group (*P* = 0.023, *d* = −0.63, CI −1.17, −0.09)
Conclusion:	"In conclusion, this is the first PTSD study to show that combining mirtazapine with SSRI treatment may have advantages in efficacy over SSRI treatment alone, similar to some findings for depression. Combined treatment with mirtazapine plus sertraline was well-tolerated and resulted in greater remission rates and greater improvement in depressive symptoms over 24 weeks of treatment."
Comments:	Small sample. Data suggest mirtazapine plus sertraline group showed significant improvement in symptoms of depression.

Author Year (Score):	**Davidson 2003 (score=5.0)**
Category:	Mirtazapine
Study type:	RCT
Conflict of Interest:	Sponsored by Organon to Dr. Davidson. No mention of COI.
Sample size:	N = 29 patients carrying a primary diagnosis of chronic PTSD by DSM-IV criteria with a score of 20 or more on the Structured Interview for PTSD.
Source of Trauma:	Multiple sources of trauma including: rape, childhood sexual abuse, physical abuse, criminal assault, military combat, accidental

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	injury, witnessing a trauma, and unexpected death of a significant other.
Age/Sex:	Mean age: 46.5 years; 6 males, 20 females
Comparison:	Group receiving 15 mg daily increased at weekly intervals up to 45 mg of mirtazapine (N=17) or an equal regimen of a placebo (N=9).
Follow-up:	Follow up at baseline, 1, 2, 3, 4, 6, and 8 weeks.
Results:	SPRINT global measure was higher for mirtazapine (64.7%) than placebo (22.2%) with p<0.05. Treatment effects greater for mirtazapine on the SIP (p=0.04) and HADS-A (p<0.05).
Conclusion:	"Mirtazapine was more effective than placebo on some measures in posttraumatic stress disorder and general anxiety symptoms"
Comments:	8 -week placebo controlled pilot study. Data suggest mirtazapine better than placebo in treating PTSD.

Author Year (Score):	**Seo 2010 (score=5.0)**
Category:	Mirtazapine
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from the Korean Research Foundation. No mention of COI.
Sample size:	N = 40 patients diagnosed with PTSD based on the Structured Clinical Interview for DSM-IV Axis I Disorders, Clinician Version.
Source of Trauma:	Multiple sources of trauma including: Traffic accidents, physical assault, sexual assault, witnessing a trauma, and other accidents.
Age/Sex:	Mean age: 37.25 years; 12 males, 28 females
Comparison:	Group receiving 15 mg/day of mirtazapine which (n=20) vs group receiving 10 mg/day of paroxetine (n=20). After 2 weeks, both could be titrated up to a max of 60 mg/day.
Follow-up:	Follow up at baseline, 2, 4, and 8 weeks.
Results:	Decrease in total CAPS-2 score baseline vs endpoint in mirtazapine (106.75 vs 68.70 p<.001) and paroxetine (104.20 vs 64.65 p<.001). Difference between groups for CAPS-2 (F = 0.16, p=0.691).
Conclusion:	"The results of this study support a possible role for mirtazapine in the treatment of PTSD symptoms. To reach a more definite conclusion, larger double-blind, placebo-controlled, head-to-head comparison studies are needed."
Comments:	Open label RCT. 8 week study. Data suggest at 8 weeks paroxetine better than mirtazapine for PTSD. Data suggest comparable efficacy.

Author Year (Score):	**Chung 2004 (score=3.5)**
Category:	Mirtazapine
Study type:	RCT
Comments:	6 week study only. Open label RCT. Data suggest mirtazapine may be effective in treating PTSD, although both medications showed improvement.

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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. Stop medication 10 days before elective surgery to avoid hypertensive crisis. Adverse effects also include: neck stiffness, nausea and vomiting, cold sweats, profuse sweating, vision problems, photophobia, chest pain, insomnia, swelling, rapid weight gain; agitation, unusual thoughts or behavior, rash. serotonin syndrome, hypertensive crisis, sleep disturbances, orthostatic hypotension, sexual dysfunction, and weight gain.
Frequency/Dose/Duration:	Phenelzine 15 mg/d flexible dosing up to 75 mg/d to achieve at least 90% MAO inhibition [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

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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.

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Evidence for the Use of Phenelzine

Author Year (Score):	**Frank 1988 (Score=5.0)**
Category:	Phenelzine
Study type:	RCT
Conflict of Interest:	Supported by the Alcohol, Drug Abuse, and Mental Health Administration. No mention of COI.
Sample size:	N = 34 veterans with PTSD.
Source of Trauma:	Combat exposure.
Age/Sex:	Mean age: 38±11.7 years; 34 males, 0 female.
Comparison:	Veterans assigned to imipramine intervention (n=12) vs veterans assigned to phenelzine group (n=11) vs. veterans assigned to placebo group (n=11).
Follow-up:	No mention of follow-up.
Results:	Impact of Event Scale in phenelzine group dropped significantly (total score from 41 to 20, p<0.003); the Scale in imipramine group dropped less significantly (total score from 40 to 30, p<0.003); the Scale in placebo group increased (total score from 35 to 36, p<0.003).
Conclusion:	"[T]he efficacy of imipramine and of phenelzine was compared with that of placebo in 34 male veterans with posttramatic stress disorder (PTSD). Both medications reduced PTSD symptoms.
Comments:	Data suggest phenelzine better than imipramine for reducing Impact of Event Scale Scores and both better than placebo.

Author Year (Score):	**Kosten 1991 (Score=4.0)**
Category:	Phenelzine
Study type:	RCT
Conflict of Interest:	Supported by Research Scientist Award, and the Veterans Administration Research Funds.
Sample size:	N=60 veterans with PTSD.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 39±2.6 years; 60 males, 0 female.
Comparison:	Veterans in phenelzine group (n=19) vs. veterans in imipramine group (n=23) vs. veterans in placebo group (n=18).
Follow-up:	No mention of follow-up.
Results:	Impact of Event Scale score in Phenelzine group dropped 45% from 30.6 to 17.0; IES score in imipramine group dropped 25% from 36.5 to 27.4; IES score in placebo group dropped 5% from 33.0 to 31.3 (p<0.01).
Conclusion:	"[B]oth medications significantly reduced PTSD symptoms, as assessed by the Impact of Events Scale (IES), but the 44% improvement on phenelzine was greater than the 25% improvement on imipramine.
Comments:	High dropout rates in all 3 groups. Phenelzine group had less combat explosion than imipramine or placebo groups which may explain treatment response.

Author Year (Score):	**Kosten 1992 (Score=4.0)**
Category:	Phenelzine
Study type:	RCT
Conflict of Interest:	Supported by Research Scientist Award, and the Veteran's Administration Research Funds. No mention of COI.

Sample size:	N=57 veterans with PTSD.
Source of Trauma:	Vietnam combat.
Age/Sex:	Mean age: 39±2.3 years; 57 males, 0 female.
Comparison:	Veterans in imipramine group (n=23) vs. veterans in phenelzine group (n=18) vs. veterans in placebo group (n=16).
Follow-up:	Follow-up at 6 and 8 weeks.
Results:	Two scales of the Impact of Event Scale scores indicated significant improvement. The intrusion IES subscale improved 4.9 scores ($p<0.0001$). The avoidance IES subscale improved 4.6 scores ($p<0.0001$). The Alexithymia Provoked Response Questionnaire (APRQ) indicated significant correlation with IES terminal avoidance scale score ($r=0.3$, $p<0.05$).
Conclusion:	"Low alexithymia on the APRQ significantly predicted improvement on the avoidance items of the Impact of Events Scale (IES) particularly among patients treated with placebo, but was not associated with changes in the intrusion items of the scale."
Comments:	Data suggest low alexithymia on the APRQ scale may be correlated to predicting improvement on the avoidance items of the IES.

Author Year (Score):	**Liebowitz 1992 (Score=4.0)**
Category:	Phenelzine
Study type:	RCT
Conflict of Interest:	Supported by the National Institute of Mental Health in Bethesda, Maryland. No mention of COI.
Sample size:	N=74 patients with social phobia who meet DSM-III criteria.
Source of Trauma:	Possible scrutiny by other individuals.
Age/Sex:	Mean age: 34.3±8.5 years; 51 males, 23 females.
Comparison:	Patients assigned to phenelzine group (n=25) vs. patients assigned to atenolol group (n=23); patients assigned to placebo group (n=26).
Follow-up:	No mention of follow-up.
Results:	The response rates indicated significant differences between phenelzine and placebo groups ($p=0.003$), and with atenolol group ($p=0.02$). The multivariate pairwise comparisons of the IE ratings was 1.53 by comparison among the three groups ($p=0.043$).
Conclusion:	"Overall, the findings support the responsivity of social phobia to monoamine oxidase inhibitors."
Comments:	Data suggest better response to phenelzine versus atenolol.

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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.

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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.

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Evidence for the Use of Nefazodone

Author Year (Score):	**Davis 2004 (Score=5.5)**
Category:	Nefazodone
Study type:	RCT/ preliminary study
Conflict of Interest:	Partially supported by Bristol-Myers Squibb. No mention of COI.
Sample size:	N = 41 patients with combat related chronic PTSD.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 53.8 years; 41 males, 0 female.
Comparison:	Patients assigned to Nefazodone (n =26) vs patients assigned to placebo group (n=15).
Follow-up:	No mention of specific follow-up time length.
Results:	Nefazodone intervention showed improvement (30% and more increase) in CAPS total score and CAPS-D (p=0.04, 0.007 respectively).
Conclusion:	"[N]efazodone was effective in treating patients with chronic PTSD and was generally well tolerated. We found significant improvements in core PTSD symptoms and secondary symptoms of depression in veterans with chronic PTSD."
Comments:	High dropouts in both group. Data suggest at 12 weeks, PTSD symptoms improved in Nefazodone group.

Author Year (Score):	**McRae 2004 (Score=5.0)**
Category:	Nefazodone
Study type:	RCT
Conflict of Interest:	Supported by Bristol-Myers Squibb. No mention of COI.
Sample size:	N=26 patients with PTSD who met DSM-IV criteria.
Source of Trauma:	No mention of specific trauma source.
Age/Sex:	Mean age: 40.27 years; 6 males, 20 females.
Comparison:	Patients in Nefazodone intervention group (n=13) vs. patients in Sertraline intervention group (n=13).
Follow-up:	No mention of follow-up.
Results:	CAPS score significantly decreased from 68.95 to 23.77 in nefazodone group ($p<0.001$). CGI-I score improved in both treatment groups (nefazodone: p=0.001; sertraline: $p<0.001$).
Conclusion:	"This study did not find significant differences in the effectiveness of nefazodone and sertraline for the treatment of PTSD."
Comments:	Data suggest comparable efficacy between both treatment groups at 12 weeks.

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Bupropion (Wellbutrin, Zyban) is an anti-depressant [415, 416] and has been used to treat depression [321, 417], anxiety [415], smoking cessation [417-421], and PTSD [419, 422].

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.

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Evidence for the Use of Bupropion

Author Year (Score):	**Becker 2007 (score=4.0)**
Category:	Bupropion
Study type:	RCT
Conflict of Interest:	Sponsored by an investigator-initiated award from GlaxoSmithKline and Veterans Affairs Merit Awards. No mention of COI.
Sample size:	N = 30 with PTSD.
Source of Trauma:	Civilian or military related PTSD.
Age/Sex:	Mean age: 50.39 years; 22 males, 6 females.
Comparison:	Bupropion SR (N = 18) – bupropion SR was begun at 100 mg every morning for the first 2 weeks. If indicated, dosing was then increased to 100 mg twice daily. At Week 4, if no significant improvement was shown, all patients were then prescribed a maximum dosage of 150 mg twice daily (300 mg/d). vs Placebo (N = 10) – patients received the placebo medication for 8 weeks.
Follow-up:	Evaluations at weeks 2, 4, 6, and 8.
Results:	There was improvement in the sample overall in the following from baseline to end point: total PTSD symptom severity [DTS; $F(1,21) = 8.67$; $P < 0.01$], symptom severity [CAPS; $F(1,20) = 9.21$; $P < 0.01$], PTSD reexperiencing symptoms [cluster B; $F(1,21) = 7.16$; $P < 0.01$], PTSD arousal symptoms [cluster D; $F(1,21) = 11.85$; $P < 0.01$], depressive symptoms [$F(1,21) = 10.75$; $P < 0.01$], negative affect [$F(1,21) = 7.28$; $P < 0.01$], and subjective sleep quality [$F(1,21) = 7.86$; $P < 0.01$].
Conclusion:	"Bupropion SR in the treatment of PTSD had no significant effect in the current sample. Factors contributing to the absence of an effect need further study. Our analysis points to the inclusion of age and concomitant antidepressant treatment as important variables in any future larger-scale study."
Comments:	Data suggest lack of efficacy for PTSD.

Author Year (Score):	**Hertzberg 2001 (score=3.5)**
Category:	PTSD and Smoking Cessation
Conclusion:	"Bupropion SR was generally well-tolerated in combination with other psychotropic medications. Bupropion SR may be effective in helping patients who desire to quit smoking and who also have a concomitant anxiety disorder, such as PTSD."
Comments:	Bupropion may benefit individuals with PTSD and desire to quit smoking.

Author Year (Score):	**Hertzberg 2013 (score=3.5)**
Category:	PTSD and Smoking Cessation
Conclusion:	"mCM may be a useful adjunctive smoking cessation treatment component for reducing smoking among smokers with PTSD, particularly early in a smoking quit attempt."
Comments:	Data suggest mCM may benefit smokers with PTSD as an adjunct therapy.

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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,

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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.

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Evidence for the Use of Alprazolam

Author Year (Score):	**Rothbaum2014 (score=6.0)**
Category:	Alprazolam
Study type:	RCT
Conflict of Interest:	Sponsored by the National Institute of Mental Health. COI, Dr. Rothbaum is a consultant to and owns equity in Virtually Better, Inc., Drs. Ressler and Davis are founding members of Extinction Pharmaceuticals / Therapade Technologies
Sample size:	N = 156 medically stable Iraq/Afghanistan veterans who met DSM-IV criteria for PTSD due to military trauma verified via the participant's discharge papers
Source of Trauma:	Military trauma.
Age/Sex:	Mean age: 35.1 years; 148 males, 8 females.
Comparison:	5 weekly 90- Minute virtual reality exposure sessions (VRE) + D-cycloserine 50 mg VS 5 weekly 90- Minute VRE sessions + 0.25 mg/d alprazolam, VS 5 weekly 90- minute VRE sessions + pill placebo
Follow-up:	Baseline screening assessment, follow-up assessments at 3, 6, and 12 months post-treatment.
Results:	Across all conditions, over course of trial, effect on Clinical Administered PTSD Scale (CAPS) (b = −12.19, CI: −16.04 to −8.33, (p < .001), d = 1.56) and effect on PTSD Symptom Scale (PSS) (b = −4.68, CI: −6.56 to −2.80, (p < .001), d = 1.16). Effect on CAPS after 12-months (b = −1.19, CI: −1.86 to −0.53, (p < .001)), effect on PSS after 12 months (b = −0.22, CI: −0.54 to 0.11, (p = .191)). learning x D-cycloserine interaction for the CAPS (b = −2.19, CI: −3.44 to −0.94, (p = .001)) and PSS (b = −0.82, CI: −1.19 to −0.45, (p = .001)).
Conclusion:	"A small number of VRE sessions were associated with reduced PTSD diagnosis and symptoms in Iraq/Afghanistan veterans, although there was no control condition for the VRE. Overall, there was no advantage of D-cycloserine on PTSD symptoms in primary analyses. In secondary analyses, benzodiazepine use during treatment may impair recovery, and D-cycloserine may enhance VRE in patients who demonstrate within-session learning. D-cycloserine augmentation treatment in PTSD patients may reduce cortisol and startle reactivity compared to the alprazolam and placebo treatment, consistent with the animal literature."
Comments:	High dropout rate. Combined alprazolam + VRET group better than D-cycloserine + VRET group.

Author Year (Score):	**Braun 1990 (score=2.5)**
Category:	Alprazolam
Comments:	Small sample, high dropouts, no blinding. Data suggest possible benefit of alprazolam for symptoms of anxiety.

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Evidence for the Use of Clonazepam

Author Year (Score):	**Cates 2004 (score=4.5)**
Category:	Clonazepam
Study type:	Crossover, RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 6 patients with PTSD.
Source of Trauma:	Combat related PTSD.
Age/Sex:	Mean age: 47-56 years (mean age not specified); 6 males, 0 females.
Comparison:	Clonazepam (N = 6) – patients received 1 mg of clonazepam during weeks 1-2, underwent a washout on week washout period and crossed over to the other drug for weeks 4 and 5. Patients received one capsule during the first week (week 1 or 3) and two capsule during the second week (weeks 2 and 4) at bedtime. Patients completed sleep diaries vs. Placebo (N = 6) – patients received the same treatment as above, but started with the placebo first.
Follow-up:	Week 2, 3, and 5.
Results:	The following symptoms were assessed: frequency of difficulty falling/staying asleep (n of nights): sleep-onset problems (Clonazepam: Mean = 4.50 ± 3.89, Placebo: mean = 9.17 ± 4.36), mid-sleep awakening (C: 7.83 ± 4.71, P: 8.67 ± 2.66), and early-morning awakening (C: 5.33 ± 5.85, P: 9.50 ± 5.32). Frequency of distressing dreams (per night) (C: 1.42 ± 0.52, P: 1.33 ± 0.45). Intensity of distressing dreams (per night) (C: 2.15 ± 0.70, P: 2.06 ± 0.60).
Conclusion:	"Clonazepam therapy was largely ineffective in improving sleep disturbances, particularly nightmares, associated with combat-related PTSD. The small sample size was a significant limitation of this study, but the prospective design and single-blind, placebo-control parameters were strengths. Further studies are needed to further define the role of this widespread clinical practice."
Comments:	Placebo controlled crossover design RCT. Very small sample (n=6). Data suggest lack of efficacy.

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Evidence for the Use of Temazepam

Author Year (Score):	**Mellman 2002 (score=4.0)**
Category:	Temazepam
Study type:	RCT
Conflict of Interest:	Supported by grant MH54006 from the national Institute of Mental Health, Bethesda, MD. No COI.
Sample size:	N=22 individuals who were admitted into a level 1 trauma center.
Source of Trauma:	Motors vehicle accident, Industrial Accident, Impersonal assaults.
Age/Sex:	14 males, 8 females; mean age 36.1±11.4.
Comparison:	Group 1: received temazepam before bed for one week, 30 mg for 5 nights and 15 for the following 2 nights. (N = 11) vs Group 2: received placebo pills for one week before bed. (N = 11)
Follow-up:	Baseline, after one night, one week post treatment.
Results:	Group 1 vs Group 2, total sleeps hours, number of awakenings, PTSD Caps Score at 1 week post treatment: 6.3±1.4 vs 5.5±1.8 (NS), 1.9±1.0 vs 2.2±2.1 (NS), 56.2±21.0 vs 40.9±24.6 (NS). Reduction of awakenings was correlated with a decrease in PTSD symptoms (r=0.55) (p<0.01).
Conclusion:	"While prescribing a benzodiazepine short term is unlikely to be harmful and may transiently alleviate distress, our findings and others suggest that it is insufficient for preventing PTSD. The findings relating reduced awakening to improvement in PTSD, however, suggests the possibility of a role for other interventions for reducing sleep disruption."
Comments:	Data suggest lack of efficacy.

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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.

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Evidence for the Use of Gabapentin

Author Year (Score):	**Stein 2007 (score=4.5)**
Category:	Gabapentin
Study type:	RCT
Conflict of Interest:	Sponsored by NIMH grants MH62037 (R21) and MH64122 (K24) to MBS. COI, nurses and physicians of the UCSD Department of Surgery, Division of Trauma for their support and assistance, Jitender Sareen, MD FRCPC, and Soraya Seedat, MBBS, Reena Deutsch, PhD, and Naomi Breslau, PhD.
Sample size:	N= 48 Participants with PTSD
Source of Trauma:	Severe physical injury requiring specialized, emerging trauma care.
Age/Sex:	Mean age: 29.4 years; 26 males, 22 females.
Comparison:	Participant taking Propranolol (n=17): 20 mg for 3 times daily (t.i.d.) and uptitrated over 2 days to 40 mg t.i.d. vs. Participant taking Gabapentin (n=14): started at 300 mg t.i.d. and uptitrated over 2 days to 400 mg t.i.d. vs. Participants on Placebo (n=17)
Follow-up:	Follow up at baseline, 1 month, 4 months, and 8 months.
Results:	No significant found in the reduction of PTSD symptoms among drugs tested. Propanol group (n-17) PCL-C means: 33.4 (SD=15.0). Gabapentin group (n=14): PCL-C means: 30.0 (SD = 10.6). Placebo group (n=17) PCL-C means: F <1.
Conclusion:	"This information suggests that the use of propranolol during the retrieval of traumatic memories may provide opportunities for the treatment of PTSD…"
Comments:	Data suggest lack of efficacy for both meds.

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Lamotrigine (Lamictal) has been used to treat seizures [447, 448], depression [449, 450], and PTSD [451].

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.

Evidence for the Use of Lamotrigine

Author Year (Score):	**Hertzberg 1999 (score=3.0)**
Comments:	Sparse methods. Small sample with high dropouts.

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Topiramate (Topamax) is an anticonvulsant [452, 453] that has been used to treat PTSD symptoms, including hyperarousal and numbness [454, 455].

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.

Evidence for the Use of Topiramate

Author Year (Score):	**Yeh 2011 (score=6.5)**
Category:	Topiramate
Study type:	RCT
Conflict of Interest:	Sponsored by Fundacᾶo de Amparo à Pesquisa do Estado de S˜ao Paulo; MCPC received a scholarship from the Ministry of Education. JJM is a CNPq Level I Researcher, and MFM, RAB, and SBA are CNPq level II researchers. No COI.
Sample size:	N = 36 civilians with a confirmed diagnosis of PTSD.
Source of Trauma:	Violence

Age/Sex:	Mean age: 40.44 years; 10 males, 21 females.
Comparison:	Topiramate (N = 17) – patients received 25 mg/day once daily, at night, and increased in 25 mg weekly until max dose of 200 mg/day was reached vs. Placebo (N = 14) – patients received the placebo drug.
Follow-up:	Baseline, 1, 2, 3, 4, 6, 8, and 12 weeks.
Results:	The efficacy analysis reports a significant reduction in comparison between topiramate and the placebo in the following: reexperiency (CAPS-B: topiramate—19.5, SD = 7.25; placebo - 13.16, SD = 6.02; *P* = 0.04, f = 4.08) and avoidance/numbing (CAPS-C: topiramate—23.5, SD = 11.37; placebo—7, SD = 9.91; P < 0.05, f = 15.46).
Conclusion:	"Topiramate was effective in improving reexperiencing and avoidance/ numbing symptom clusters in patients with PTSD. This study supports the use of anticonvulsants for the improvement of symptoms of PTSD."
Comments:	Data suggest greater improvement of PTSD symptoms in topiramate group.

Author Year (Score):	**Tucker 2007 (score=6.0)**
Category:	Topiramate
Study type:	RCT
Conflict of Interest:	Sponsored by Ortho-McNeil Neurologics, Inc., Titusville, N.J. COI, one or more authors have received or will receive financial benefits from participation in this study.
Sample size:	N = 38 patients with PTSD.
Source of Trauma:	Civilian, non-combat-related PTSD.
Age/Sex:	Mean age: 41.5 years; 8 males, 30 females.
Comparison:	Topiramate (N=19) – Study medication was started at 25 mg/day and was titrated by 25-50 mg/week during an 8-week period following a designated washout period. Topiramate was given twice daily vs. placebo (N=19) – Patients received the placebo treatment.
Follow-up:	No mention of follow-up.
Results:	Patients in the topiramate group exhibited significantly greater reductions compared with the placebo group in re-experiencing (CAPS cluster B: topiramate, 74.9%; placebo, 50.2%, p=0.038) and TOP-8 overall severity (topiramate, 68.0%; placebo, 41.6%; p=0.025).
Conclusion:	"These preliminary results suggest that further, adequately powered studies of topiramate for the treatment of civilian PTSD are warranted."
Comments:	Small sample. Data suggest a non-statistically significant trend toward improvement from Topiramate.

Author Year (Score):	**Lindley 2007 (Score=5.0)**
Category:	Topiramate
Study type:	RCT
Conflict of Interest:	Sponsored by an investigator-initiated research grant from Ortho-McNeil Pharmaceutical, Inc. No mention of COI.
Sample size:	N= 40 male veterans with PTSD.
Source of Trauma:	Combat
Age/Sex:	Mean age: 53.4 years; 40 males, 0 females.

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Comparison:	Topiramate (n=15) – Patients received 25 mg BID of topiramate. The dosage was increased by 50 mg/d each week until a maximally tolerated dosage was achieved or 200 mg/d was reached vs. Placebo (n=9) – Patients received 25 mg BID of the placebo.
Follow-up:	No follow-up mentioned.
Results:	Baseline Clinician-Administered PTSD Scale scores were 62.1 ± 13.9 for placebo and 61.0 ± 22.2 for topiramate. The last PGI-I score obtained fell near the minimally improved range for both groups (placebo, 2.9 ± 1.1, vs topiramate, 2.7 ± 1.2; minimally improved = 3).
Conclusion:	"Primary outcome measures failed to demonstrate a significant effect for topiramate over placebo; however, high dropout rate in the treatment group prohibits definitive conclusions about the efficacy of topiramate in this population."
Comments:	High dropout rate in Topiramate group. Data suggest lack of efficacy.

Author Year (Score):	**Batki 2014 (score=7.5)**
Category:	Topiramate for Concomitant PTSD and Alcohol Disorder
Study type:	RCT
Conflict of Interest:	Sponsored by grants from the Department of Defense, National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health. DLP, BL, AW, KD, and EH have no disclosures to make. SLB has served as a consultant to Gilead Sciences and TN has consulted to Genentech. TN has received study medication from Actelion for a study funded by the Department of Defense and received study medication from Glaxo Smith Kline for a study funded by the Department of Veterans Affairs.
Sample size:	N= 30 veterans with PTSD and alcohol use disorder (AUD).
Source of Trauma:	Combat and civilian.
Age/Sex:	Mean age: 49.43 years; 28 males, 2 females.
Comparison:	Topiramate (n=13) – patients received an initial dose of 25 mg/day, which was increased to 300 mg/day by the end of the trial vs. Placebo (n=14) – patients received 25 mg of the placebo drug.
Follow-up:	Weekly for 12 weeks.
Results:	There was a near-significant trend for a main effect of treatment , which is the decrease of drinking day with the use of topiramate [p=0.063, RR=0.430; 95% CI=(0.18-1.05)]. The PCL total score at baseline was 57.1±13.4, at weeks 1-12 was 42.3±16.4, p=0.001, 95% CI -1.84 to -0.62.
Conclusion:	"These preliminary results indicate that in veterans with co-occurring PTSD and AUD, topiramate may be effective in reducing alcohol consumption, alcohol craving, and PTSD symptom severity – particularly hyperarousal symptoms. Topiramate was associated with transient cognitive impairment but was otherwise well tolerated."
Comments:	Data suggest topiramate may be useful in reducing drinking frequency in individuals with concomitant PTSD and alcohol use disorder.

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Valproic acid (Valproate, Divalproex) has been used to treat seizures [456-458], as a mood stabilizer for bipolar disorder, and for some anxiety disorders [459, 460] and PTSD [461].

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.

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Evidence for the Use of Valproic Acid

Author Year (Score):	**Davis 2008 (score=6.5)**
Category:	Valproic Acid
Study type:	RCT
Conflict of Interest:	No conflict of interest, supported by a VA Research and Development Merit Award and an investigator-initiated grant from Abbott Laboratories, Chicago, IL.
Sample size:	N = 85
Source of Trauma:	Combat related
Age/Sex:	Mean age: 52.2; 83 males, 2 females
Comparison:	Patients treated with placebo (N = 41) vs patients treated with divalproex (N = 44)
Follow-up:	Follow up conducted at the 8 week end date
Results:	The study was tested and conducted on the Clinician-Administered PTSD Scale (CAPS). And the results show results of baseline score of 75.2 for divalproex and 77.3 for placebo. Then at the end of 8 weeks, 60.1 for divalproex and 60.8 for placebo.
Conclusion:	"Divalproex monotherapy was not effective in the treatment of chronic PTSD in predominantly older male combat veterans. Further study is needed to determine the efficacy of divalproex in the management of PTSD in women or civilians or in combination with antidepressants."
Comments:	Data suggest lack of efficacy of Valproic acid.

Author Year (Score):	**Hamner 2009 (score=4.5)**
Category:	Valproic Acid
Comments:	Modest sample size. Data suggest lack of efficacy.

Author Year (Score):	**Kuriyama 2011 (score=3.0)**
Category:	Valproic Acid
Comments:	Sparse methods

Author Year (Score):	**Kuriyama 2012 (score=3.0)**
Category:	Valproic Acid
Comments:	Methods are poorly descried, and participant characteristics are not cited.

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Tiagabine (Gabatril) an anticonvulsant that has also been used for anxiety and PTSD [463-466].

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.

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Evidence for the Use of Tiagabine

Author Year (Score):	**Connor, 2005 (Open label score=4.0, Double blind score=5.5)**
Category:	Tiagabine
Study type:	RCT
Conflict of Interest:	Sponsored by a grant from Cephalon Inc. No mention of COI.
Sample size:	Open label: N = 29 subjects with PTSD as assessed by the DSM-IV structured interview. Double blind: N = 18 subjects with PTSD as assessed by the DSM-IV structured interview that demonstrated at least minimal improvement in the open-label phase.
Source of Trauma:	Sexual trauma, other interpersonal violence, accidents, threat of harm to loved one or friend, and unwanted therapeutic abortion.
Age/Sex:	Open label: Mean age: 41.3 years; 10 males, 19 females. Double blind: No mention of age or gender.
Comparison:	Open label: Baseline (N=26) vs after 12 weeks of tiagabine at 2 mg for 1 week then titrated upwards in 4 mg increments per week (N=26). Double blind: Continued Tiagabine group (N=10) vs placebo group tapered off in decrements of 2 mg every 3 days (N=8)
Follow-up:	Open label: Weeks 1, 2, 3, 4, 8 and 12. Double blind: Continuing from open label weeks 13, 14, 16, 20, and 24
Results:	Open label: Sprint score at baseline of 23.0 vs at week 12 of 9.2 ($p<.0001$). SIP score at baseline of 37.3 vs at week 12 of 17.2 ($p<.0001$) and DTS score at baseline of 84.1 vs at week 12 of 41.1 ($p<.0001$). Double Blind: Remission of Tiagabine group (N = 4/6) vs placebo (N=0/4) ($p<0.08$).
Conclusion:	"These findings suggest a possible role for the SGRI tiagabine in the treatment of PTSD. As the role of GABAergic drugs in PTSD is poorly defined, larger, randomized, double-blind, placebo-controlled trials are needed."
Comments:	Small sample size. Open label trial. Data suggest a possible benefit for Tiagabine for PTSD as relapse occurred more often when switching from study medication to placebo.

Author Year (Score):	**Davidson, 2007 (score=4.0)**
Category:	Tiagabine
Study type:	RCT
Conflict of Interest:	Sponsored by Cephalon Inc. COI: Dr. Davidson has received support from Cephalon. Dr. Stein has been a consultant for Cephalon. Dr. Pollack has been on the advisory board and received research grants from Cephalon.
Sample size:	N = 232 patients who met the DSM-IV criteria for PTSD using the Clinician-Administered PTSD scale.
Source of Trauma:	Physical and sexual assault/violence, witnessing harm or death, serious accident/fire/injury, combat, natural or technological disaster.
Age/Sex:	Mean age: 42.6 ± 11.8 years; 78 males, 154 females.
Comparison:	4 mg/d individually titrated of up to 4 mg/d weekly to a max of 16 mg/d tiagabine group (N=116) vs placebo (N=116).
Follow-up:	Follow up at baseline, week 6 and week 12.
Results:	Mean reduction in CAPS total score was 30.7 for tiagabine and 30.2 for placebo ($p=0.85$). Rates of remission for tiagabine were 16% vs 14% for placebo ($p=0.88$). Mean change on the Connor-Davidson Resilience Scale for tiagabine was 6.4 vs 8.1 for placebo

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	(p=0.45) Mean change on the Sheehan Disability scale for tiagabine was -5.5 vs -5.9 for placebo (p=0.74)
Conclusion:	"[T]his placebo-controlled study showed that tiagabine was not significantly different from placebo in reducing symptoms of PTSD in patients with PTSD. Tiagabine was generally well tolerated and not associated with changes in weight, sexual function, worsening of depressive status, or symptoms of a discontinuation syndrome. Although drugs that target the GABA system have shown benefits in the treatment of anxiety disorders, 34 – 36 additional studies are needed to assess their potential for the treatment of PTSD."
Comments:	Data suggest lack of efficacy of Tiagabine.

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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.

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Evidence for the Use of Aripiprazole

Author Year (Score):	**Naylor 2015 (score =4.0)**
Category:	Aripiprazole
Study type:	RCT
Conflict of Interest:	Sponsored by VA Mid-Atlantic MIRECC, Department of Veterans Affairs Advanced Research Career Development Award (Marx), and VA Career Development Transition Award (Marx). Dr. Naylor is sponsored by Department of Veterans Affairs Rehabilitation Research and Development Career Development Award (1lK2RX000908). No COI.
Sample size:	N = 14 participants with PTSD
Source of Trauma:	Combat related Trauma
Age/Sex:	Mean age: 33.8 years; 9 males, 5 females.
Comparison:	Participant given Aripiprazole (n=7): After two week of placebo, Aripiprazole were administered 5mg once a day orally for 2 weeks, 5–10 mg taken once a day orally for 2 weeks, 5–10 mg taken once a day orally for 2 weeks, and 20 mg taken once a day orally for 2 weeks. Vs. Participant on Placebo (n=7)
Follow-up:	Follow up at week 2, 6, and 10.
Results:	Treatment response CAPS scores: Aripiprazole group week 2 (mean ± SE): 93.40 (4.60); week 10: 63.80 (11.74) Vs. Placebo group week 2 (mean ± SE): 82.29 (7.22); week 10: 72.71 (7.95) Comparison (P=0.17)
Conclusion:	"Adjunctive aripiprazole appears to be a safe and well tolerated intervention for PTSD and frequently co-occurring depressive and psychotic symptoms among Veterans who served in the US military after 11 September 2001."
Comments:	Although a weak trend is present, the trial's data are statistically negative.

Author Year (Score):	**Mello 2008 (score=3.5)**
Category:	Aripiprazole
Comments:	Data show improvement in some PTSD symptoms with aripiprazole.

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Quetiapine (Seroquel) is an atypical antipsychotic that also exerts α1-blocking activity [472, 473] which has been used for the treatment of schizophrenia, bipolar disorder [474, 475], and PTSD [408, 409, 472, 475-477].

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.

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Evidence for the Use of Quetiapine

Author Year (Score):	**Villarreal 2016 (score=4.0)**
Category:	Quetiapine
Study type:	RCT
Conflict of Interest:	Sponsored by an investigator-initiated grant from AstraZeneca to Dr. Hamner. No COI.
Sample size:	N = 80 patients with chronic PTSD
Source of Trauma:	No mention of source of trauma.
Age/Sex:	Mean age: 52.0 years, 75 males, 5 females
Comparison:	Quetiapine: (n=42) received 25 mg- 400 mg doses titrated over time vs Placebo (n=38)
Follow-up:	2, 4, 8, 12 weeks
Results:	CAPS scores for quetiapine group were 75±16 and 71±12 for placebo group (t=-0.76, p=0.45). DSM-IV scores were higher in treatment group than in placebo (m=21 vs m=17, p=0.02). Effect on interaction of visit and treatment were f=2.88. df=4, 240, p=0.03, which indicates that quetiapine group showed lower CAPS scores than placebo group.
Conclusion:	"Quetiapine monotherapy was efficacious in the treatment of PTSD. These findings suggest quetiapine as a single agent is effective in treating military PTSD."
Comments:	High dropout rates (32.8% dropped in run-in phase; then 31.0% dropouts in RCT's drug arm with mostly adverse effects (dry mouth, somnolence, sedation), and 42.6% dropouts mostly lack of efficacy in placebo arm). Data suggest PTSD symptoms improved with quetiapine.

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Risperidone (Risperdal) is an atypical antipsychotic that has been used to treat schizophrenia, bipolar disorder [481, 482], and PTSD [483-486].

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.

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Evidence for the Use of Risperidone

Author Year (Score):	**Krystal 2011 (Score=7.0)**
Category:	Risperidone
Study type:	RCT
Conflict of Interest:	Supported by the Department of Veterans Affairs Office of Research and Development. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N = 267 patients diagnosed with military service related PTSD.
Source of Trauma:	Military service
Age/Sex:	Mean age: 54.4 ± 10.7 years; 258 males, 9 females.
Comparison:	Patients received 4 mg once daily risperidone intervention (n = 133) vs patients received placebo (n = 134).
Follow-up:	Follow-up at 6, 12, 18, and 24 weeks.
Results:	No significant effects on CAPS total score by risperidone intervention (p=0.11): -16.3 (95% CI: -19.7 to -12.9).
Conclusion:	"Among patients with military-related PTSD with SRI-resistant symptoms, 6-month treatment with risperidone compared with placebo did not reduce PTSD Symptoms."
Comments:	Data suggest at 4 months risperidone showed lack of efficacy in reducing PTSD symptoms.

Author Year (Score):	**Byrne 2017 (No score) Secondary analysis of Krystal 2011**
Category:	Risperidone
Study type:	Secondary analysis of Krystal, 2011
Conflict of Interest:	Supported by the Veteran Affairs National Center for PTSD and Consortium to Alleviate PTSD. Authors declared no COI.
Sample size:	N = 267 patients diagnosed with military service related PTSD.
Source of Trauma:	Military service
Age/Sex:	Mean age: 54.4 ± 10.7 years; 258 males, 9 females.
Comparison:	Patients received 4 mg once daily risperidone intervention (n = 133) vs patients received placebo (n = 134).
Follow-up:	Follow-up at 6, 12, 18, and 24 weeks.
Results:	50% out of the 194 veterans showed reduced CAPS score; but 49% of the veterans indicated delayed improvement.
Conclusion:	"While results are indicative of nonspecific pharmacotherapeutic effects, they suggest that specific PTSD symptom clusters and impairment are associated with variable improvement in veterans with antidepressant resistant PTSD."
Comments:	Secondary analysis suggesting that PTSD symptom clusters are associated with variable improvement in individuals with antidepressant resistant PTSD.

Author Year (Score):	**Bartzokis 2004 (Score=5.0)**
Category:	Risperidone
Study type:	RCT
Conflict of Interest:	Supported by the Department of Veterans Affairs, Janssen research foundation, and the Marie Wilson Howells endowment. No mention of COI.
Sample size:	N=65 patients with combat related chronic PTSD.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 51.6 ± 4.2 years; 65 males, 0 female.

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Comparison:	Patients randomly assigned to risperidone treatment group (n=33) vs. patients assigned to placebo group (n=32).
Follow-up:	Follow-up at 3 months.
Results:	Compared with placebo group, patients with risperidone intervention showed significantly more 20% reduction in CAPS total score (p=0.002). CAPS-D (p<0.01) and CAPS-Total (p<0.05) scores were statistically significant between the comparison of two groups.
Conclusion:	"[A]djunctive risperidone improved a broad range of psychiatric symptoms in patients with chronic combat-related PTSD."
Comments:	Data suggest risperidone may improve PTSD symptoms.

Author Year (Score):	**Rothbaum 2008 (Score=4.5)**
Category:	Risperidone
Study type:	RCT
Conflict of Interest:	Supported by Titusville N.J. and Janssen L.P. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=20 patients with PTSD completed all phases of intervention.
Source of Trauma:	Civilian trauma.
Age/Sex:	Mean age: 34.2 years; 4 males, 16 females.
Comparison:	Patients received risperidone intervention (n=9) vs. patients received placebo (n=11).
Follow-up:	No mention of follow-up.
Results:	Mean decreased CAPS score after intervention: 28.5 ± 26.6. Risperidone group showed greater improvement in CAPS sleep difficulty item, comparing with the placebo group (p=0.09).
Conclusion:	"[R]isperidone augmentation was helpful in those subjects who did not remit with sertraline alone, particular in the areas of global improvement, positive affect, and sleep."
Comments:	Small sample sizes. Data suggest risperidone may have adjunctive efficacy when added to sertraline.

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Olanzapine (Zyprexa) is an atypical antipsychotic agent [487, 488] that has been used to treat schizophrenia and mania in bipolar disorder [487, 489, 490]. It also has been used to treat PTSD symptoms of sleep disturbances and nightmares [488, 491-493].

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

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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.

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Evidence for the Use of Olanzapine

Author Year (Score):	**Carey 2012 (score=5.0)**
Category:	Olanzapine
Study type:	RCT
Conflict of Interest:	Sponsored by Eli Lilly. No COI.
Sample size:	N = 28 participants with non-combat related chronic PTSD.
Source of Trauma:	Non-combat PTSD.
Age/Sex:	Mean age: 40.75 years; 11 males, 17 females.
Comparison:	Olanzapine (N = 14) – patients received 5 mg olanzapine for 1 week, followed by 7.5 mg for 1 week and then 10 mg for 2 weeks till a max dose of 15 mg was reached vs. placebo (N = 14) – patients received 5 mg placebo for 1 week, followed by 7.5 mg for 1 week and then 10 mg for 2 weeks till a max dose of 15 mg was reached
Follow-up:	8 weeks.
Results:	The olanzapine assigned group demonstrated a significantly greater improvement in PTSD symptoms (mean change = -35.86±19.85; 57.7% improvement) than the placebo group (mean change = -19.29±28.77; 23.7% improvement) from baseline to the week 8 endpoint using LOCF data (p = 0.018). also, at week 4: (olanzapine: 9.29mg±1.53; placebo: 9.82mg±0.67; p = 0.014)
Conclusion:	"To our knowledge, this is the first controlled evidence of the efficacy of olanzapine monotherapy in an exclusively non-combat related chronic PTSD group. Despite the small sample size, these data suggest that olanzapine may have a role in the treatment of PTSD. These findings warrant replication in a larger sample."
Comments:	8-week trial of non-combat PTSD. Data suggest olanzapine exhibited statistically significant PTSD improvement vs. placebo.

Author Year (Score):	**Stein 2002 (score=4.0)**
Category:	Olanzapine
Study type:	RCT
Conflict of Interest:	Sponsored by Eli Lilly. Dr. Stein is a paid consultant for Eli Lilly.
Sample size:	N = 19 patients with PTSD.
Source of Trauma:	Chronic military-related PTSD.

Age/Sex:	Mean age: 53.25 years; 19 males, 0 females.
Comparison:	Olanzapine (n=10) – patients were given 10 mg at bedtime for the first two weeks; the dose was increased to 20 mg at the end of the 8-week trial vs. Placebo (n=9) – patients were given 10 mg of the placebo treatment for 8 weeks.
Follow-up:	8 weeks.
Results:	The primary outcome measures changes in the following symptom domains. Posttraumatic stress (Placebo: mean value = 84.0±16.2, Olanzapine: mean value = 86.1±22.1, p=0.81), Depression (Placebo: 35.9±13.9, Olanzapine: 36.6±12.7, p=0.91), and sleep (placebo: 15.9±3.4, olanzapine: 16.1±2.9, p=0.89).
Conclusion:	"This is most likely the first double-blind, placebo controlled study of an adjunct to SSRIs for PTSD. Despite the small group size, the findings suggest a role for olanzapine or other atypical antipsychotics in treating SSRI-resistant PTSD. Sleep symptoms may especially benefit."
Comments:	Sparse methods. Data suggest olanzapine significantly improved PTSD symptoms compared to placebo.

Author Year (Score):	**Butterfield 2001 (score=4.0)**
Category:	Olanzapine
Comments:	Small sample. Some baseline differences in outcomes and no demographic data by group provided. Data suggest lack of efficacy.

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.

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Evidence for the Use of Propranolol

Author Year (Score):	**Hoge 2012 (score=5.5)**
Category:	Propranolol
Study type:	RCT
Conflict of Interest:	Sponsored by NIMH grant #MH068603 to R.K.P. No COI.
Sample size:	N= 43 Participant with PTSD.
Source of Trauma:	No specific trauma source described.
Age/Sex:	Mean age: 33.5; 18 males, 23 females.
Comparison:	Participants taking Propranolol (n=21): Received initial oral dose of 40 mg short-acting propranolol. Another 60 mg long-acting propranolol was given if systolic blood pressure doesn't fall under 100 mmHg after the first hour. Assessment was repeated at 4, 5, 12, and 13 weeks vs. Participants on Placebo (n=20): Another placebo pill was given if systolic blood pressure does not fall under 100 mmHG after the first hour.
Follow-up:	Follow up at 1 month, and 3 month.
Results:	No significant effects of Drugs on any outcome measured. Correlation of CAP scores and psychological probability: 4-week, r = 0.46, n = 37 (*P* = 0.004); 12-week, r = 0.36, n = 30 (*P* = 0.04).
Conclusion:	"The physiological results provide some limited support for a model of PTSD in which a traumatic conditioned response is reduced by posttrauma propranolol. However, the clinical results from this study do not support the preventive use of propranolol in the acute aftermath of a traumatic event."
Comments:	Data suggest lack of efficacy

Author Year (Score):	**Stein 2007 (score=4.5)**
Category:	Propranolol
Study type:	RCT
Conflict of Interest:	Sponsored by NIMH grants MH62037 (R21) and MH64122 (K24) to MBS. COI, nurses and physicians of the UCSD Department of Surgery, Division of Trauma for their support and assistance, Jitender Sareen, MD FRCPC, and Soraya Seedat, MBBS, Reena Deutsch, PhD, and Naomi Breslau, PhD.
Sample size:	N= 48 Participants with PTSD
Source of Trauma:	Severe physical injury requiring specialized, emerging trauma care.
Age/Sex:	Mean age: 29.4 years; 26 males, 22 females.
Comparison:	Participant taking Propranolol (n=17): 20 mg for 3 times daily (TID) and uptitrated over 2 days to 40 mg TID vs. participant taking Gabapentin (n=14): started at 300 mg TID and uptitrated over 2 days to 400 mg TID vs. Participants on Placebo (n=17)
Follow-up:	Follow up at baseline, 1 month, 4 months, and 8 months.
Results:	No significant found in the reduction of PTSD symptoms among drugs tested. Propanol group (n-17) PCL-C means: 33.4 (SD=15.0). Gabapentin group (n=14): PCL-C means: 30.0 (SD = 10.6). Placebo group (n=17) PCL-C means: *F* <1.
Conclusion:	"This information suggests that the use of propranolol during the retrieval of traumatic memories may provide opportunities for the treatment of PTSD…"
Comments:	Data suggest lack of efficacy for both meds.

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Author Year (Score):	**Mahabir 2015 (score=4.5)**
Category:	Propranolol
Study type:	RCT
Conflict of Interest:	Sponsored by Canadian Institutes of Health Research. COI, J.T. designed the study and conducted the medical assessments. D.S. and A.R.A. performed clinical interviews and cognitive testing. M.M. gathered behavioural data, and undertook the analysis of all data with the assistance of A.R.A. Author M. M. wrote the manuscript, with conceptual advice from D.S., A.R.A. and J.T.
Sample size:	N=41 participant with PTSD
Source of Trauma:	No specific trauma source described
Age/Sex:	Mean age: 43.4 years; 11 males, 30 females.
Comparison:	Participants raking propranolol (n=20): single dose of 1g/kg of propranolol. Every 30 minutes heart rate (HR) and blood pressure (BP) were monitored vs. Participants on placebo (n=21): single dose of 1g/kg o placebo. Every 30 minutes heart rate (HR) and blood pressure (BP) were monitored
Follow-up:	No mention of follow up.
Results:	Propanol group PS Index composite scaled scores is shown significant. (Propanol:23.40±6.26; Placebo: 17.69±4.76; t_{21}=2.49, p=021)
Conclusion:	"Our preliminary results demonstrated that cognitive functioning improved following pro- pranolol administration in PTSD patients. The implications are discussed with regards to the processing of traumatic events."
Comments:	Data suggest propranolol significantly improved processing speed in PTSD patient.

Author Year (Score):	**Pitman 2002 (score=3.5)**
Category:	Propranolol
Comments:	Data suggest propranolol may prevent some PTSD.

Prazosin (Minipress) is an alpha-1 adrenoreceptor antagonist that is an antihypertensive medication [503-506]. Prazosin has been used to treat PTSD [328, 504-515].

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

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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.

Evidence for the Use of Prazosin

Author Year (Score):	**Germain 2012 (Score=7.0)**
Category:	Prazosin
Study type:	RCT
Conflict of Interest:	Supported by National Institutes of Health, and Department of Defense Congressionally Directed Medical Research Program. No mention of COI.
Sample size:	N = 50 veterans with sleep disturbances.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 40.9±13.2 years; 45 males, 5 females.
Comparison:	Veterans with prazosin intervention (n=18) vs. veterans with behavioral sleep intervention (n=17) vs veterans with placebo (n=15).
Follow-up:	Follow-up at 4 months.
Results:	Insomnia severity reduced significantly in prazosin and BSI intervention groups measured by Insomnia Severity Index ($p<0.01$). Overall sleep quality and sleep disturbances were improved in three groups measured by PSQI-A ($p<0.01$), and by PSQI ($p<0.01$). No significant differences were found measured by CGI Scale.
Conclusion:	"BSI and prazosin were both associated with significant sleep improvements and reductions in daytime PTSD symptoms in this sample of military veterans."
Comments:	BSI better than prazosin for improved sleep. Data suggest both prazosin and BSI groups resulted in improved sleep disturbance as well as PTSD symptom severity.

Author Year (Score):	**Raskind 2013 (Score=6.5)**
Category:	Prazosin
Study type:	RCT
Conflict of Interest:	Supported by U.S. Army Medical Research and Material Command, NIH grant, and Department of Veterans Affairs. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N= 67 veterans returned from Iraq and Afghanistan.
Source of Trauma:	Iraq and Afghanistan Combat.
Age/Sex:	Mean age: 30.4 years; 57 males, 10 females.
Comparison:	Veterans assigned to prazosin intervention group (n=32) vs. placebo group (n=35).
Follow-up:	No mention of follow-up.

Results:	Prazosin group indicated better primary outcomes over placebo group. CAPS nightmare item score decreased differently between two groups: prazosin=3.1 vs. placebo=1.2 ($p<0.001$). PSQI endpoint scores differed from two groups: prazosin=5.6 vs. placebo= 2.8 ($p=0.003$).
Conclusion:	"Prazosin is effective for Combat related PTSD with trauma nightmares in active-duty soldiers, and benefits are clinically meaningful."
Comments:	Data suggest prazosin was significantly better for all 3 primary outcomes compared to placebo.

Author Year (Score):	**Simpson 2015 (Score=6.0)**
Category:	Prazosin
Study type:	RCT
Conflict of Interest:	Supported by NIA grant, Washington Center of Excellence in Substance Abuse Treatment and Education, and VA Puget Sound Health Care System. No mention of COI.
Sample size:	N=30 patients with comorbid PTSD and alcohol dependence.
Source of Trauma:	Alcohol assumption/ heavy drinking.
Age/Sex:	Mean age: 43.3 ±11.7 years; 19 males, 11 females.
Comparison:	Patients with prazosin intervention (n=15) vs. patients with placebo (n=15).
Follow-up:	Follow-up at 6 weeks.
Results:	In the 6^{th} week, prazosin group indicated greater decrease than placebo group in percent drinking days per week ($x^2(6) = 19.3$; $p=0.004$). Greater reduction for percent heavy drinking days per week showed in prazosin group ($x^2(6) =21.3$; $p=0.002$). In the 12^{th} week, prazosin group indicated lower mean percent of drinking days (M=13.0±14.7) than placebo group (M=46.1±25.4).
Conclusion:	"Consistent with the extant research evaluating medications for comorbid PTSD/AD, the current evaluation of prazosin also found decreased alcohol consumption but no medication effect on PTSD symptomatology."
Comments:	Data suggest prazosin may benefit those with PTSD and AD by decreasing number of heavy drinking days but did not improve PTSD symptoms.

Author Year (Score):	**Petrakis 2016 (Score=5.0)**
Category:	Prazosin
Study type:	RCT
Conflict of Interest:	Supported by the VISN I Mental Illness Research Education and Clinical Center, and the Department of Defense. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N=96 veterans with comorbid PTSD and alcohol dependence.
Source of Trauma:	Combat.
Age/Sex:	Mean age: 44 years; 90 males, 6 females.
Comparison:	Veterans assigned to prazosin intervention (n=50) vs. veterans assigned to placebo (n=46).
Follow-up:	No mention of specific follow-up time length.
Results:	Intervention time affect PTSD severity significantly ($p=0.00$), medication and model site had no effect. PSQI sleep quality index was affected significantly by time ($p=0.0001$). Time also decreased the average number of drinking during intervention ($p=0.0001$).

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Conclusion:	"Prazosin was not effective in treating PTSD symptoms, improving sleep, or reducing alcohol consumption overall in this dually diagnosed group."
Comments:	Lack of efficacy. Data suggest prazosin no better than placebo for improving PTSD symptoms nor improving sleep or reducing AD.

Author Year (Score):	**Khazaie, 2016 (Score=3.0)**
Category:	Prazosin
Comments:	Sparse methods. Data suggest lack of efficacy with no improvement in PTSD symptoms and/ or sleep disturbances.

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Guanfacine (Intuniv), a cognition-enhancing medication, is an α2-adrenergic receptor agonist that was previously used to treat hypertension [519, 520]. It has been used to treat attention deficit hyperactivity disorder (ADHD) in children and adolescents [521, 522] and PTSD [416, 519, 523].

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.

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Evidence for the Use of Guanfacine

Author Year (Score):	**Neylan 2006 (score=5.0)**
Category:	Guanfacine
Study type:	RCT
Conflict of Interest:	Supported by the VA Sierra Pacific Mental Illness Research, Education, and Clinical Center (MIRECC). One author receives research support from Pfizer and Forest Pharmaceuticals.
Sample size:	N = 63 healthy male and females veterans with chronic PTSD.
Source of Trauma:	Military Services
Age/Sex:	No mention of age or sex.
Comparison:	Group 1: participants received guanfacine (N =29) vs. Group 2: patients received placebo (N =34)
Follow-up:	Baseline, weeks 1, 2, 3, 4, 6, 8, 10, 12, 14.
Results:	Group 1, PTSD scale score, mean Impact Event Scale score, baseline vs final follow-up: 68.3 vs. 63.0 ($p<0.01$), 2.13 vs 1.78 ($p<0.001$). Group 1 vs Group 2: side effects dry mouth prevalence and light headed prevalence: 59% vs 15% ($p<0.001$) and 24% vs 3% ($p=0.019$).
Conclusion:	"[T]he effect size of zero suggests no promise for demonstrating efficacy, even with larger groups. Controlled studies are needed to determine if anti-adrenergic agents with other mechanisms of action hold greater promise for the treatment of chronic PTSD.
Comments:	Sparse methods. Data suggest lack of efficacy.

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Clonidine (Catapres) has been used to treat hypertension [355, 524-530], nightmares [529, 531, 532], opiate withdrawal [533, 534], and PTSD [530, 535].

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.

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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.

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Evidence for the Use of Doxazosin

Author Year (Score):	**Rodgman 2016 (score=5.0)**
Category:	Doxazosin
Study type:	RCT
Conflict of Interest:	Sponsored by grant from Michael E. DeBakey VA Medical Center and a grant from NIH. No COI.
Sample size:	N = 8 patients with PTSD
Source of Trauma:	Military
Age/Sex:	Mean age: 34.8±8.3 years; 8 males, 0 females.
Comparison:	Doxazosin: (n=8) received 4 mg/d of doxazosin every day and increased 4 mg/d every 4 days vs Placebo (n=7)
Follow-up:	None
Results:	$CAPS_{17}$ scores on treatment were $F_{1,13}$=0 (p=.992) and $F_{1,13}$=1.7 for time (p=.978).PCL-M scores were $F_{1,13}$=0 (p=.963) for treatment and $F_{1,13}$=6.33 on time (p=.026). Patients that received doxazosin rather than placebo had lower PCL-M scores.
Conclusion:	"Doxazosin XL may be an effective alternative to prazosin for the treatment of some PTSD symptoms."
Comments:	Pilot study with small sample. Data suggest doxazosin XL was associated with reductions in PCL-M scores over time.

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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.

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Evidence for the Use of Hydrocortisone

Author Year (Score):	**Yehuda 2015 (Score=6.5)**
Category:	Hydrocortisone
Study type:	RCT
Conflict of Interest:	Supported by the Lightfighters Trust Foundation. The authors declared no COI.
Sample size:	N = 24 military veterans with PTSD.
Source of Trauma:	War.
Age/Sex:	Mean age: 49.6 years; 24 males, 0 female.
Comparison:	Veterans received hydrocortisone intervention (n=12) vs veterans received placebo (n=12). All received treatment prior to prolonged exposure therapy sessions
Follow-up:	Follow-up at 6 weeks.
Results:	Veterans in hydrocortisone group showed significant change in CAPS total score (Cohen's d=0.43; 95%CI 0.78 to 0.05).
Conclusion:	"[H]ydrocortisone augmentation of PE may result in greater retention in treatment and thereby promote PTSD symptom improvement."
Comments:	Experimental study. High dropout rate in placebo group. Data suggest Hydrocortisone may stabilize HPA regulation negative feedback sensitivity maintained by the glucocorticoid receptor.

Author Year (Score):	**Delahanty 2013 (Score=5.0)**
Category:	Hydrocortisone
Study type:	RCT
Conflict of Interest:	Supports by the National Institute of Mental Health, and Ohio Board of Regents. The authors declared no COI.
Sample size:	N=64 patients with traumatic injury history with PTSD.
Source of Trauma:	Injury.
Age/Sex:	Mean age: 30.6±10.7 years; 42 males, 22 females.
Comparison:	Patients with hydrocortisone intervention (n=31) vs. patients with placebo (n=33).
Follow-up:	Follow-up at 1 and 3 months.
Results:	CAPS score indicated significant effect on time among intervention group (p=0.01). Fewer PTSD symptoms showed in hydrocortisone group (from 26.0±4.0 to 19.4±4.0) and placebo group (from 36.5±3.9 to 31.3±3.9).
Conclusion:	"Low-dose hydrocortisone may be a promising approach to the prevention of PTSD in acutely injured trauma patients, and may be particularly efficacious in acutely injured trauma victims without a history of significant psychopathology."
Comments:	Data suggest administration of hydrocortisone may reduce PTSD symptoms and depressive symptoms.

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Author Year (Score):	**Grossman 2006 (Score=4.5)**
Category:	Hydrocortisone
Study type:	Experimental crossover RCT
Conflict of Interest:	Supported by NIMH 1KO8MH01543-01A1, NIMH RO1MH49555, and NIH 5 M01 RR0071. No mention of COI.
Sample size:	N=27 subjects with medical health and off medication for more than three months.
Source of Trauma:	No mention of specific trauma source.
Age/Sex:	Age range: 20 to 55 years; 19 males, 8 females.
Comparison:	Patients with PTSD history (n=15) vs. comparison individuals (n=12).
Follow-up:	No mention of follow-up.
Results:	Verbal declarative memory indicated significant groups interactions (p=0.04). Working memory indicated significant groups interactions (p=0.022).
Conclusion:	"Heightened vulnerability of declarative memory in subjects with PTSD may indicate hippocampal involvement, whereas working memory vulnerability suggests additional brain regions (prefrontal, cingulate, temporal, and parietal cortices) and neurotransmitter systems (dopamine and serotonin) particularly sensitive to glucocorticoids in persons with PTSD."
Comments:	Experimental study. No short to long term followup. Data suggest individuals with PTSD have an increased sensitivity to glucocorticoids.

Author Year (Score):	**Gill 2011 (No score)**
Category:	Hydrocortisone
Study type:	Experimental study (non RCT)
Comments:	Data suggest PTSD may be distinguished from MDD with sustained elevated serum IL-6 levels.

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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.

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Evidence for the Use of Nutraceuticals

Author Year (Score):	**Kaplan 1996 (score=5.5)**
Category:	Nutraceuticals
Study type:	RCT crossover
Conflict of Interest:	No mention of COI or sponsorship.
Sample size:	N = 13 with PTSD who satisfied the DSM-III-R criteria
Source of Trauma:	Combat-related, accidents, physical assault, and other
Age/Sex:	Mean age: 39.7 years; 8 males, 5 females
Comparison:	Inositol group: received 12 grams (in powder form) per day/2 teaspoons twice a day in juice or tea, for four weeks (n=12) vs. Placebo group: same amount and instructions as treatment group, for four weeks (n=12). All patients received both treatments, with a 2 week washout period between treatments
Follow-up:	No follow-up post-intervention
Results:	Mean overall Impact of Event Scale (IES) scores at baseline and after 4 weeks of treatment, respectively: Inositol group – 35.8±14, 32.0±11, Placebo group – 34.9±12, 35.3±15. No significant difference found between treatment and placebo groups for IES overall score difference ($p > 0.05$).
Conclusion:	"This preliminary double-blind crossover study showed no effect of inositol on PTSD core symptoms of intrusion and avoidance."
Comments:	Small sample size. Data suggest lack of efficacy.

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Omega-3 fatty acids are a class of essential fatty acids contained within certain foods and have been used for treatment of PTSD. Omega-3 fatty acids can come in many different forms [554-566].

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.

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Author Year (Score):	**Matsumura 2016 (score=6.5)**
Category:	Omega-3 Fatty Acids
Study type:	RCT
Conflict of Interest:	No mention of sponsorship or COI.
Sample size:	N = 83 patients with PTSD who survived severe accident-related injuries.
Source of Trauma:	Accidents: motor vehicle, falling, work place.
Age/Sex:	Mean age: 39.3 years; 69 males, 14 females.
Comparison:	Omega-3: (n= 37) Patients took 300 mg x 7 capsules per day for 12 weeks. The daily dose of omega-3 PUFAs capsules contained 1470 mg DHA and 147 mg EPA. vs Placebo: (n= 46) patients took 300 mg x 7 capsules per day for 12 weeks. The placebo contained a daily dose of 987 mg rapeseed oil, 525 mg soybean oil, 525 mg olive oil, and 63 mg fish oil.
Follow-up:	3 months
Results:	For heart-rate, two-way ANOVA revealed a significant main effect of group($F[1,81]=4.36$, $p=.04$, $\eta_p^2 = .051$) but not period ($F[1,81]=0.01$, $p=.93$, $\eta_p^2=.000$), and group-x period interaction ($F[1,81]=2.24$, p.14, $\eta_p^2=.027$). for skin conductance two-way ANOVA revealed a significant main effect of period ($F[1, 81]=29.95$, $p<.001$, $\eta_p^2=.270$) but not group ($F[1,81]=0.15$, $p=.70$, $\eta_p^2=.002$), and group x period interaction ($F[1,81]= 2.08$, $p=.15$, $\eta_p^2=0.025$).
Conclusion:	"These findings suggest that post-trauma supplementation of omega-3 PUFAs might be effective for the secondary prevention of psychophysiological symptoms of PTSD."
Comments:	Population of mild PTSD individuals. Data suggest omega-3 polyunsaturated fatty acids lowered the heart rate at rest and during script-driven imagery.

Author Year (Score):	**Matsuoka 2015 (score=6.5)**
Category:	Omega-3 Fatty Acids
Study type:	RCT
Conflict of Interest:	Supported by CREST from the Japan Science and Technology Agency. Dr. Matsuoka has received research grants from the Japan Science and Technology Agency.; the National Center of Neurology and Psychiatry, Japan; and the Ministry of Health, Labour, and Welfare of Japan. He has been a paid speaker for Ono, Mochida, Takeda, Suntory Wellness, Otsuka and the DHA and EPA association. One or more of the authors have received or will receive benefits for personal or professional use.
Sample size:	N = 110 accident-injured patients.
Source of Trauma:	Accident-related.
Age/Sex:	Mean age: 39.6 years; 90 males, 20 females.
Comparison:	DHA: (n=53) patients received 1,470 mg/d of DHA plus 147 mg/d of eicosapentaenoic acid for 12 weeks. vs EPA: (n=57) patients received the placebo for 12 weeks.
Follow-up:	3 months
Results:	The effects of the intervention on Outcome Measures at 3 months: CAPS total mean score in DHA was 10.78 and in placebo was 9.22, Effects = 1.56, 95% CI, -3.90 to 7.01, =0.572. Full-blown PTSD: 2 (DHA), 1 (placebo), effects = 2.44, 95% CI 0.23-26.10, p=.459. Full-blown and partial PTSD: 5 (DHA), 3 (placebo), Effects = 2.04, 95% CI 0.52-8.07, p=0.311.

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Conclusion:	"Docosahexaenoic acid supplementation was not superior to placebo for the secondary prevention of PTSD symptoms at 3 months after sever accidental injury. The efficacy of a different ratio of DHA and EPA and higher doses of omega-3 fatty acids as secondary prevention of PTSD remains to be determined"
Comments:	Data suggest that at 3-months DHA was ineffective for secondary prevention of PTSD.

Marijuana has two major neuroactive phytocannabinoids: tetrahydrocannabinol (THC) and cannabidiol (CBD). THC has a euphoric and psychotomimetic effect, whereas CDB affects pain receptors [567-569].

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.

Author Year (Score):	**Jetly 2015 (score=5.0)**
Category:	Marijuana
Study type:	RCT crossover
Conflict of Interest:	No COI. Sponsored by the Canadian Forces Surgeon General's Health Research Program.
Sample size:	N = 10 Canadian military personnel with PTSD diagnosed following the DSM-IV-TR criteria, experiencing trauma-related nightmares despite undergoing standard treatment
Source of Trauma:	Combat
Age/Sex:	Mean age: 43.6 years; 10 males, 0 females.
Comparison:	Nabilone group: started at 0.5 mg dosage, titrated weekly to maximum of 3.0 mg, for 7 weeks (N = 10) vs. Placebo group, for 7 weeks (N = 9). 2 week wash out period between treatments. All subjects underwent both treatment except for one, who did not complete the second trial period due to being assigned a different location.
Follow-up:	No follow-up post intervention
Results:	Clinician-Administered PTSD Scale (CAPS) mean change from baseline scores – Nabilone group: -3.6, Placebo group: -1.0 (p = 0.03). Clinical Global Impression of Change (CGI-C) mean change from baseline scores – Nabilone group: 1.9, Placebo group: 3.2 (p = 0.05). General Well Being Questionnaire (WBQ) mean change from baseline scores – Nabilone group: 20.8, Placebo group: -0.4 (p = 0.04)
Conclusion:	"This study gives added support for the potential use of synthetic endocannabinoids, such as nabilone as a medication for treatment of PTSD-related nightmares. However, these findings need to be replicated in a larger cohort. There is a need for further exploration of the effect of nabilone on other symptoms of PTSD such as re-experiencing, hypervigilance and insomnia."
Comments:	Small sample size (n=10) with sparse methods. Although there is reported improvement in PTSD-associated nightmares, there were 50% treatment related adverse effects in the nabilone group and 60% in the placebo group.

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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**

ationale:	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,

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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.

Evidence for the Use of Transcranial Magnetic Stimulation (TMS)/Repetitive Magnetic Transcranial Stimulation

Author Year (Score):	**Isserles 2012 (score=6.5)**
Category:	Transcranial Magnetic Stimulation
Study type:	RCT
Conflict of Interest:	Dr. Isserles receives financial support from Brainsway, Inc., which developed the H-coils and supported this study. Prof. Zangen and Dr. Roth are key-inventors of the H-coils, own equity in Brainsway, Inc and receive financial support from this company. E. Zlotnick received financial support from Brainsway, Inc. No COI.
Sample size:	N= 30 patients with PTSD
Source of Trauma:	No mention of trauma source.
Age/Sex:	Mean age:44.5 years; 20 males, 6 females
Comparison:	Group A: received Deep Transcranial Magnetic Stimulation 3 weekly 20-min sessions for 4 weeks after brief exposure to the traumatic event with the script-driven imagery Procedure (n=9) vs. Group B: received 3 weekly 20-min sessions for 4 weeks of DTMS after brief exposure to a non-traumatic event (n=8) vs. Group C: received 3 weekly 20-min sessions for 4 weeks of sham stimulation after brief exposure to the traumatic event (n=9)
Follow-up:	Follow up: 2 weeks and 2 months
Results:	Significant improvement was demonstrated in the intrusive component of the Clinician-Administered PTSD Scale (CAPS scale) in patients administered DTMS after exposure to the traumatic event script, while patients in the control groups showed no significant improvement. Similar trend was demonstrated in the Total-CAPS score as in the other rating scales. A significant reduction in the HR response to the traumatic script was evident in group A, further supporting the above results.
Conclusion:	"Combining brief script-driven exposure with DTMS can induce therapeutic effects in PTSD patients. A wide multi-center study is suggested to substantiate these findings."
Comments:	Pilot study. Suggest DTMS may be beneficial for fear extinction in PTSD patients but larger studies need to substantiate this.

Author Year (Score):	**Watts 2012 (score=6.5)**
Category:	rTranscranial Magnetic Stimulation
Study type:	RCT
Conflict of Interest:	Supported by funding from the Hitchcock Foundation. No mention of COI.
Sample size:	N= 20 subjects with PTSD
Source of Trauma:	Military Service, Assault, Motor vehicle accidents, or combination of multiple.
Age/Sex:	Mean age: 55.5 years; 2 females, 18 males.
Comparison:	Group 1: (n=10) received 10 rTMS sessions delivered at 1 Hz to the right dorsolateral prefrontal cortex (DLPRC) Vs. Group 2: (n=10) received 10 sham rTMS sessions to the same area.
Follow-up:	Follow up: 2 months
Results:	Transcranial magnetic stimulation delivered at 1 Hz to the right DLPRC resulted in statistically and clinically significant improvements in core PTSD symptoms and depressive symptoms compared with sham treatments. The effectiveness showed some degradation during the 2 months after treatments were stopped.
Conclusion:	"In summary, this blinded sham controlled trial of 10 sessions of 1 Hz rTMS delivered to the right DLPRC showed that patients with PTSD demonstrate therapeutic effects for PTSD greater than sham rTMS to the same region. This was a small pilot study that supports the growing evidence for the effectiveness of rTMS for the treatment of PTSD."
Comments:	Small sample. Data suggest rTMS improved PTSD symptoms for 2 months.

Author Year (Score):	**Nam 2013 (score=6.0)**
Category:	rTranscranial Magnetic Stimulation
Study type:	RCT
Conflict of Interest:	Supported by grant of Korean Research Foundation (2012-0006579) and Seoul R&BD Program (SS110008). No mention of COI
Sample size:	N= 18 patients with PTSD
Source of Trauma:	Physical assault, motor vehicle accidents, and domestic violence.
Age/Sex:	Mean age: 37 years; 6 males, 10 females.
Comparison:	Active Group: received 3 weeks of 20-min per weekday (total of 15 treatment days) sessions of 1-Hz low-frequency rTMS group (n=9) Vs. Sham group: received identical rTMS treatment except lateral wing of coil was raised 90° off head and edge of coil still touching scalp for 3 weeks of 20 min per weekday sessions (15 total treatments) (n=7)
Follow-up:	Assessments done at baseline and at 2, 4, and 8 weeks
Results:	All Clinician-Administered PTSD Scale (CAPS) scores improved significantly over the study period. We found significant differences in the re-experiencing scores (F=7.47, p=0.004) and total scores (F=6.45, p=0.008) on the CAPS. The CAPS avoidance scores showed a trend toward significance (F=2.74, p=0.055), but no significant differences in the CAPS hyperarousal scores were observed.
Conclusion:	"The present study showed low-frequency rTMS to be an effective and tolerable option for the treatment of PTSD. Trials using variable indices of rTMS to the right prefrontal cortex and explorations of the differences in the effects on specific symptom

	clusters may be promising avenues of research regarding the use of rTMS for PTSD."
Comments:	Small sample (n=18). Data suggest low frequency rTMS showed efficacy versus sham for PTSD symptoms.

Author Year (Score):	**Boggio 2010 (score=6.0)**
Category:	rTranscranial Magnetic Stimulation
Study type:	RCT
Conflict of Interest:	Supported by a grant from Northstar Neuroscience. No mention of COI.
Sample size:	N = 30 patients
Source of Trauma:	Sexual and non-sexual assault, death of relative, feeling of impending doom.
Age/Sex:	Mean age: 44.5±4.4 years; 9 males, 21 females.
Comparison:	Active Right Group: received 10 active TMS treatments, 5 days per week for two weeks, right side of scalp (n= 10) vs Active Left Group: received 10 active TMS treatments, 5 days per week for two weeks, left side of scalp (n=10) vs Sham: received 10 sham rTMS treatments with no actual magnetic stimulation released from coil (n=10)
Follow-up:	Follow up was 3 months
Results:	Results show that both active conditions—20 Hz rTMS of left and right DLPFC— induced a significant decrease in PTSD symptoms as indexed by the PTSD Checklist and Treatment Outcome PTSD Scale; however, right rTMS induced a larger effect as compared to left rTMS. In addition, there was a significant improvement of mood after left rTMS and a significant reduction of anxiety following right rTMS. Improvements in PTSD symptoms were long lasting; effects were still significant at the 3-month follow-up. Finally, neuropsychological evaluation showed that active 20 Hz rTMS is not associated with cognitive worsening and is safe for use in patients with PTSD.
Conclusion:	"These results support the notion that modulation of prefrontal cortex can alleviate the core symptoms of PTSD and suggest that high-frequency rTMS of right DLPFC might be the optimal treatment strategy."
Comments:	Small sample. Data suggest rTMS may be beneficial for reducing PTSD symptoms with right rTMS showing more efficacy than left rTMS.

Author Year (Score):	**George 2014 (score=5.0)**
Category:	rTranscranial Magnetic Stimulation
Study type:	RCT
Conflict of Interest:	Supported by U.S. Army Medical Research and Materiel Command. No COI.
Sample size:	N = 41 patients
Source of Trauma:	Suicide attempt
Age/Sex:	Mean age: 42.5± 15.7; 35 males, 6 females.
Comparison:	Active Group: received 10 Hz of rTMS for 5 sec train, 10 sec intertrain intervals for 30 min sessions 3 times daily for 3 days (n=20) Vs. Sham: received sham rTMS that used a metal insert to block magnetic field and electrodes on the scalp to deliver matched somatosensory sensation (n=21)
Follow-up:	Follow up for 6 months.

Results:	From the mITT analyses, SSI scores declined rapidly over the 3 days for both groups (sham change -15.3 points, active change -15.4 points), with a trend for more rapid decline on the first day with active rTMS (sham change -6.4 points, active -10.7 points, P = 0.12). This decline was more pronounced in the completers subgroup [sham change -5.9 (95% CI: -10.1, -1.7), active -13 points (95% CI: -18.7, -7.4); P = 0.054]. Subjective ratings of 'being bothered by thoughts of suicide' declined non-significantly more with active rTMS than with sham at the end of 9 sessions of treatment in the mITT analysis [sham change -31.9 (95% CI: -41.7, -22.0), active change -42.5 (95% CI: -53.8, -31.2); P = 0.17].
Conclusion:	"Delivering high doses of left prefrontal rTMS over three days (54,000 stimuli) to suicidal inpatients is possible and safe, with few side effects and no worsening of suicidal thinking. The suggestions of a rapid anti-suicide effect (day 1 SSI data, Visual Analogue Scale data over the 3 days) need to be tested for replication in a larger sample."
Comments:	Pilot study. 3 day trial only suggesting high dose of rTMS is safe for suicidal inpatients.

Author Year (Score):	**Cohen 2004 (score=5.0)**
Category:	rTranscranial Magnetic Stimulation
Study type:	RCT
Conflict of Interest:	Supported by a grant from the Israel Defense Force. No mention of COI.
Sample size:	N = 24 patients with PTSD
Source of Trauma:	Included: military service, motor vehicle accident, sexual and nonsexual assault, death of relative, work accidents.
Age/Sex:	Mean age: 41.8 years; 17 males, 7 females.
Comparison:	Group 1: (n=6) Sham rTMS received 20 min treatments over 10 work days Vs. Group 2: (n=8) received slow frequency rTMS (1Hz per 5 seconds of train) Vs. Group 3: received high frequency rTMS (10 Hz per 2 seconds of train)(n=10)
Follow-up:	Follow up 14 days after the end of treatment
Results:	The 10 daily treatments of 10- Hz rTMS at 80% motor threshold over the right dorsolateral prefrontal cortex had therapeutic effects on PTSD patients. PTSD core symptoms (re-experiencing, avoidance) markedly improved with this treatment. Moreover, high-frequency rTMS over the right dorsolateral prefrontal cortex alleviated anxiety symptoms in PTSD patients.
Conclusion:	"This double-blind, controlled trial suggests that in PTSD patients, 10 daily sessions of right dorsolateral prefrontal rTMS at a frequency of 10 Hz have greater therapeutic effects than slow-frequency or sham stimulation."
Comments:	Short term trial (2 weeks). Data suggest rTMS at 10 Hz improved core PTSD symptoms.

Author Year (Score):	**Rosenberg 2002 (score=3.0)**
Category:	rTranscranial Magnetic Stimulation
Comments:	No blinding. No sham. Small sample open label trial. Antidepressant use was uncontrolled and variable. Short treatment time – only 10 days. Data suggest possible benefit of rTMS for depression, insomnia, anxiety and hostility but core PTSD symptoms improved minimally if at all. Results sustained for 2 months in 9/12 completers for depression.

Deep brain stimulation involves the implantation of a medical device (neurostimulator) to provide high-frequency electrical stimulation of subcortical structures, mainly the amygdala and ventral capsule [592-598]. Deep brain stimulation has been used for Parkinson disease [599], highly resistant obsessive-compulsive disorder [600], depression [601, 602], and PTSD [594, 603-607].

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.

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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.

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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.

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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.

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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.

Evidence for the Use of Acupuncture

Author Year (Score):	**Engel 2014 (score=7.0)**
Category:	Acupuncture
Study type:	RCT
Conflict of Interest:	Sponsored by the Uniformed Services University of the Health Sciences (USUHS) under Award No. MDA905-03-C-0003. No COI. No COI.
Sample size:	N = 55 active duty military personnel with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 34.8 years; 38 males, 17 females.
Comparison:	Acupuncture (n=28) Patients received usual PTSD care plus eight 60-minute sessions of acupuncture conducted twice weekly. Vs. Usual PTSD Care (n=27) Patients received the usual PTSD care only.
Follow-up:	4, 8, and 12 weeks.
Results:	Statistically significant differences favoring acupuncture were found between the 2 treatment groups for the primary outcome, PCL ($w^{2/3}$ =97.8, P < 0.0001), and for CAPS ($w^{2/3}$ =9.2, P < 0.05). Mean PCL score significantly decreased in the acupuncture with UPC group at 4 weeks (58.1 ± 11.4 vs. 38.8 ± 11.6; t_{241} = 13.4, P< 0.0001), at 8 weeks (37.8 ± 15.0; t_{153}=11.0, P< 0.0001) and 12 weeks (37.7 ± 15.9; t_{158}=10.5, P< 0.0001).
Conclusion:	"Acupuncture was effective for reducing PTSD symptoms. Limitations included small sample size and inability to parse specific treatment mechanisms. Larger multisite trials with longer follow-up, comparisons to standard PTSD treatments, and

	assessments of treatment acceptability are needed. Acupuncture is a novel therapeutic option that may help to improve population reach of PTSD treatment."
Comments:	Usual care bias. Data suggest improved PTSD symptoms severity in acupuncture group.
Author Year (Score):	**Prisco 2013 (score=4.5)**
Category:	Acupuncture
Study type:	RCT
Conflict of Interest:	No COI. Sponsored by a grant from the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development, NRI-08-121.
Sample size:	N = 35 veterans with PTSD.
Source of Trauma:	Combat-related.
Age/Sex:	Mean age: 37.8 years; 25 males, 10 females.
Comparison:	True acupuncture (n=8) participants were offered two true acupuncture treatments per week for 18 consecutive weeks for a total of 16 treatments. Vs Sham acupuncture (n=8) participants were offered two sham acupuncture treatments per week for 18 consecutive weeks for a total of 16 treatments. Vs. Wait-list control (n=9) participants received conventional care.
Follow-up:	1 and 2 months.
Results:	Subjects in the true auricular acupuncture group had a statistically significant improvement (p = 0.0165) in sleep quality as measured by the ISI at time (t) = 1 month. This group had a trend toward lower MSD TST at t = 2 months (p = 0.078), lower WA TST at t = 1 month (p = 0.0893), and toward higher MSD nap times than the other two groups post-treatment (p = 0.0666).
Conclusion:	"Acupuncturists should consider incorporating sleep hygiene education into their clinical practices and/or collaborate with insomnia health care professionals when working with individuals with insomnia. This study also supports the finding that perceived sleep quality and objective WA measurements are not significantly correlated."
Comments:	Waitlist control bias, however had sham group. Auricular acupuncture. Small sample sizes. Data show inconsistent results between groups and over time.

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

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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

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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

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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

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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?

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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

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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

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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

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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

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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)

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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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