Post-traumatic Stress Disorder

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KEYWORDS

• Post-traumatic stress disorder • Trauma • Psychiatry • Psychotherapy
• Pharmacotherapy • Assessment

KEY POINTS

- Post-traumatic stress disorder (PTSD) assessment, whether by structured interviews like the CAPS-5 (Clinician-Administered PTSD Scale for DSM-5 [Diagnostic and Statistical Manual of Mental Disorders, 5th edition]) in psychiatric settings or the PCL-5 (PTSD Checklist for DSM-5) in nonpsychiatric settings, is vital for the diagnosis of PTSD to ensure its treatment.
- Evidence-based psychotherapy is the first-line treatment for PTSD.
- Prolonged exposure, cognitive processing therapy, and eye movement desensitization and reprocessing are the forms of psychotherapy with the best evidence for treating PTSD and are recommended by numerous PTSD treatment guidelines.
- Pharmacotherapy is common in clinical practice and often used to reduce overall PTSD severity or target specific symptoms (eg, insomnia).
- The serotonin reuptake inhibiting antidepressants, particularly the US Food and Drug Administration-approved medications sertraline and paroxetine, are the most highly validated pharmacotherapies for PTSD.

POST-TRAUMATIC STRESS DISORDER

Post-traumatic stress disorder (PTSD) is a psychiatric disorder characterized by the development of intrusive symptoms, avoidance of trauma-related cues, negative alterations in cognition and mood, and marked alterations in arousal and reactivity following exposure to a traumatic event (**Table 1**).[1] In a national sample of more than 36,000 US adults, the past-year prevalence of PTSD was 4.7%, and lifetime prevalence was 6.1%.[2] Several sociodemographic characteristics, including younger age, female gender, and lower education and income were associated with higher rates of PTSD.

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Table 1
Criteria of post-traumatic stress disorder

Trauma Exposure	Intrusions	Avoidance	Negative Alterations in Cognitions and Mood	Alterations in Arousal and Reactivity	Other
Actual or threatened death, serious injury, or sexual violence in 1 (or more) of the following ways: 1. Directly experiencing the traumatic event 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 4. Experiencing repeated or extreme exposure to aversive details of the traumatic events	1. Recurrently, involuntary, and intrusive distressing memories of the traumatic event(s) 2. Recurrent distressing dreams in which the content and/or affect of the dream are related to the traumatic event(s) 3. Dissociative reactions in which the individual feels or acts as if the traumatic event(s) were reoccurring 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 physiologic reactions to internal or external cues that symbolize or resemble an aspect of the traumatic event(s)	Persistent avoidance of stimuli associated with the traumatic event(s), as evidenced by 1. Avoidance of or efforts to avoid distressing memories, thoughts, or feelings about or closely associated with the traumatic events(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)	1. Inability to remember an important aspect of the traumatic event(s) 2. Persistent and exaggerated negative beliefs or expectations about oneself, others, or the world 3. Persistent, distorted cognitions about the cause or consequences of the traumatic event(s) that lead the individual to blame themselves or others 4. Persistent negative emotional state 5. Markedly diminished interest or participation I significant activities 6. Feelings of detachment or estrangement from others 7. Persistent inability to experience positive emotions	1. Irritable behavior or angry outbursts 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	1. Duration of symptoms is more than 1 month 2. Disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning 3. Disturbance is not attributable to the physiologic effects of a substance or another medical condition

Data from American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders DSM-5 Fifth Edition*. 5th ed. American Psychiatric Association Publishing; 2013. Accessed May 7, 2020. https://www.appi.org/Products/DSM-Library/Diagnostic-and-Statistical-Manual-of-Mental-Disord?sku=2554.

Assessment of Trauma Exposure and Post-traumatic Stress Disorder

There are several measures that can be used to assess exposure to potentially traumatic events and PTSD symptoms in various settings (**Table 2** for the gold-standard measures). The LEC-5 (Life Events Checklist for DSM-5 [Diagnostic and Statistical Manual for Mental Disorders, 5th edition]) is a self-report screening measure for exposure to 16 potentially traumatic events (PTEs) and a different event not listed. It was developed to be administered before the CAPS-5 (Clinician-Administered PTSD Scale for DSM-5) to evaluate exposure to PTEs.[3]

The gold standard of assessing PTSD is the CAPS-5.[4] The CAPS-5 is an in-depth structured diagnostic clinical interview that assesses individual symptoms of PTSD and diagnostic status. Given the scope of assessment, this is a time-intensive instrument, and administration typically takes between 45 and 60 minutes; as such, it is unlikely that it would be administered outside of specialty psychiatric settings.

The PTSD Checklist for DSM-5 (PCL-5) is a 20-item self-report measure that assesses DSM-5 PTSD symptoms.[5] The PCL-5 takes approximately 5 to 10 minutes to complete, making it easier to administer in nonpsychiatric settings where time is limited.

The Primary Care PTSD Screen for DSM-5 (PC-PTSD-5)[6] is a 6-item assessment of exposure to PTEs and PTSD symptoms that is more suitable for time-limited primary care settings. A cut-score of 3 indicates a positive PTSD screen and was determined to maximize quality of sensitivity and specificity.[6,7]

Psychotherapies for Post-Traumatic Stress Disorder

Current treatment guidelines recommend 3 front-line trauma-focused treatments—prolonged exposure (PE), cognitive processing therapy (PE), and eye movement desensitization and reprocessing (EMDR); there is currently insufficient evidence supporting preventive interventions (**Table 3**).[8–10]

Prolonged exposure

PE was developed by Edna Foa, and is a manualized, 8- to 15-session treatment with 90-minute sessions. PE targets avoidance as the symptom that prevents recovery, through helping the client engage in activities they have been avoiding because of trauma and repeated exposure to traumatic memories. PE is one of the most studied treatments for PTSD, with over 20 randomized controlled trials (RCTs).[11] Meta-analytic findings of RCTs and comparing with wait-list control conditions have found that it yields large treatment effect size reductions in PTSD symptoms and loss of diagnosis.[12]

Cognitive processing therapy

CPT was developed by Patricia Resick. and is a manualized, 12-session treatment with 60-miuten sessions. It focuses on addressing cognitive symptoms associated with PTSD that maintain avoidance of negative affect. Like PE, CPT is a rigorously studied treatment, with over 20 RCTs across various traumas, populations, and countries.[11] Meta-analyses assessing RCTs compared with wait-list control conditions and treatment as usual (TAU) have found that CPT yields large effect size reductions in PTSD symptoms and loss of diagnosis.[12,13]

Eye movement desensitization and reprocessing

EMDR[14] was developed by Francine Shapiro., and is typically administered in weekly sessions of up to 90 minutes over the course of 3 months, although length of treatment varies based on the needs of the individual.[15] It focuses on reducing the intensity of traumatic memories through eye movements; however, this mechanism is the ongoing

Table 2
Assessment of potentially traumatic events and post-traumatic stress disorder

Instrument	Type	Usage	Versions	Psychometrics
Life Events Checklist for DSM-5 (LEC-5)[3]	Self-report	To be administered before the CAPS-5 to evaluate exposure to PTEs[3]	Three versions: 1. To determine if an event occurred 2. To determine the worst event for those with multiple exposures to PTEs 3. An interview to establish if a PTE meets the criterion necessary for a diagnosis of PTSD	In various samples, including combat veterans and college students, displayed temporal stability, convergent validity, and predicted distress and PTSD symptoms[3]
CAPS-5[4]	Structured diagnostic interview[4]	Assesses PTSD diagnostic status and symptom severity, including assessment of all PTSD criteria; assessment of the dissociative subtype; and global ratings of distress, impairment, and symptom severity that has been developed for the current diagnostic criteria for PTSD in the DSM-5	One version, which takes approximately 45–60 min, designed to be administered by trained clinicians, clinical researchers, and paraprofessionals	Extensive research in a variety of samples, demonstrating strong internal consistency, interrater reliability, and test-retest reliability, while additionally being strongly correlated with other measures of PTSD[4]
PCL-5[5]	Self-report	Screening individuals for PTSD, making a provisional diagnosis, and monitoring change during and after treatment	4 versions: 1. Past month 2. Past week 3. With PTE assessment 4. With LEC-5 and PTE assessment	Extensive validation research in a variety of military and civilian samples, displaying high internal consistency, test-retest reliability, and convergent and discriminant reliability[5,62,63]
Primary Care PTSD Screen for DSM-5 (PC-PTSD-5)[6]	Self-report	Screening trauma exposure and PTSD symptoms in time-limited primary care settings	One version with 6 yes/no items	Validation done to create a cut-score of 3 to maximize quality of sensitivity and specificity[6,7]

Table 3
Summary of evidence of psychotherapies for the prevention and treatment of PTSD

Indication	Psychotherapy	Description	VA/DoD Guidelines (2017)[10]	APA Guidelines (2017)[c,64]	NICE Guidelines (2018)[9]	ISTSS Guidelines (2020)[8]
Prevention	Psychological first aid	Early psychosocial intervention applied during or immediately after a trauma that focuses on determining the basic physical and mental needs of an individual[65]	NA	NA	NA	Insufficient evidence
	Critical incident stress debriefing	Individual or group treatment provided hours or days after the trauma that focuses on emotional ventilation, trauma processing, and psychoeducation[66]	Not recommended, harmful	NA	Not recommended, harmful	Insufficient evidence
Treatment	Prolonged exposure	Teaches individuals to gradually approach trauma-related memories, feelings, and situations, leading to reduced avoidance and decreased PTSD symptoms[67]	High quality of evidence	High quality of evidence	High quality of evidence	High quality of evidence
	Cognitive processing therapy	Teaches individuals who to challenge and modify unhelpful beliefs related to the trauma to create new understandings of the trauma, which reduce its impact on daily life[68]	High quality of evidence	High quality of evidence	High quality of evidence	High quality of evidence
	Eye movement desensitization and reprocessing	Processes the memories of traumatic experiences that contain disturbing emotions, thoughts, beliefs, and physical sensations, thus reducing and eliminating symptoms[43,69,70]	High quality of evidence	Moderate rating of evidence	High quality of evidence	High quality of evidence

Abbreviations: DoD, department of defense; ISTSS, international society for traumatic stress studies; NICE, national institute for health and care excellence; PTSD, posttraumatic stress disorder; VA, Veterans Health Administration.

subject of scientific debate.[16] EMDR has been increasingly researched, with over 40 trials assessed in 1 meta-analysis.[16] EMDR has been found to have a strong evidence of effect for treating PTSD.[17,18]

Overall, when it comes to the treatment of PTSD, there is evidence that the treatments with the strongest support are PE and CPT.[17] However, meta-analyses have also found that there is not strong evidence for unequivocal superiority of any particular intervention, indicating that what is important is that affected individuals receive treatment.[19]

Special Group Considerations

When screening and working with individuals with PTSD, there are special group considerations. Women tend to develop PTSD at higher rates compared with men, which is partially accounted for by the high rates of sexual assault that women experience, as sexual assault carries a higher risk of developing PTSD than most other traumas.[20] Veterans are another group with higher rates of PTSD relative to the general population, largely owing to military service-related trauma exposures, with a meta-analysis of PTSD prevalence in the post-9/11 era finding the average prevalence PTSD across 33 studies was 23%.[21]

Minoritized groups, such as refugees, racial/ethnic minorities, and lesbian, gay, bisexual, transgender (LGBT+) people are also at increased risk for PTSD. Refugees are a heterogenous group, with much variation in experiences, such that research has found varying prevalence rates of PTSD within various refugee populations; however, a meta-analysis of 66 articles with 150 prevalence estimates found the prevalence of PTSD in refugees settled in high income countries was 34%.[22] Additionally, refugee populations often experience multiple traumas, including torture, combat, and being close to death.[23] Refugee populations may also have different cultural expressions of psychological distress (eg, increased somatization), which may challenge the assessment and treatment of PTSD.

Certain racial/ethnic minority groups and LGBT + individuals have also been found to have increased risk of PTSD. For example, a study of the general US adult population using the current diagnostic criteria for PTSD, Native Americans had significantly elevated odds of PTSD relative to non-Hispanic whites.[2] In research on specific populations (eg, veterans and 9/11 responders), the prevalence or conditional risk of PTSD was higher among Black/African-American and Latinx/Hispanic individuals.[24–28] Further, among both men and women, those who identify as lesbian/gay or bisexual had higher prevalence of PTSD relative to those who identified as heterosexual.[29] The increased prevalence of PTSD has been found to be associated with different trauma exposures, such that there is greater exposure to types of trauma (eg, interpersonal violence) that carry a greater risk of PTSD,[26,28,29,30,31] and with racial discrimination, which has been found to compromise trauma recovery and be associated with greater severity of PTSD symptoms.[32,33]

Considerations for Pharmacologic Prevention Efforts of Post-Traumatic Stress Disorder

In the first hours and days after a traumatic experience, many individuals report symptoms of acute stress, including increased arousal, insomnia, and agitation.[34] While benzodiazepines (BZDs) are effective in reducing these symptoms, they are ineffective for the prevention of PTSD.[35] Patients newly prescribed with BZDs should be informed about the potential of dependence and carefully monitored. Evidence for other pharmacologic agents, including beta-blockers, opiates, and hydrocortisone, for the prevention of PTSD in the aftermath of a traumatic experience is scarce and of low quality.[36]

Pharmacotherapies for Post-Traumatic Stress Disorder

Treatment guidelines

Most guidelines for the treatment of PTSD, including the VA/DoD,[10] NICE,[9] and Australian guidelines,[37] recommend psychotherapy as first-line treatment and pharmacotherapies only as second-line treatments. This recommendation is based on reviews and meta-analyses showing that pharmacotherapies are less effective than trauma-focused psychotherapeutic interventions in reducing PTSD severity.[18,38,39] However, different groups of patients may be attracted to psychotherapy and pharmacotherapy studies. Also, psychotherapy studies often report higher dropout rates than pharmacotherapy studies. Further, meta-analyses comparing psychotherapy and pharmacotherapy studies often neglect important study design differences between these studies. First, there is no way to hide from therapists and their patients whether the active or placebo psychotherapy is being administered. Second, randomized controlled trials (RCTs) investigating the effectiveness of psychotherapeutic interventions often compare the active treatment against a waitlist condition, in which participants receive no treatment at all. In RCTs testing pharmacologic agents, usually both, the active medication and the placebo group, are often provided with TAU, which can include psychotherapy. Hence, such studies usually report a smaller difference between the 2 investigated conditions.[40] In accordance, 1 landmark study with a head-to-head design found equal efficacy of psychopharmacotherapy, psychotherapy, and the combination of both.[41]

With regard to monotherapy, the highest quality and largest amount of evidence exists for the efficacy of sertraline, paroxetine, fluoxetine (all 3 selective serotonin reuptake inhibitors [SSRIs][a]) and venlafaxine extended release (serotonin norepinephrine reuptake inhibitor [SNRI][b]).[38,39] Based on the mechanism of action of these medications, the whole class of SSRIs can be assumed to be effective.[42] The SSRI and SNRI medications essentially displaced older antidepressants shown to have efficacy for PTSD , the tricyclic antidepressants and monoamine oxidase inhibitors, because of their superior safety and tolerability profiles. However, a tricyclic showed similar efficacy to an SSRI in a head-to-head comparison, suggesting the older medications might be underutilized in patients resistant to the new medications.[43] In addition, the efficacy of quetiapine, an atypical antipsychotic, has been documented also.[44] However, because of its adverse effect profile and lack of additional evidence, its role as a monotherapeutic agent is debated among experts (also see **Table 4**).[8]

Clinical practice

In clinical practice, pharmacotherapy is common for individuals with PTSD.[45,46] For example, in a cohort of more than 700,000 veterans diagnosed with PTSD, the mean number of psychotropic medications prescribed was 3.5 (standard deviation [SD] = 2.7). More than 80% of these veterans received an antidepressant; more than 20% received an atypical antipsychotic agent, and almost 40% were prescribed a sedative hypnotic.[45,47] There are multiple reasons why pharmacotherapy is common among individuals with PTSD. The severity of PTSD symptoms often negatively impacts psychological and daily functioning, requiring pharmacologic stabilization. Importantly, the participation in trauma-focused treatments requires individual to be psychologically stable, which can sometimes only be achieved with pharmacologic treatment. Moreover, even the best currently available psychotherapeutic interventions have limited effectiveness and a relatively high drop-out rate.[48] Thus, psychological treatments alone are often not sufficient to manage symptoms of PTSD, and many individuals therefore receive additional pharmacologic treatment. Such treatment aims to decrease overall severity of PTSD symptoms, or target specific symptoms

Table 4
Summary of evidence for pharmacotherapy for the prevention and treatment of post-traumatic stress disorder

Indication	Drug	FDA Approved	VA/DOD Guidelines (2017)[10]	APA Guidelines (2017)[c,64]	NICE Guidelines (2018)[9]	ISTSS Guidelines (2020)[8]
Prevention	Hydrocortisone	-	Insufficient evidence	NA	-	+ (weak)
	Benzodiazepines[a]	-	Insufficient evidence	NA	-	NA
	Propranolol	-	Insufficient evidence	NA	-	Insufficient evidence
Monotherapy	Sertraline	+	+	+	+	+
	Paroxetine	+	+	+	+	+
	Fluoxetine	-	+	+	+	+
	Venlafaxine	-	+	+	+	+
	Quetiapine	-	-	NA	NA	+ (weak)
	Risperidone	-	-	Insufficient evidence	NA	NA
	Topiramate	-	-	Insufficient evidence	NA	Insufficient evidence
	Other SSRIs[a]		Insufficient evidence	NA	+	NA
	Tricyclic antidepressants[a]	-	+ weak[d]	NA	NA	Insufficient evidence
Augmentation	Quetiapine	-	NA	NA	NA	NA
	Risperidone	-	-	NA	NA	+
	Prazosin[b]	-	Insufficient evidence	NA	NA	+

Note. +, recommendation for; -, recommendation against; NA, not addressed.
[a] Class of medications.
[b] For nightmares.
[c] Update ongoing.
[d] Weak recommendation for imipramine and amitriptyline only. Please add the following citation as reference 71: Davidson J, Kudler H, Smith R, Mahorney SL, Lipper S, Hammett E, Saunders WB, Cavenar JO Jr. Treatment of posttraumatic stress disorder with amitriptyline and placebo. Arch Gen Psychiatry. 1990 Mar;47(3):259-66. doi: 10.1001/archpsyc.1990.01810150059010. PMID: 2407208.

(eg, insomnia, agitation) or common comorbidities. Although SSRIs are the first-line treatment for the former, numerous agents can be used for the two latter.

Comorbidity Considerations

PTSD is often comorbid with other conditions,[2] including substance use disorder (SUD), borderline personality disorder (BPD), and insomnia. Given the high levels of comorbidities in individuals with PTSD, treatments that address PTSD and common comorbid conditions have been developed.

SUD is highly comorbid with PTSD, with up to 65% of patients with PTSD have been found to have a comorbid SUD.[49] SUD can be addressed with psychological and pharmacologic treatments. Although there are well-established pharmacologic treatments for PTSD and alcohol use disorder (AUD), evidence regarding treatment for co-occurring PTSD and AUD is limited and generally mixed. This is the case for agents commonly prescribed for either of the 2 conditions (eg, SSRIs or naltrexone) or hypothesized to be beneficial when both conditions co-occur (eg, zonisamide).[50,51] However, the combination of established treatments for PTSD and AUD is mostly well-tolerated and should be considered in clinical practice even in absence of strong evidence.[50] Evidence regarding treatment of PTSD and opioid use disorder (OUD) is even more scarce and mostly limited to retrospective studies.[52] Hence, clinical management often includes the combination of pharmacologic treatments established for PTSD or OUD and should be guided by clinical experience. With regard to psychological treatments, Concurrent Treatment of PTSD and Substance Use Disorder Using Prolonged Exposure (COPE) was developed for treatment of these comorbidities and consists of integrated cognitive-behavioral relapse prevention skills with PE. COPE has been found to significantly reduce PTSD symptom severity compared with TAU and to treat SUD at comparable levels to TAU in an RCT of SUD treatment-seeking participants.[49] Similarly, in an RCT of treatment-seeking veterans, COPE reduced PTSD symptoms and increased PTSD remission compared with an integrated coping skills treatment and decreased substance use equivalently to the coping skills treatment.[53] Overall, COPE has been found to be a feasible, safe, and efficacious treatment for comorbid PTSD and SUD.[49,53]

Dialectical Behavior Therapy-Prolonged Exposure (DBT-PE) was developed to treat those with comorbid PTSD and BPD, as those with PTSD have high odds of also having lifetime (odds ratio [OR] = 2.8) and past-year BPD (OR = 3.3).[2] DBT is a treatment that was developed to treat those with BPD.[54] DBT-PE combined the 2 treatments, integrating individual therapy, group skills training, and phone coaching of DBT with the trauma-focused exposure therapy of PE.[54,55] In both an RCT and an effectiveness study in community mental health settings, DBT-PE was found to be safe and feasible for those with comorbid PTSD and BPD, and resulted in lasting reductions in PTSD, suicidal behaviors, and psychological distress, although the effect sizes were attenuated in the effectiveness study compared with the highly-controlled efficacy study.[54,55]

Among the most debilitating symptoms of PTSD are nightmares, and 70% to 87% of patients with PTSD report comorbid insomnia.[56,57] This is reflected in the class and types of medications that are prescribed to veterans. Many of the most prescribed medications do have hypnotic effects (eg, Trazodone, the most commonly prescribed antidepressant for in veterans with PTSD in Veterans Administration clinics) or atypical antipsychotics.[45] With regard to the latter, adjunctive treatment with risperidone was found to improve sleep quality and nightmares in veterans with chronic, antidepressant-resistant, military-related PTSD.[58] Similarly, there is evidence that prazosin, an $\alpha 1$ adrenergic receptor antagonist approved as an antihypertensive drug,

reduces trauma-related nightmares.[59] Yet, the evidence base for this effect is mixed, with a well-powered RCT failing to demonstrate an effect[60] and thus the interpretation of the cumulative evidence is debated among experts (see **Table 4**). Cognitive-behavioral treatments for insomnia, including cognitive-behavioral therapy for insomnia, imagery rehearsal therapy, and exposure, rescripting, and relaxation therapy, were found to reduce both PTSD symptoms and improve insomnia severity and sleep quality in a meta-analysis of 12 RCTs.[61]

CLINICS CARE POINTS

- Nonpsychiatrists can screen for PTSD using the PCL-5, PC-PTSD, and the LEC-5.
- Trauma-focused psychotherapies are first-line treatments for PTSD. Treatments such as PE, CPT, and EMDR are recommended by a variety of treatment guidelines to the quality and depth of empirical evidence.
- SSRIs are first-line pharmacologic treatments for PTSD.
- Comorbidities, including substance use disorder and insomnia, are common among individuals with PTSD and may require additional and specific pharmacologic or psychological treatment

DISCLOSURE

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