Posttraumatic Stress Disorder

A VA Clinician's Guide to Optimal Treatment of Posttraumatic Stress Disorder (PTSD)

VA

U.S. Department of Veterans Affairs

Veterans Health Administration

PBM Academic Detailing Service

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Key Facts

Posttraumatic Stress Disorder (PTSD) is a disorder frequently seen in our Veteran population that can have a negative impact on sleep, mood, work productivity, and interpersonal relationships.[2]

It is important to ask about suicidal thoughts in Veterans with PTSD, regardless of the presence or absence of other psychiatric problems.

The prevalence of PTSD is rising. Between 2004 and 2012, the percentage of all active-duty service members with a diagnosis of PTSD increased from one to five percent, largely attributable to the conflicts in Afghanistan and Iraq.[1]

Individuals with PTSD are at a higher risk of[2,3]:

- Attempting suicide:
  - Six times increased risk of suicidality with PTSD alone
- Unhealthy or risky behaviors including:
  - Smoking
  - Substance use
  - Poor self-care

Patients with combat-related PTSD have a high prevalence of comorbid disorders.[2,13–21]

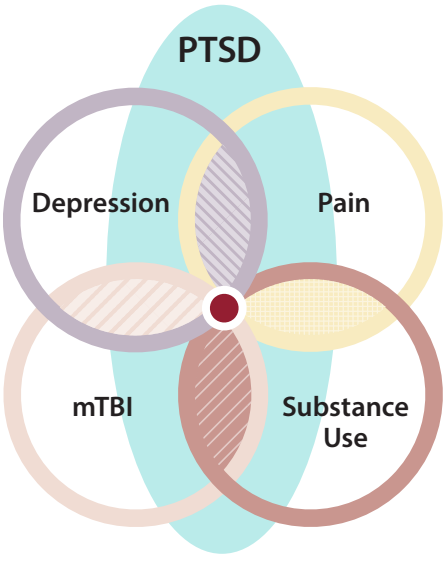
Figure 1. Common Comorbidities Associated with PTSD[2–12]

Depression

- Depression is three to five times more likely in those with PTSD.
- Risk of attempting suicide increases by nine fold.

Chronic Pain

- 15% to 35% of Veterans with chronic pain also have PTSD.



Mild Tramatic Brain Injury (mTBI)

- Many Veterans with mTBI also have PTSD, but most Veterans with PTSD don't have mTBI.
- Among Veterans with mTBI, estimates of PTSD range from 12% to 89%.

Substance Use Disorder (SUD)

- 63% to 76% of Veterans with SUD also meet criteria for PTSD.

Diagnosing PTSD and Engaging Veterans in Shared Decision Making

Figure 2. Shared Decision Making and Measurement-Based Care[2,22–24]

Patients Should be Screened Periodically for PTSD Using Validated Measures

Primary Care PTSD Screen (PC-PTSD-5) | PTSD Checklist (PCL-5)

For patients screened positive for PTSD: (PC-PTSD-5 with three or more YES answers; PCL-5>33)
Complete an appropriate diagnostic evaluation that includes determination of DSM criteria*

Measure the severity of PTSD after diagnosis using the PCL-5 or other quantitative self-report measure of PTSD severity.

When treating PTSD in the primary care setting, use collaborative care interventions that facilitate active engagement in evidence-based treatments.

Engage patients in shared decision making by educating patients about effective treatment options (**https://www.ptsd.va.gov/apps/decisionaid/**).

Develop a treatment plan based on patient specific goals, values, and preferences.

Screening Tools

PC-PTSD-5

- A score of > three is considered a positive screen.

PCL-5

- The PCL has several purposes, including:
  - Screening individuals for PTSD
  - Aiding in diagnostic assessment of PTSD
  - Monitoring symptom change during and after treatment.
- The PCL takes five to 10 minutes to complete and patients can self-administer while in the waiting room.
- A score of 33 or higher appears to signal a need for more evaluation.
- A reduction of five points suggests a positive response to therapy.
- A 10-point change represents a clinically significant change.

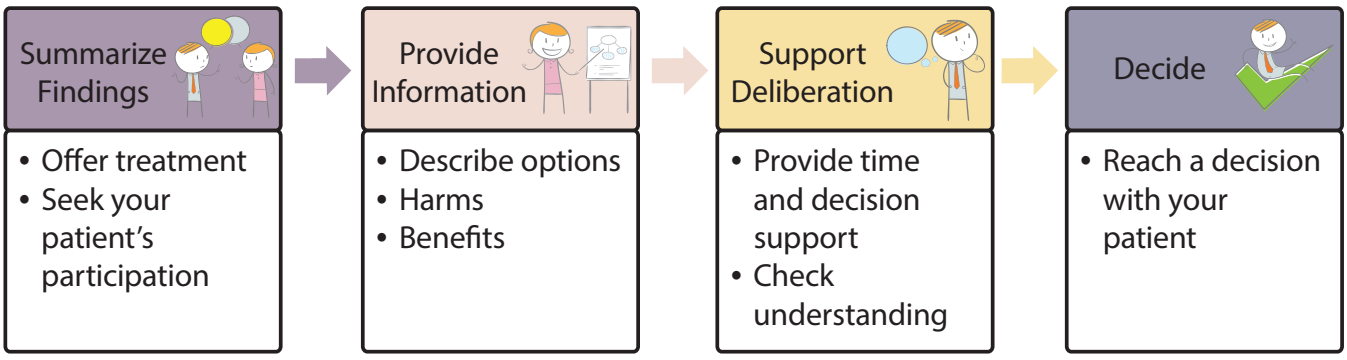
*DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, fifth edition.

Patients with probable PTSD should undergo an appropriate diagnostic evaluation including a review of trauma history and associated symptoms, medical history, treatment history, relevant family history, and acute risk of harm to self or others.[2]

Patients with probable PTSD should undergo an appropriate diagnostic evaluation.

Once PTSD has been diagnosed, engage patients in shared decision making about treatment. Let your patient know the effective treatment options for PTSD and the risks and benefits of each.[2]

Figure 3. Steps to Shared Decision Making[22]



Shared Decision Making is NOT:

- **Giving your patient a brochure**
- **Telling your patient about only one option**
- **Doing whatever your patient wants**

Management of PTSD: First-Line Treatment Options

Trauma-focused psychotherapies are the first-line treatment option for PTSD. They are defined as any therapy that uses cognitive, emotional, or behavioral techniques to facilitate processing a traumatic experience and in which the trauma focus is a central component of the therapeutic process.[2]

- Effective for patients with PTSD, even those who have considerable complexity, chronicity and comorbidity.[25–34]
- Improvements are long lasting and side effects are minimal; most common is discomfort confronting the trauma memory.[29,35]

Figure 4. Evidence-based Trauma-focused Psychotherapies[29]

Evidence-based Psychotherapy	Cognitive Processing Therapy*	Prolonged Exposure*	Eye Movement Desensitization & Reprocessing
How Does it Work?	Helps reframe negative thoughts about the trauma	Teaches how to gain control by facing fears	Facilitates accessing the traumatic memory network
What Does the Treatment Entail?	Talk about thoughts; may have a written component	Talk about the trauma. Start doing safe things previously avoided. Listen to session recordings	Call the trauma to mind while focusing on an external motion or sound

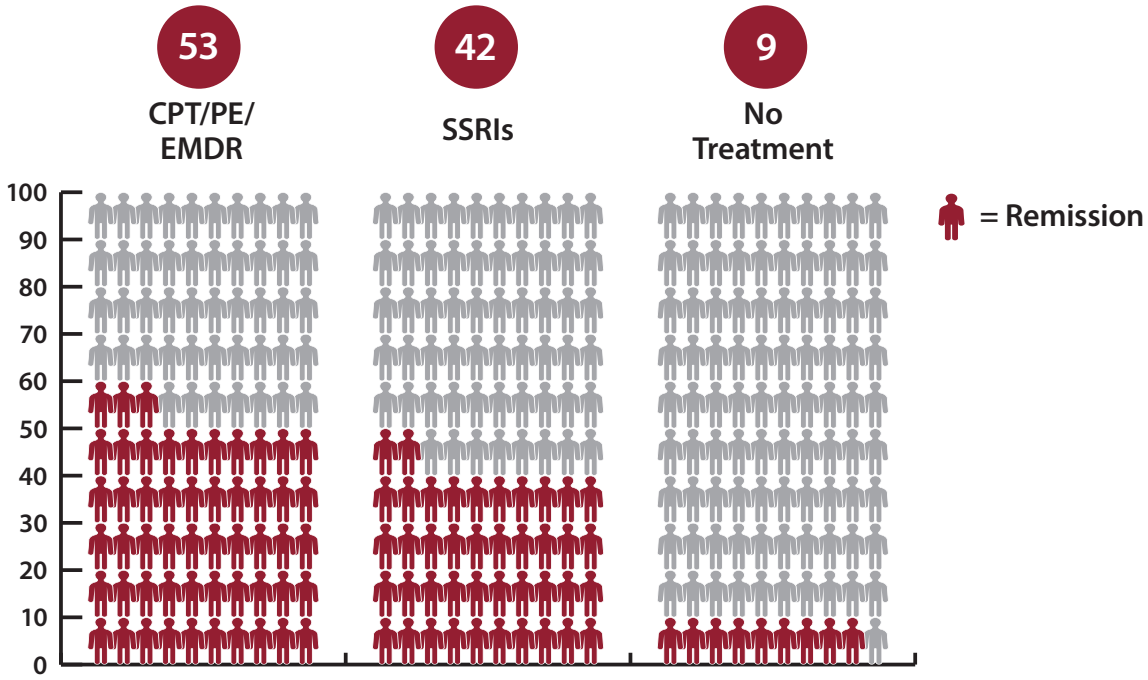
*Demonstrated efficacy using secure video teleconferencing modality and offering VA supported apps.

Additional trauma-focused therapies for consideration include: specific cognitive behavioral therapies for PTSD; brief eclectic psychotherapy (BEP); narrative exposure therapy (NET); and written narrative exposure.

Why is Pharmacotherapy not Recommended as a First-line Treatment for PTSD?

When psychotherapies were compared in meta-anaylsis to pharmacotherapies, results strongly indicate that trauma-focused psychotherapies imparted greater change in core PTSD symptoms.[36,37] In addition, there is a growing body of literature that indicates patients prefer psychotherapy over pharmacotherapy.[38–40]

Figure 5. Remission Rates are Greater for Evidence-based Psychotherapy Three Months After Treatment[41]



CPT = cognitive processing therapy; EDMR = eye movement desensitization and reprocessing; PE = prolonged exposure;
SSRIs = selective serotonin reuptake inhibitors (pharmacotherapy).

Offer trauma-focused psychotherapy treatment when available.

Management of PTSD: Second-Line Treatment Options

When individual trauma-focused psychotherapy is not readily available or not preferred by the patient, then pharmacotherapy and/or manualized individual non-trauma-focused psychotherapy are recommended as second-line treatment options.[2]

Table 1. Non-trauma-focused Psychotherapy

Therapy	Focus
Present-Centered Therapy	Current problems in a patient's life related to PTSD
Stress Inoculation Training	Cognitive restructuring that targets thinking patterns that induce stress responses
Interpersonal Psychotherapy	Impact the trauma has had on an individual's interpersonal relationships

Of the pharmacotherapy options, antidepressants have the strongest evidence for reducing PTSD symptoms.[36]

Figure 6. VA/DoD PTSD Clinical Practice Guideline 2017: Medications Recommended for PTSD[2]

Recommended Agents

- Paroxetine*
- Sertraline*
- Fluoxetine
- Venlafaxine

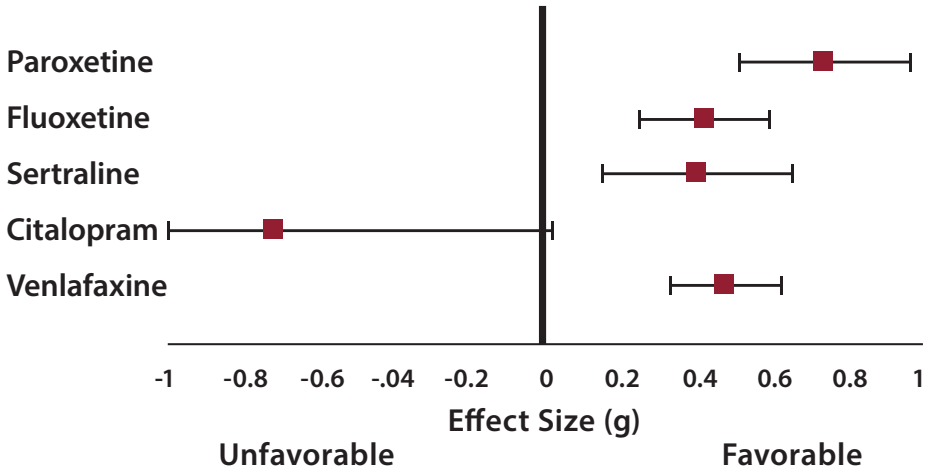
Suggested Agents

- Nefazodone**
- Imipramine
- Phenelzine**

Should be reserved for patients who have failed one or more recommended agents.

*FDA approved for PTSD; **Requires close monitoring.

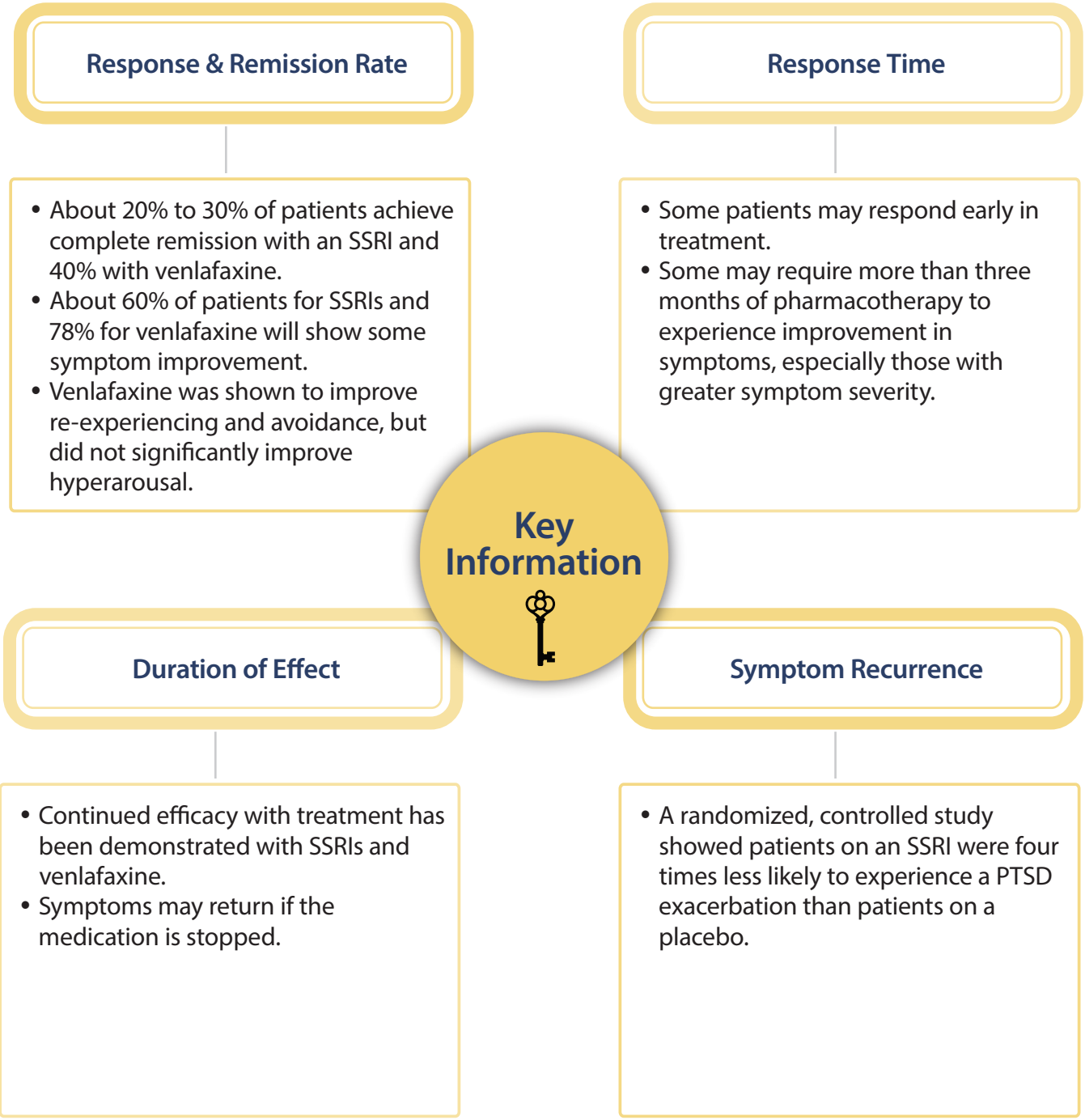
Figure 7. Antidepressant Used for Treatment Of PTSD[36]



A meta-analysis of 112 studies measured the effect size (g) of pharmacotherapies compared to control. Of the medication classes, the evidence was most convincing for antidepressants. Among antidepressants, paroxetine (g = 0.74, CI 0.51 to 0.97), fluoxetine (g = 0.43, CI 0.25 to 0.6), sertraline (g = 0.41, CI 0.15 to 0.66), and venlafaxine (g = 0.48, CI 0.33 to 0.63) were shown to have the strongest evidence. A nonsignificant negative effect was seen with citalopram (g = -0.71, CI -1.45 to 0.02) based on one study. Effect size was determined by change in PTSD symptom measure. By convention, effect sizes of 0.8 are considered large, 0.5 medium, and 0.2 small.

Relative to trauma-focused psychotherapy, data suggests pharmacotherapy imparts a lesser degree of change in the core PTSD symptoms.[36,37]

Figure 8. Key Information on Antidepressant Use in PTSD[40,41,42,43,44–46]



While nefazodone, imipramine, and phenelzine have evidence to support their use, these antidepressants require close monitoring due to their serious potential adverse effects and should be reserved for patients who have failed other preferred treatment options.

Table 2. Side Effects and Monitoring of Nefazodone, Imipramine and Phenelzine[47]

Medication	Rare but Serious Side Effects	Monitoring
Nefazodone	Liver toxicity	Baseline liver function tests (LFTs); Repeat LFTs monthly for the first six months, then every six months for duration of therapy.
Imipramine	Anticholinergic, cardiovascular (arrhythmias, palpitations, heart block, QT prolongation)	Electrocardiograms
Phenelzine	Hypertensive crisis if patient does not follow low tyramine diet; Avoid medications contraindicated with monoamine oxidase inhibitors, such as stimulants (e.g., for ADHD).	Dietary and medication restrictions

If recommended treatments have not been beneficial, consider the following alternative or adjunct options for patients with PTSD refractory to standard treatments.

Table 3. Additional Antidepressants that have Demonstrated Results as Monotherapy or Adjunctive Therapy in Limited Small Studies[48–54*]

Medication	Monotherapy or Adjunctive	Studied in Combat-related PTSD
Duloxetine	Monotherapy	X
Escitalopram	Monotherapy	
Fluvoxamine	Monotherapy	X
Mirtazapine	Both	X

*The 2017 VA/Department of Defense (DoD) Clinical Practice Guide does not recommend for or against monotherapy or augmentation with these agents. Additional information can be found in the Academic Detailing Service PTSD Quick Reference Guide.

Medications have been shown to have limited and variable responses. If the patient initially declines trauma-focused psychotherapy, it is reasonable to offer referral to psychotherapy again after medication effects plateau or if side effects occur.

Offer treatment with paroxetine, sertraline, fluoxetine, or venlafaxine and/or individual non-trauma-focused psychotherapy.

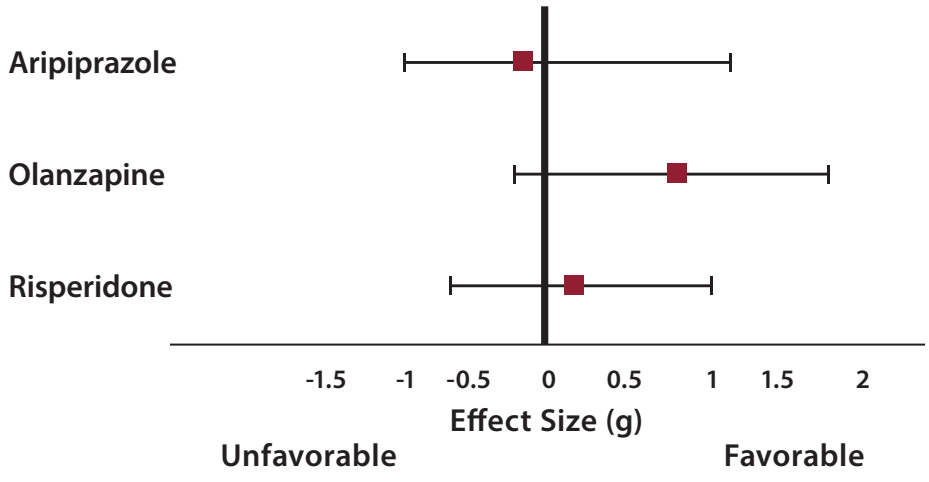
Agents to Avoid: Antipsychotics

Antipsychotics are not recommended for the treatment of PTSD.[2] It is extremely important to distinguish PTSD symptoms from a primary psychotic disorder through a comprehensive assessment of the psychotic symptoms. This approach will optimize potential benefits of PTSD treatment and minimize the risks associated with inappropriate use of antipsychotics.

- There is limited evidence for the use of antipsychotics in combat-related PTSD treatment, and they can cause significant harm.[2,37,55,56,57]
- Monotherapy with quetiapine was recently found to be more effective than placebo in combat Veterans, but the study has not been replicated, and had significant attrition rates.[2,58]

The largest randomized placebo-controlled trial found that adjunctive risperidone did not improve overall PTSD symptoms in Veterans with PTSD.[55]

Figure 9. Core PTSD Symptoms Show No Significant Improvement with the Addition of Antipsychotics.[37]

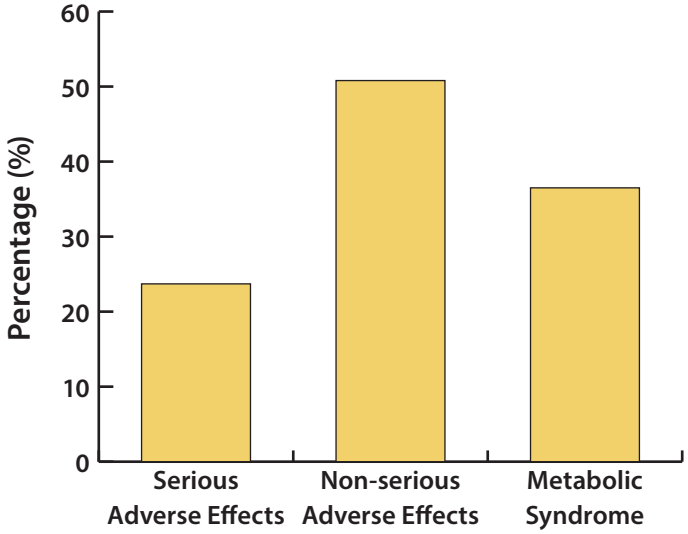


This meta-analysis evaluated the effect size of adjunctive antipsychotic medication treatment on core symptoms of PTSD (using various standard PTSD rating scales) with antidepressants over an eight to 12 week period versus control. No significant effect was seen on core symptoms of PTSD with the three most well studied antipsychotics.

Risks of antipsychotics include:[60,61]

- Motor Symptoms
  - Dystonic Reactions
  - Akathisia
  - Tremor/Parkinsonism
  - Tardive dyskinesia
  - Neuroleptic malignant syndrome
- Metabolic adverse effects
  - Weight gain
  - Type 2 diabetes mellitus
  - Hypercholesterolemia/ Hypertriglyceridemia
- Cardiovascular adverse effects
  - Atrial hypertension
  - Sudden cardiac death

Figure 10. High Incidence of Adverse Effects with Atypical Antipsychotics in Patients over 40 years old[59]



A study of 332 patients receiving aripiprazole, olanzapine, quetiapine or risperidone for up to two years reported a high incidence of serious adverse effects (23.7%) including deaths, hospitalizations and emergency room visits. A high incidence of non-serious adverse events (50.8%) and metabolic syndrome (36.5%) were also seen.

Avoid starting antipsychotic medications and discuss discontinuation in Veterans with PTSD.

Agents to Avoid: Benzodiazepines

Benzodiazepines are ineffective for the treatment and prevention of PTSD and any potential benefits are outweighed by the risks.[2,62]

Figure 11. Risks of Benzodiazepine Use in PTSD Treatment[2,62–66,67,68–69,70–73]

Increased PTSD Severity

Benzodiazepines do not reduce the core symptoms of PTSD or improve PTSD-related sleep dysfunction.

Decreased Efficacy of Trauma-focused Psychotherapy

The numbing and memory-impairing effects of benzodiazepines may reduce the effectiveness of trauma-focused psychotherapy.

Increased Risk of Substance Use

Co-occurring substance use disorders are very high in PTSD, so concurrent use of benzodiazepines creates an increased risk of overdose and potential problems with tolerance and dependence.

Difficult Withdrawal

Withdrawal of benzodiazepines can worsen existing PTSD symptoms, resulting in increased anxiety, sleep disturbances, rage, hyper-alertness, increased nightmares and intrusive thoughts.

Aggravating Aggressive Behaviors

Although aggressive behaviors are not commonly observed with PTSD, they are more likely to occur with disinhibiting substances (alcohol, benzodiazepines) — particularly if other aggravating situations are present (e.g. financial stressors, homelessness).

Increased Suicidality and Health Care Utilization

Veterans with PTSD who receive a benzodiazepine within one year of diagnosis have been found to have higher rates of health care utilization and are more likely to have suicidal thoughts, behaviors, and to die by suicide.

Other Risks

Benzodiazepines may also cause depression and falls, increase risk of car accidents by 60%, and are commonly involved in intentional and unintentional overdose deaths.

Avoid starting benzodiazepines for Veterans with PTSD and discuss a slow taper and discontinuation with patients who have been taking benzodiazepines for more than four weeks.

Management of PTSD: Sleep Disturbances

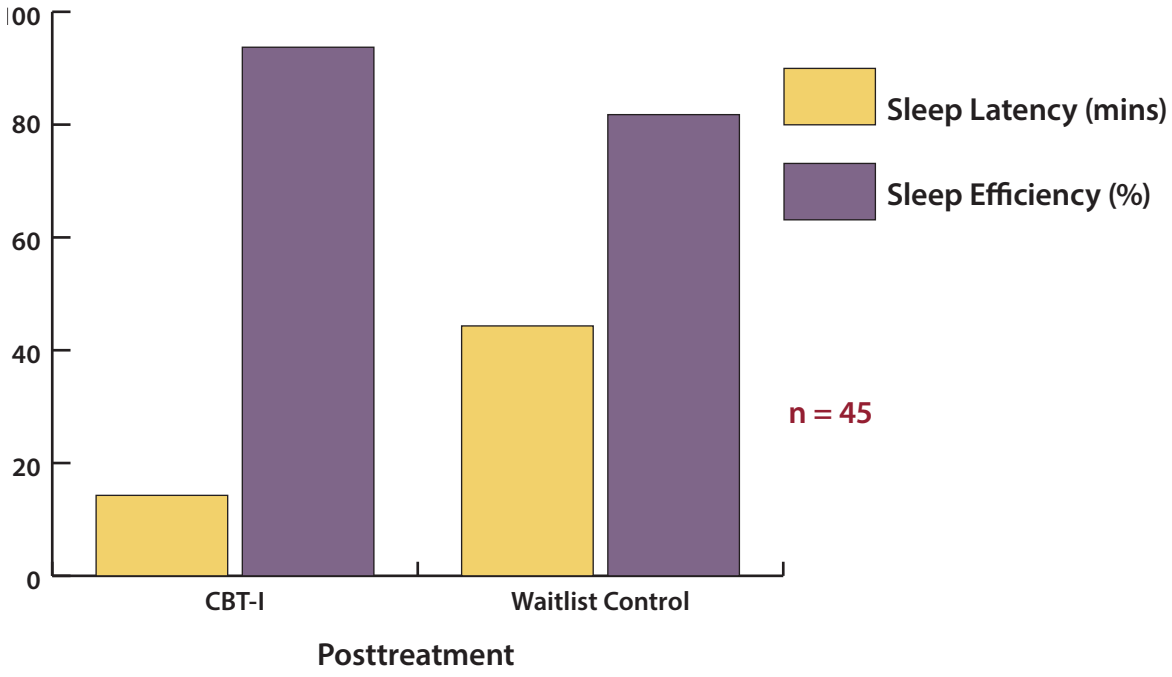
Between 90% and 100% of patients diagnosed with PTSD experience sleep disturbances, including insomnia and nightmares, that often persist after evidence-based PTSD treatment.[1,74,75]

Cognitive Behavior Therapy for Insomnia (CBT-I) is recommended as the first-line treatment for insomnia and has been shown to improve sleep in individuals with PTSD.[76–81]

Patients with PTSD often develop perpetuating behavioral and psychological factors that can lead to further wakefulness, negative expectations and distorted beliefs about their insomnia disorder. CBT-I can be used to address these factors.

CBT-I provides sustained improvement in sleep, improved psychosocial functioning, and reduction in PTSD and depressive symptoms.[81]

Figure 12. CBT-I Improves Sleep in Veterans with PTSD[80]



Eight sessions of weekly CBT-I were provided (n = 29) and results compared to waitlist control (n = 16). CBT-I results were superior to those of the waitlist control group on all sleep diary outcomes and polysomnography-measured total sleep time with durable gains maintained at six months. Overall psychosocial functioning improved following CBT-I.

Sleep latency: Time it takes to fall asleep. Sleep efficiency: Percent of time in bed spent sleeping.

The CBT-I Coach is a VA app designed to supplement CBT-I. It can also be used on its own but is not designed to replace therapy for those who need it. **https://mobile.va.gov/app/cbt-i-coach**.

Offer CBT-I to Veterans with insomnia and PTSD.

It is important to examine potential causes of sleep disturbance independently of PTSD.

Obstructive Sleep Apnea (OSA)

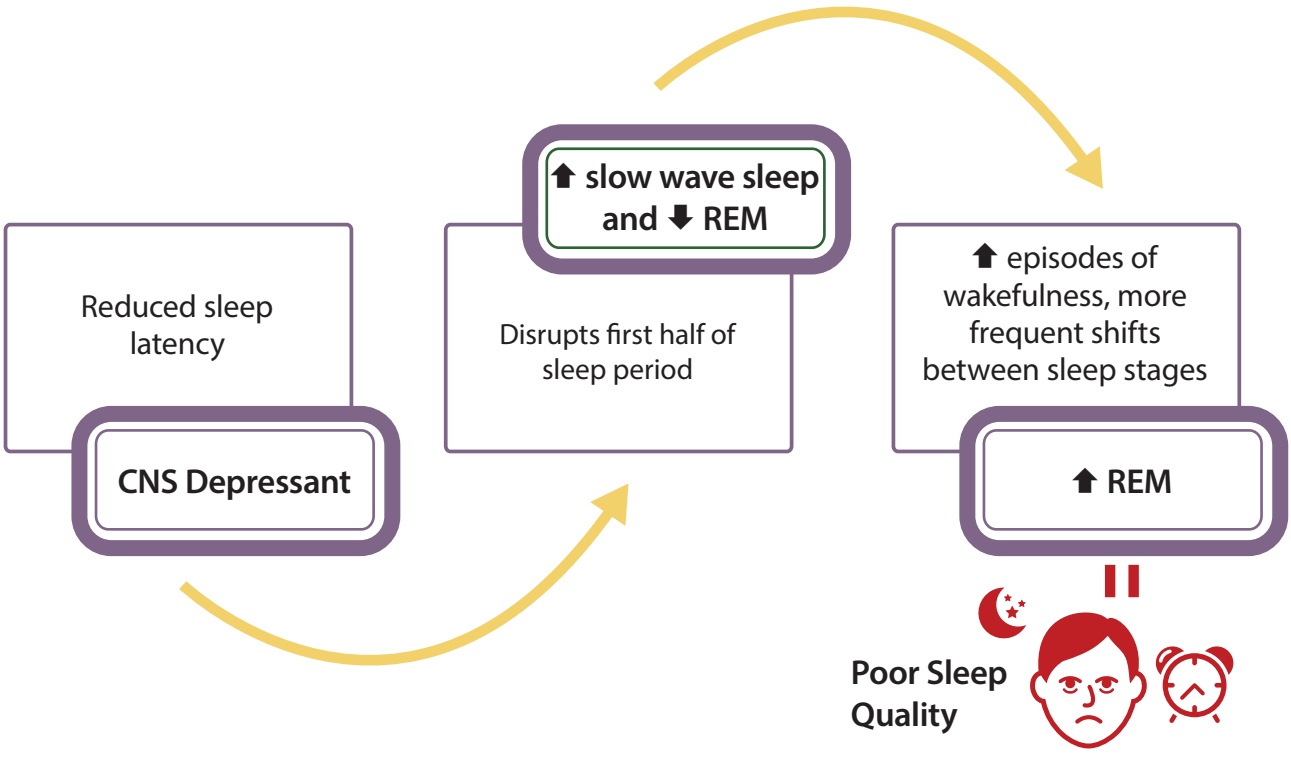
It is reported that approximately 69% of Veterans with PTSD had an apnea-hypopnea index (AHI) >10, indicative of at least mild OSA.[2]

- Untreated OSA can worsen sleep-related symptoms of PTSD.[82]
- Continuous Positive Airway Pressure (CPAP) therapy has been found to reduce the number of nightmares per week and overall PTSD symptoms. [82–84]

Alcohol

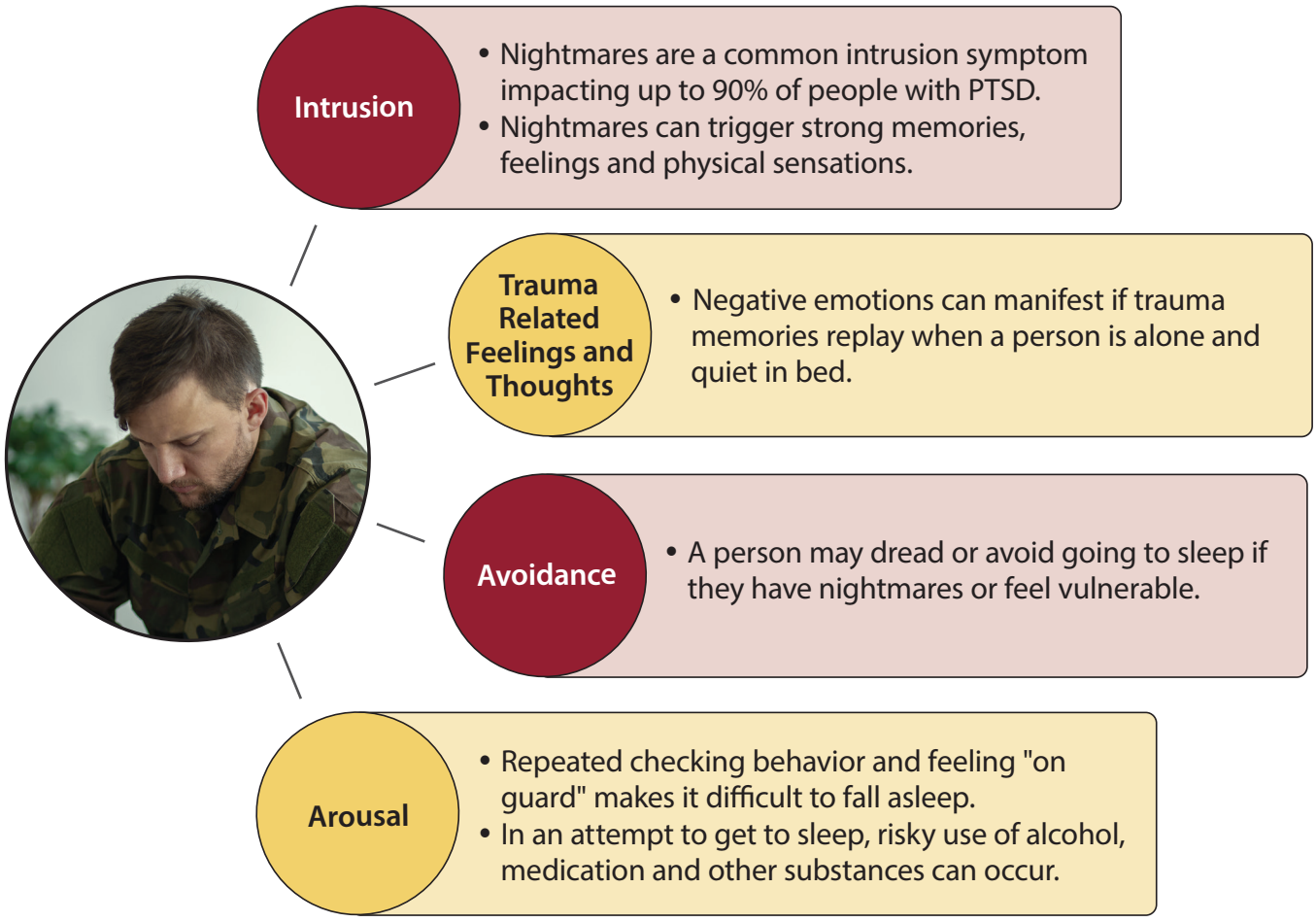
Veterans also may be self-medicating with alcohol. Over time, the initial effect on sleep latency diminishes while the sleep disruption persists.

Figure 13. Alcohol Disrupts the Sleep Cycle[85]



Management of PTSD: Nightmares

Figure 14. Nightmares have Significant Impact on Veterans with PTSD.[2,3,4]



Despite prazosin improving PTSD-related nightmares in several smaller randomized trials,[86–89] a recent randomized multicenter trial conducted at 13 Department of Veterans Affairs Medical Centers failed to show positive benefits from prazosin for global PTSD symptoms or nightmares.[90]

The recommendation on prazosin to treat trauma-related nightmares has changed. The revised Clinical Practice Guidelines now state there is insufficient evidence to recommend prazosin for trauma-related nightmares.

Based on prazosin's minimal side effects and limited treatment options available, prazosin may still be an effective treatment option for some patients experiencing PTSD-related nightmares. If a patient has had success with it, then continue its use. If prescribed for new patients, monitor and document objective improvement (e.g., with PCL or sleep quality assessment).

Table 4. PTSD-Related Nightmares: Treatments that have Demonstrated Response in Small or Limited Studies.[2,88–91,93–94,95–98]

	Prazosin*	Imagery rehearsal therapy (IRT)	Low-dose Trazodone*	Doxazosin*
Studied dosing range	2–20 mg	N/A	25–200 mg	2–8 mg
Evidence	Mixed	Mixed	Limited	Limited
Summary of Evidence	Small studies show reduced nightmare severity and increase in total sleep time. Large VA multi-center randomized controlled trial did not find beneficial results. Subset of patients may still benefit from this treatment (e.g. elevated CNS adrenoreceptor activation**).	<u>IRT</u> Higher-quality trials show no benefit or are inconclusive in Veterans. <u>CBT-I + IRT</u> A single eight-week randomized trial in 40 combat Veterans reported improvement in sleep, PTSD severity, and decrease in PTSD-related nighttime symptoms.	A survey found that 72% of Veterans reported reduction in nightmares from 3.3 per week to 1.3 per week. Multiple-baseline trial of six Veterans reported improvement in sleep and reduction of nightmares.	Small open label studies and retrospective chart review show reduced nightmare severity in non-Veteran populations. A two-week double-blind placebo-controlled trial of eight Veterans found no effect of treatment on CAPS scores but found a trend for improvement in hyperarousal scores and treatment x time effect on PCL ($p = 0.003$).

The treatments listed have limited evidence for their use in the treatment of PTSD-related nightmares. CNS = central nervous system; *Can cause postural hypotension and falls, caution is advised in patients with a history of falls and in elderly patients. **Higher standing baseline blood pressure may be a biomarker of activation.[91] Additional medications studied include topiramate and clonidine. Utility of both may be limited by side effects.

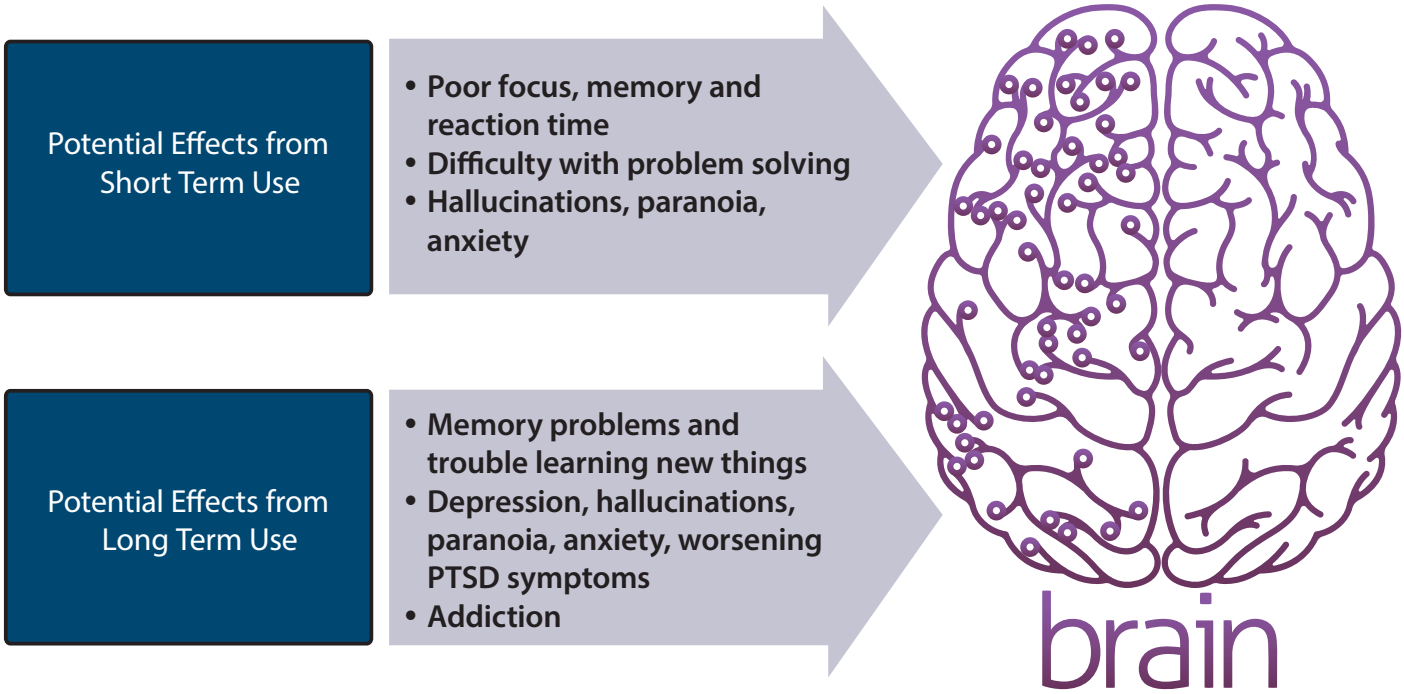
When using medications to treat PTSD-related nightmares, document objective improvement in symptoms and discontinue treatment if it's not effective.

PTSD and Marijuana

There is currently a lack of large, well-designed studies evaluating the efficacy of cannabinoids in patients with PTSD.[99–103] They are not recommended for the treatment of PTSD due to the lack of evidence, known adverse effects, and associated risks.[2]

- Preliminary evidence suggests that cannabinoids may reduce PTSD symptoms, particularly nightmares.[2,99]
- Potential benefits of cannabinoids are offset by their serious side effects.[2,100,102–104]

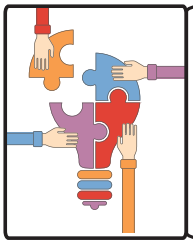
Figure 15. Potential Side Effects of Marijuana[102]



Summary

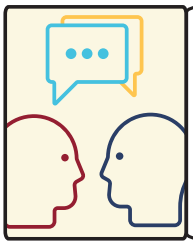
Foster Hope and Posttraumatic Growth

- Fight PTSD stigma, myths and misconceptions
- Work to fit the right treatment to the right person at the right time
- Share that with treatment recovery is possible



Engage Veterans in Shared Decision Making

- Provide people with PTSD the full menu of treatments
- Educate and compare pros & cons of all options
- Match up treatments with Veteran's values and preferences



Offer Individual Trauma-focused Therapy First

- Clear the path to the most effective and lasting PTSD treatment
- Hardwire a process for referring patients to PE (prolonged exposure), CPT (cognitive processing therapy) & EMDR (eye movement desensitization & reprocessing)

Choose Medications that Help Not Harm

- Provide proven treatments for the core symptoms of PTSD like sertraline, paroxetine, fluoxetine & venlafaxine
- Avoid prescribing benzodiazepines & off-label antipsychotics

Don't Let Comorbidities Derail PTSD Care

- Emphasize non-pharmacologic approaches for chronic pain, sleep problems & anger control issues
- Connect people with alcohol or opioid use disorders to effective medications & support

Measure Progress and Re-Evaluate

- Use objective tools to screen & track improvement such as the Primary Care PTSD Screen (PC-PTSD) & PTSD Checklist (PCL)
- Arrange and follow through on referrals

Not all patients will respond to the recommended evidence-based psychotherapies and/or pharmacotherapies. Determining what to do for these Veterans is a clinically important question. The PTSD consultation program can help guide this decision.

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We thank our expert reviewers:

Paula P. Schnurr, Ph.D.
Sonya B. Norman, Ph.D.
Lisa C. Smith, MD
Nancy Bernardy, Ph.D.
Jessica Hamblen, Ph.D.
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These are general recommendations only. The treating provider should make clinical decisions based on an individual patient's clinical condition.

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January 2019

IB 10-751, P96755, V2 **www.va.gov**