Implementing AHRQ Effective Health Care Reviews

Helping Clinicians Make Better Treatment Choices

Psychological and Pharmacologic Treatments for Adults with PTSD

Practice Pointers by Aaron Saguil, MD, MPH

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Key Clinical Issue

What are the benefits and harms of psychotherapies and pharmacologic agents for the treatment of adults with posttraumatic stress disorder (PTSD)?

Evidence-Based Answer

Cognitive behavior therapy (CBT) and CBT-mixed treatments had high strength of evidence for benefit in improving PTSD-related outcomes, such as reduced PTSD symptoms, reduced depression symptoms, and resolution of PTSD diagnosis. (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) Cognitive processing therapy, cognitive therapy, eye movement desensitization and reprocessing (EMDR), and narrative exposure therapy had moderate strength of evidence for benefit. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) Fluoxetine, paroxetine, and venlafaxine had moderate strength of evidence for reducing PTSD symptoms. (SOR: B, based on inconsistent or limited-quality patient-oriented evidence.) There was insufficient evidence to compare psychotherapy with pharmacotherapy and to compare serious adverse events among treatments.[1]

Practice Pointers

Family physicians regularly diagnose and treat PTSD, which affects 8% of men and 20% of women in the general population.[2] Similarly, 16% of female veterans receiving care in Veterans Health Administration facilities have PTSD.[3] Male veterans have higher rates of PTSD than the general population; PTSD has been diagnosed in one out of four male combat veterans serving in Operation Enduring Freedom or Operation Iraqi Freedom.[3] Untreated, PTSD can lead to substance abuse and suicide.[2]

This Agency for Healthcare Research and Quality (AHRQ) systematic review updates a 2013 report and includes 193 studies. Because several different outcome scales were used across trials (e.g., the Clinician-Administered PTSD Scale, which measures the presence and intensity of PTSD-related symptoms), the

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to produce evidence to improve health care and to make sure the evidence is understood and used. A key clinical question based on the AHRQ Effective Health Care Program systematic review of the literature is presented, followed by an evidence-based answer based upon the review. AHRQ's summary is accompanied by an interpretation by an *AFP* author that will help guide clinicians in making treatment decisions. For the full review, clinician summary, and consumer summary, go to https://effectivehealthcare.ahrq.gov/topics/ptsd-adult-treatment-update/research-2018.

This series is coordinated by Kenny Lin, MD, MPH, Deputy Editor.

A collection of Implementing AHRQ Effective Health Care Reviews published in *AFP* is available at https://www.aafp.org/afp/ahrq.

CME **This clinical content** conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 541.

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CLINICAL BOTTOM LINE

Summary of Efficacy and Strength of Evidence of PTSD Psychological Treatments

Treatment	Symptom	No. of trials (no. of participants)	Findings	Strength of evidence
Cognitive processing therapy	PTSD symptoms*	5 (399)	Reduced PTSD symptoms SMD = −1.35 (95% CI, −1.77 to −0.94)	●●○
	Loss of PTSD diagnosis	4 (299)	Greater loss of PTSD diagnosis RD = 0.44 (95% CI, 0.26 to 0.62)	●●○
	Depression symptoms†	5 (399)	Reduced depression symptoms SMD = −1.09 (95% CI, −1.52 to −0.65)	●●○
Cognitive therapy	PTSD symptoms*	4 (283)	Reduced PTSD symptoms SMD of individual studies ranged from −2.0 to −0.3 All studies favored treatment (all studies $P < .05$)	●●○
	Loss of PTSD diagnosis	4 (283)	Greater loss of PTSD diagnosis RD = 0.55 (95% CI, 0.28 to 0.82) All studies favored treatment (3 of 4 studies $P < .05$)	●●○
	Depression symptoms†	4 (283)	Reduced depression symptoms Between-group mean differences of individual trials ranged from −11.1 to −8.3 All studies favored treatment (4 of 4 studies $P < .05$)	●●○
Cognitive behavior therapy (exposure)	PTSD symptoms*	13 (885) 8 (689)	Reduced PTSD symptoms SMD = −1.23 (95% CI, −1.50 to −0.97) SMD for the Clinician-Administered PTSD Scale = −1.12 (95% CI, −1.42 to −0.82)	●●●
	Loss of PTSD diagnosis	6 (409)	Greater loss of PTSD diagnosis RD = 0.56 (95% CI, 0.35 to 0.78)	●●●‡
	Depression symptoms†	10 (715)	Reduced depression symptoms SMD = −0.76 (95% CI, −0.91 to −0.60)	●●●

continues

Strength of evidence scale

- ●●● **High:** High confidence that the evidence reflects the true effect. Further research is very unlikely to change the confidence in the estimate of effect.
- ●●○ **Moderate:** Moderate confidence that the evidence reflects the true effect. Further research may change the confidence in the estimate of effect and may change the estimate.
- ●○○ **Low:** Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
- ○○○ **Insufficient:** Evidence either is unavailable or does not permit a conclusion.

Note: Outcomes graded as insufficient are not included in this table.

PTSD = posttraumatic stress disorder; RD = risk difference; SMD = standardized mean difference.

*—SMD from the Clinician-Administered PTSD Scale and other various PTSD symptom scales.
†—SMD from the Beck Depression Inventory and other various depression symptom scales.
‡—Strength of evidence increased from moderate to high because of additional evidence of efficacy published since prior PTSD review.
§—Strength of evidence increased from low to moderate because of additional evidence of efficacy published since prior PTSD review.

authors interpreted a standardized mean difference (SMD) of 0.5 (a medium effect size) as being clinically significant, although definitive thresholds for clinical significance have not been established.

CBT focusing on imagined, written, virtual reality, and real-life exposures reduced PTSD symptoms by an SMD of −1.23 (95% CI, −1.5 to −0.97), led to a greater loss of PTSD diagnosis with a risk difference of 0.56 (95% CI, 0.35 to 0.78),

CLINICAL BOTTOM LINE *(continued)*

Summary of Efficacy and Strength of Evidence of PTSD Psychological Treatments

Treatment	Symptom	No. of trials (no. of participants)	Findings	Strength of evidence
Cognitive behavior therapy (mixed)	PTSD symptoms*	21 (1,349)	Reduced PTSD symptoms SMD = −1.01 (95% CI, −1.28 to −0.74)	●●●‡
		11 (709)	SMD = −1.24 (95% CI, −1.67 to −0.81)	
	Loss of PTSD diagnosis	9 (474)	Greater loss of PTSD diagnosis RD = 0.29 (95% CI, 0.11 to 0.41)	●●●‡
	Depression symptoms†	15 (929)	Reduced depression symptoms SMD = −0.87 (95% CI, −1.14 to −0.61)	●●●‡
Eye movement desensitization and reprocessing	PTSD symptoms*	8 (449)	Reduced PTSD symptoms SMD = −1.08 (95% CI, −1.82 to −0.35)	●●○§
	Loss of PTSD diagnosis	7 (427)	Greater loss of PTSD diagnosis RD = 0.43 (95% CI, 0.25 to 0.61)	●●○
	Depression symptoms†	7 (347)	Reduced depression symptoms SMD = −0.91 (95% CI, −1.58 to −0.24)	●●○
Brief eclectic psychotherapy	Loss of PTSD diagnosis	3 (96)	Greater loss of PTSD diagnosis RD of individual studies ranged from 0.13 to 0.58 All studies favored treatment ($P < .05$)	●○○
	Depression symptoms†	3 (96)	Reduced depression symptoms Different depression scales used; all 3 studies favored treatment (3 of 3 studies $P < .05$)	●○○

continues

Strength of evidence scale

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§—Strength of evidence increased from low to moderate because of additional evidence of efficacy published since prior PTSD review.

and reduced depression symptoms by an SMD of −0.76 (95% CI, −0.91 to −0.60). CBT using mixed modalities (i.e., cognitive restructuring, exposure, guided imagery, mindfulness training, psychoeducation, self-monitoring, and/or stress management) reduced PTSD symptoms by an SMD of −1.01 (95% CI, −1.28 to −0.74), led to a greater loss of PTSD diagnosis with a risk difference of 0.29 (95% CI, 0.11 to 0.41), and reduced depression symptoms by an SMD of −0.87 (95% CI, −1.14 to −0.61). Both interventions were rated as having a high strength of evidence. Cognitive processing therapy, cognitive therapy, EMDR, and narrative exposure therapy had the same magnitude of PTSD outcomes reduction, with moderate strength of evidence because of imprecision in study results.

There was moderate strength of evidence to support the pharmacologic treatments fluoxetine (SMD = −0.28; 95% CI, −0.42 to −0.14; four studies, n = 835), paroxetine (SMD = −0.56 to −0.44; two studies, n = 348), and

CLINICAL BOTTOM LINE *(continued)*

Summary of Efficacy and Strength of Evidence of PTSD Psychological Treatments

Treatment	Symptom	No. of trials (no. of participants)	Findings	Strength of evidence
Imagery rehearsal therapy	PTSD symptoms*	1 (168)	Reduced PTSD symptoms Between-group mean difference = −21.0 ($P < .05$)	●○○
Narrative exposure therapy	PTSD symptoms	3 (232)	Reduced PTSD symptoms SMD ranged from −1.95 to −0.79 across 3 individual studies (3 of 3 studies $P < .05$)	●●○
	Loss of PTSD diagnosis	2 (198)	Greater loss of PTSD diagnosis RD of 0.06 and 0.43 in individual studies Both studies favored treatment (1 of 2 studies $P < .05$)	●○○
Seeking safety	PTSD symptoms*	3 (232)	Reduced PTSD symptoms SMD of individual trials ranged from −0.22 to 0.04 2 of 3 trials favored treatment (0 of 3 studies $P < .05$)	●○○ for no difference
Trauma affect regulation	PTSD symptoms*	2 (173)	Reduced PTSD symptoms Between-group mean difference of −17.4 and −2.7 in individual studies Both favored treatment (1 of 2 studies $P < .05$)	●○○

Strength of evidence scale

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venlafaxine (SMD = −0.35 to −0.26; two studies, n = 687) for the reduction of PTSD symptoms. There was low strength of evidence that sertraline, prazosin, topiramate, olanzapine, and risperidone were effective for improving PTSD-related outcomes.

The AHRQ review findings are similar to the recommendations from the U.S. Department of Veterans Affairs (VA)/U.S. Department of Defense (DoD) clinical practice guideline.[3] This guideline states that the trauma-focused psychotherapies with the strongest evidence are prolonged exposure, cognitive processing therapy, and EMDR; there is sufficient evidence to also recommend narrative exposure and other types of CBT. Non–trauma-focused psychotherapies that were reported as potentially helpful include stress inoculation training, present-centered therapy, and interpersonal psychotherapy. The pharmacotherapies recommended in the VA/DoD guideline include fluoxetine, paroxetine, venlafaxine, and sertraline; the guideline recommends against the use of atypical antipsychotic medications, topiramate, and amitriptyline.

CLINICAL BOTTOM LINE

Summary of Efficacy and Strength of Evidence of PTSD Pharmacologic Treatments

Treatment	Symptom	No. of trials (no. of participants)	Findings	Strength of evidence
Fluoxetine (selective serotonin reuptake inhibitor)	PTSD symptoms*	4 (835)	Reduced PTSD symptoms SMD = −0.28 (95% CI, −0.42 to −0.14)	●●○
	Depression symptoms†	3 (771)	Similar reduction in depression symptoms SMD = −0.20 (95% CI, −0.40 to 0.00)	●○○‡ for no difference
Paroxetine (selective serotonin reuptake inhibitor)	PTSD symptoms*	2 (348)	Reduced PTSD symptoms SMD of −0.56 to −0.44 in individual studies Both studies favored treatment (2 of 2 studies $P < .05$)	●●○
	PTSD symptom remission	2 (348)	Greater PTSD symptom reduction RD of 0.13 and 0.19 across 2 individual studies (1 of 2 studies $P < .05$)	●●○
	Depression symptoms†	2 (348)	Reduced depression symptoms SMD ranged from −0.60 to −0.34 across individual studies Both studies favored treatment (2 of 2 studies $P < .05$)	●●○
Sertraline (selective serotonin reuptake inhibitor)	PTSD symptoms*	7 (1,085)	Reduced PTSD symptoms SMD = −0.20 (95% CI, −0.36 to −0.04)	●○○§
	Depression symptoms†	7 (1,085)	Similar reduction in depression symptoms SMD = −0.14 (95% CI, −0.33 to 0.06)	●○○‖ for no difference

continues

Strength of evidence scale

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- ●○○ **Low:** Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
- ○○○ **Insufficient:** Evidence either is unavailable or does not permit a conclusion.

Note: Outcomes graded as insufficient are not included in this table. Insufficient evidence was provided for divalproex (anticonvulsant), tiagabine (anticonvulsant), citalopram (selective serotonin reuptake inhibitor), all tricyclic antidepressants, bupropion (other second-generation antidepressant), and mirtazapine (other second-generation antidepressant). No studies that met inclusion criteria rated as having low or medium risk of bias evaluated lamotrigine (anticonvulsant), any benzodiazepine, desvenlafaxine (serotonin-norepinephrine reuptake inhibitor), duloxetine (serotonin-norepinephrine reuptake inhibitor), nefazodone (other second-generation antidepressant), or trazodone (other second-generation antidepressant).

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†—SMD from the Beck Depression Inventory or from various other depression symptom scales.
‡—Strength of evidence changed from moderate in the prior review to low for no difference in the updated review. Only two of three studies favored treatment, one favored placebo. Imprecision, inconsistency, and effect sizes near the null prompted the change in grade.
§—Strength of evidence changed from moderate in the prior review to low in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, and findings were imprecise.
‖—Strength of evidence changed from low to low for no difference in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, findings were imprecise, and most individual study estimates were close to the null.
¶—Strength of evidence changed from insufficient to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
**—Strength of evidence changed from low to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
††—Strength of evidence changed from moderate in the prior review to low in the updated review. The findings were imprecise, only one of three individual studies found significant differences between study groups, and the sample sizes were small.

Summary of Efficacy and Strength of Evidence of PTSD Pharmacologic Treatments

Treatment	Symptom	No. of trials (no. of participants)	Findings	Strength of evidence
Venlafaxine (serotonin-norepinephrine reuptake inhibitor)	PTSD symptoms*	2 (687)	Reduced PTSD symptoms SMD of −0.35 and −0.26 for 2 individual studies	●●○
	PTSD symptom remission	2 (687)	Greater PTSD symptom remission RD of 0.12 and 0.15 across individual studies	●●○¶
	Depression symptoms†	2 (687)	Reduced depression symptoms Between-group mean difference of −2.6 and −1.6 across individual studies	●●○**
Prazosin (alpha blocker)	PTSD symptoms*	3 (117)	Reduced PTSD symptoms SMD = −0.52 (95% CI, −0.90 to −0.14)	●○○
Topiramate (anticonvulsant)	PTSD symptoms*	3 (142)	Reduced PTSD symptoms SMD ranged from −1.85 to −0.38 across individual studies	●○○††
Olanzapine (antipsychotic)	PTSD symptoms*	2 (47)	Reduced PTSD symptoms SMD of −1.15 and −0.96 across individual studies, both significantly favored treatment	●○○
		3 (62)	SMD ranged from −1.15 to 0.89 across individual studies All studies favored treatment (2 of 3 studies $P < 0.05$)	
Risperidone (antipsychotic)	PTSD symptoms*	4 (422)	Reduced PTSD symptoms SMD = −0.26 (95% CI, −0.52 to −0.01)	●○○

Strength of evidence scale

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||—Strength of evidence changed from low to low for no difference in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, findings were imprecise, and most individual study estimates were close to the null.
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††—Strength of evidence changed from moderate in the prior review to low in the updated review. The findings were imprecise; only one of three individual studies found significant differences between study groups, and the sample sizes were small.

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For the family physician in the clinic, the VA/DoD guideline recommends screening adults at risk of PTSD (e.g., those exposed to traumatic events such as war, natural disaster, or violence) with the Primary Care PTSD Screen (available at https://www.ptsd.va.gov/professional/assessment/screens/pc-ptsd.asp) or the PTSD Checklist (available at https://www.mirecc.va.gov/cih-visn2/Documents/Clinical/PCL-5_with_Info_Sheet.pdf). Those who screen positive should have a structured interview using a tool such as the Clinician-Administered PTSD Scale. Once the diagnosis is made, the VA/DoD guideline recommends starting with individual trauma-focused psychotherapy, based on evidence that psychotherapy results in a greater change in symptoms with more persistent benefits. Pharmacotherapy may be used when psychotherapy is not available.[3]

Editor's Note: *AFP*'s SOR ratings are different from the AHRQ Strength of Evidence (SOE) ratings. Dr. Saguil is a contributing editor for *AFP*.

The views expressed in this piece are the author's own and do not reflect the views of the Uniformed Services University of the Health Sciences, the U.S. Army, or the Department of Defense.

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3. U.S. Department of Veterans Affairs, U.S. Department of Defense. VA/DoD clinical practice guidelines. Management of posttraumatic stress disorder and acute stress reaction 2017. https://www.healthquality.va.gov/guidelines/MH/ptsd/VADoDPTSDCPGFinal012418.pdf. Accessed October 8, 2018. ■