

# Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: 2023 Update of the Evidence Base for the PTSD Trials Standardized Data Repository

## Executive Summary



### Main Points

- This update adds 60 newly published randomized controlled trials (RCTs) on posttraumatic stress disorder (PTSD) and comorbid PTSD/substance use disorder (SUD) to the previous Agency for Healthcare Research and Quality (AHRQ) report on this topic<sup>1</sup> and the National Center for PTSD (NCPTSD) PTSD Trials Standardized Data Repository (PTSD-Repository);<sup>2</sup> the new total of included RCTs is 496.
- Across all 496 RCTs:
  - The most commonly studied intervention was psychotherapy (44%), followed by pharmacologic interventions (19%), and complementary and integrative health (6%); 7 percent of studies used both pharmacologic and psychotherapeutic interventions.
  - Overall, most studies were conducted in the United States (59%) and had sample sizes in the range of 25 to 99 participants (58%), with a relatively small number of studies enrolling more than 200 participants (8%).
  - Data on race was reported in 57 percent of studies and ethnicity in 31 percent; 42 percent did not provide information on race or ethnicity.
  - Almost a third of studies (32%) targeted specific types of trauma; combat-related trauma was the most commonly targeted (15% of all studies), followed by terrorism/political violence/forced displacement (5%) and accidents (2%); 51 percent allowed a mix of trauma types, and 17 percent did not provide information on participant trauma types.

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- Across the 60 newly added RCTs:
  - The most commonly studied intervention was psychotherapy (40%), followed by complementary and integrative health (10%) and nonpharmacologic biologic interventions (8%); 8 percent of studies used both pharmacologic and psychotherapeutic interventions.
  - Just over half of the newly added RCTs were conducted in the United States (53%), enrolled community (not specifically military) participants, and had sample sizes in the range of 25 to 99 participants (53%); a relatively small number of studies enrolled more than 200 participants (7%).
  - 20 percent of studies targeted a specific trauma type, and about half of studies allowed a mix of trauma types (53%); 27 percent did not provide information on participant trauma types.
- This update also includes risk of bias (RoB) using the updated Cochrane RoB 2 tool for randomized trials for all 496 included RCTs.
  - Across all 496 RCTs, RoB was rated as low RoB for 14 percent, some concerns for 27 percent, and high for the remaining studies (60%).
  - Of the 60 newly added RCTs, RoB was rated as low RoB for 17 percent, some concerns for 17 percent, and high for the remaining studies (67%).



## Background and Purpose

PTSD is a disorder that results from being exposed to a traumatic event. People with PTSD have symptoms such as flashbacks, avoidance of trauma-related stimuli, negative beliefs about themselves and/or others, and hypervigilance. These symptoms reduce quality of life and function. The purpose of this report is to update the previous AHRQ report<sup>1</sup> by identifying and abstracting data from newly published RCTs examining treatment for PTSD and comorbid PTSD/SUD: this project builds upon our previous work.<sup>1,2,3,4</sup> These data will inform the subsequent update and expansion of the [PTSD-Repository](#) (a publicly accessible clinical trials database maintained by the NCPTSD).<sup>5</sup> A comprehensive data repository allows future systematic reviews to easily identify includable studies and extract data relevant to their review. The PTSD-Repository can also help identify research gaps to determine future research priorities and encourage researchers to adopt standard data elements in research and reporting. In addition, it can serve as a source for patients, clinicians, and policymakers to search for evidence on the effectiveness of specific interventions and augment existing patient education tools.



## Methods

We followed methods outlined in the AHRQ Evidence-based Practice Center Program Methods Guidance (<https://effectivehealthcare.ahrq.gov/topics/ebp-methods-guide/overview>) where applicable.<sup>6</sup> For this update, we searched PTSDpubs (formerly PILOTS), Ovid<sup>®</sup> MEDLINE<sup>®</sup>, Cochrane CENTRAL, PsycINFO<sup>®</sup>, Embase<sup>®</sup>, CINAHL<sup>®</sup>, and Scopus<sup>®</sup> for eligible RCTs published from August 1, 2021, to March 3, 2023. We

dually reviewed citations from the literature search and potentially includable full-text articles for eligibility, resolving disagreement by consensus. We developed evidence tables for the prior updates<sup>1,2</sup> and for this update; one team member abstracted data from included RCTs into these evidence tables and a second reviewer checked for accuracy and completeness. An investigator assessed RoB for newly added studies using Cochrane's RoB 2: A Revised Tool for Assessing Risk of Bias in Randomized Trials,<sup>7</sup> and a second reviewer checked for accuracy. For studies included prior to our implementation of RoB 2 (k=388), an investigator reassessed a subset of the 388 studies using RoB 2 and a second reviewer checked for accuracy. We provide summary statistics for RoB 2 assessment of all 496 studies in this update.



## Results

In this update, we added 60 RCTs examining treatments for PTSD for a total of 496 included RCTs overall. The updated report now includes 136 pharmacologic studies (trials with at least one medication arm) and 360 nonpharmacologic studies (trials with no medication arms). The 496 trials were published from 1988 to 2023. Across all 496 RCTs, the most commonly studied intervention was psychotherapy (44%), followed by pharmacologic interventions (19%), and complementary and integrative health (6%); 7 percent of studies used both pharmacologic and psychotherapeutic interventions. Overall, most studies were conducted in the United States (59%), and enrolled community (i.e., not specifically military) populations (54%). A total of 42,467 participants are represented; sample sizes ranged from 8 to 943 with most studies (58%) enrolling 25 to 99 participants. Across all 496 RCTs, RoB was rated as low RoB for 14 percent, some concerns for 27 percent, and high for the remaining studies (60%).

Among the 60 newly added RCTs, psychotherapy interventions were the most commonly employed (40%), followed by complementary and integrative health (10%). About half of studies were conducted in the United States (53%), enrolled community participants (53%), and enrolled participants with a mix of trauma types (53%). The newly added studies had sample sizes ranging from 20 to 916, with most studies having a sample size between 25 and 99 participants (53%). The Clinician-Administered PTSD Scale (CAPS) and the PTSD CheckList (PCL) were measures most frequently used to assess continuous PTSD outcomes, used in 40 percent and 39 percent of studies, respectively. PTSD diagnostic change or clinically meaningful response were assessed in 50 percent of studies. Among non-PTSD outcomes, depression was the most commonly assessed (60% of the newly added studies). Of the 60 newly added RCTs, 67 percent were rated as high RoB, 17 percent were rated as some concerns, and 17 percent were rated as low RoB.



## Limitations

Study inclusion was limited to studies published in English. Many data elements were not reported or were reported in an inconsistent manner across the available body of literature. Data elements that were infrequently reported include the number of participants with a history of traumatic brain injuries, SUD, or suicidal ideation/behavior, and mean number of trauma types per participant.



## Implications and Conclusions

This report updates the previous AHRQ report on this topic<sup>1</sup> with comprehensive data, calculated standardized effect sizes for PTSD outcomes, and RoB assessment from 60 recently published trials. This update also includes RoB assessment for all 436 previously included studies. As with the previous AHRQ reports on this topic,<sup>1,2,3</sup> this update will be used by NCPTSD to inform updates to the PTSD-Repository, a publicly available PTSD trials database (accessible at <https://www.ptsd.va.gov/ptsdrepository/index.asp>) that allows clinical, research, education, and policy stakeholders to understand current research on treatment effectiveness and harms, and enables these stakeholders to more quickly and accurately make informed decisions about future research, mental health policy, and clinical care priorities. These updates ensure that all available evidence is included and accessible for a broad range of users. Updating RoB assessment to the same scale for all studies and adding standardized effect sizes will allow for more efficient and accurate comparisons across PTSD trials.



## References

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2. O'Neil ME, Cheney TP, Hsu FC, et al. Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: An Update of the PTSD-Repository Evidence Base. Comparative Effectiveness Review No. 235. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 20(21)-EHC029. Rockville, MD: Agency for Healthcare Research and Quality; November 2020. doi: 10.23970/AHRQEPCCER235.

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## Full Report

O'Neil ME, Cheney TP, Yu Y, Hart EL, Holmes RS, Blazina I, Clauss K, Veazie SP, Griffin JC, Jungbauer R, Zaccari B, Fu R, Carlson KF, Chou R. Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: 2023 Update of the Evidence Base for the PTSD Trials Standardized Data Repository. Systematic Review. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 75Q80120D00006.) AHRQ Publication No. 23-EHC028. Rockville, MD: Agency for Healthcare Research and Quality; September 2023. DOI: <https://doi.org/10.23970/AHRQEPCTSD2023>. Posted final reports are located on the Effective Health Care Program search [page](#).

