



Systematic Review

Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: 2022 Update of the PTSD-Repository Evidence Base

Executive Summary



Main Points

- This update adds 48 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) report¹ and National Center for PTSD (NCPTSD) PTSD Trials Standardized Data Repository (PTSD-Repository);² the new total of included RCTs is 437.
- Across the 48 newly published RCTs, the most commonly studied intervention was psychotherapy (50%), followed by complementary and integrative health (17%) and pharmacologic interventions (16%); 8 percent of studies used both pharmacologic and psychotherapeutic interventions.
- Almost half of studies were conducted in the United States (46%), or enrolled community participants (52%). Most studies had sample sizes in the range of 25 to 99 participants (69%), with a relatively small number of studies enrolling more than 200 participants (8%).
- The PTSD Checklist (PCL) and the Clinician-Administered PTSD Scale (CAPS) were measures most frequently used to assess continuous PTSD outcomes, used in 62% and 52% of studies, respectively. PTSD diagnostic change or clinically meaningful response was assessed in 58 percent of studies. Among non-PTSD outcomes, depression was the most commonly assessed (67% of studies).
- For studies added in this update, we abstracted data to calculate standardized effect sizes for continuous PTSD outcomes, and risk of bias (RoB) was assessed using the updated Cochrane RoB 2 tool for randomized trials. Of these 48 RCTs, 52 percent were rated as high RoB, 31 percent were rated as low RoB, and the remaining studies were rated as some concerns (15%). Note that, for previously included studies (n=389), RoB is being progressively reassessed using RoB 2 and will be provided in a future update, along with calculated standardized effect sizes.





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. This project builds upon our previous work;^{1,3,4} the purpose of this report is to identify and abstract data from RCTs examining treatment for PTSD and comorbid PTSD/SUD to update the previous AHRQ report¹ which will inform the subsequent update and expansion of the [PTSD-Repository](#) (a publicly accessible clinical trials database maintained by the NCPTSD).² 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/ceer-methods-guide/overview>) where applicable.⁵ For this update, we searched PTSDpubs (formerly PILOTS), Ovid[®] MEDLINE[®], Cochrane CENTRAL, PsycINFO[®], Embase[®], CINAHL[®], and Scopus[®] for eligible RCTs published from June 1, 2018, to January 26, 2022. We dually reviewed citations from the literature search and potentially includable full-text articles for eligibility, resolving disagreement by consensus. One team member abstracted data from included RCTs published prior to July 30, 2021, into evidence tables developed for the last update¹ and a second reviewer checked for accuracy and completeness. Note that studies published after July 30, 2021 will be included in the next annual update. An investigator assessed RoB for newly added studies and a subset of the 389 studies previously included in the PTSD-Repository using Cochrane's RoB 2: A Revised Tool for Assessing Risk of Bias in Randomized Trials,⁶ and a second reviewer checked for accuracy. Note that we do not provide summary statistics for RoB assessment of all 437 studies in this update, since we will not complete updated RoB assessment for all 389 studies from the previous report in this phase; complete RoB assessment using the updated Cochrane RoB 2 tool and summary statistics will be provided in future annual updates.



Results

In this update, we added 48 RCTs examining treatments for PTSD for a total of 437 included RCTs overall. The updated report now includes 125 pharmacologic studies (trials with at least one medication arm) and 312 nonpharmacologic studies (trials with no medication arms). Among the 48 newly added RCTs, psychotherapy interventions were the most commonly employed (50%), followed by complementary and integrative health (17%). Approximately half of studies were conducted in the United States (46%), enrolled community participants (52%) and participants with a mix of trauma types (48%). Studies typically had sample sizes ranging from 25 to 99 participants (69%). The PCL and the CAPS were measures most frequently used to assess continuous PTSD outcomes, used in 62% and 52% of studies, respectively. PTSD diagnostic change or clinically meaningful response were assessed in 58 percent of studies. Among non-PTSD outcomes, depression was the most commonly assessed (67% of studies). Of the 48 newly added RCTs, 52 percent were rated as high RoB, 15 percent were rated as some concerns, and 31 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 with comprehensive data, calculated standardized effect sizes for PTSD outcomes, and RoB assessment from 48 recently published trials. As with the previous AHRQ reports, 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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3. O'Neil M, McDonagh M, Hsu F, et al. Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: Groundwork for a Publicly Available Repository of Randomized Controlled Trial Data. Technical Brief No. 32. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 19-EHC018-EF. Rockville, MD: Agency for Healthcare Research and Quality; May 2019. doi: 10.23970/AHRQEPCTB32. PMID: 31145565.
4. O'Neil ME, Harik JM, McDonagh MS, et al. Development of the PTSD-Repository: a publicly available repository of randomized controlled trials for posttraumatic stress disorder. *J Trauma Stress*. 2020 Aug;33(4):410-9. doi: 10.1002/jts.22520. PMID: 32667076
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Full Report

O'Neil ME, Cheney TP, Yu Y, Hart EL, Holmes RS, Blazina I, Veazie SP, Griffin JC, Fu R, Carlson KF, Chou R. Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: 2022 Update of the PTSD-Repository Evidence Base. Systematic Review. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 75Q80120D00006.) AHRQ Publication No. 22(23)-EHC040. Rockville, MD: Agency for Healthcare Research and Quality; October 2022. DOI: <https://doi.org/10.23970/AHRQEPCTSD2022>. Posted final reports are located on the Effective Health Care Program search [page](#).

