

Pharmacologic and Nonpharmacologic Treatments for PTSD: An Update of the PTSD-Repository Evidence Base

Evidence Summary



Main Points

- This update adds newly published studies on posttraumatic stress disorder (PTSD, 47 randomized controlled trials [RCTs]), studies targeting comorbid PTSD and substance use disorders (SUDs, 21 RCTs), and variables related to comorbidities such as SUDs and suicidal ideation/behavior, to the PTSD-Repository, a database of RCTs of interventions to treat PTSD.
- We abstracted data from 389 RCTs, which included psychotherapeutic interventions (63%), pharmacologic interventions (25%), and complementary and integrative or nonpharmacologic biological treatments (12%).
- Reporting was incomplete for many data elements in published studies: less than half of studies reported on the loss of PTSD diagnosis (i.e., no longer meeting criteria for PTSD) or clinically meaningful response/remission of symptoms.
- Risk of bias (ROB) was assessed for all included studies; most were rated as having a medium ROB (57%), and only 6 percent were rated as having a low ROB.
- An exploration of an expanded ROB system was developed and pilot tested.



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 functioning. The purpose of this project was to update and expand the PTSD Trials Standardized Data Repository (PTSD-Repository), a publicly accessible clinical trials database maintained by the National Center for PTSD (NCPTSD). 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. It will also 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. The PTSD-Repository included data published between 1980 and May 22, 2020 from 318 RCTs of interventions targeting treatment of PTSD. This update expands on our previous work (Agency for Healthcare Research and Quality [AHRQ] Technical Brief No. 32)^{1,2} by adding RCTs published since that work was completed, broadening some inclusion criteria (e.g., studies of comorbid PTSD/SUD) and elements of data abstracted (e.g., inclusion/exclusion criteria related to suicide and psychotic disorders), and conducting ROB assessments for all studies included in the repository (both those found in this update and those included previously). We also explored expanding specific elements of the ROB criteria that may affect studies of PTSD more particularly, pilot testing on a small set of RCTs.



Methods

We followed methods outlined in the AHRQ Evidence-based Practice Center (EPC) Program Methods Guidance (<https://effectivehealthcare.ahrq.gov/topics/er-methods-guide/overview>) where applicable.³ For this update, we searched PTSDpubs (formerly PILOTS), Ovid[®] MEDLINE[®], Cochrane CENTRAL, PsycINFO[®], Embase[®], CINAHL[®], and Scopus[®] for eligible RCTs published from June 2018 to May 22, 2020. We also reviewed studies excluded in Technical Brief No. 32¹ (a prior version of this report) for interventions targeting comorbid PTSD and SUD that would meet the expanded inclusion criterion. 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 into evidence tables developed for Technical Brief No. 32,¹ and a second reviewer checked for accuracy and completeness. An investigator assessed ROB for previously included studies and newly added studies following the methods used in a prior review of PTSD intervention studies, Comparative Effectiveness Review No. 207,⁴ and a second reviewer checked for accuracy. At the request of the sponsor, NCPTSD, and with guidance from NCPTSD and a Technical Expert Panel with expertise in ROB assessment methods, we explored development of additional, or refinement of existing, ROB elements relevant to the PTSD-Repository. The revised criteria were tested on a small subset of studies.



Results

In this update, we added 47 RCTs targeting PTSD and 21 targeting comorbid PTSD/SUD for a total of 389 RCTs included in the PTSD-Repository. The updated report now includes 115 pharmacologic studies (trials with at least one medication arm) and 274 nonpharmacologic studies (trials with no medication arms – all other types of studies including psychotherapy, nonpharmacologic biologic, and complementary and integrative

health interventions were classified as nonpharmacologic). The trials were published from 1988 to 2020, with the majority published within the last 10 years.

Psychotherapeutic interventions were the most commonly studied (63%), followed by pharmacologic interventions (25%). The majority of studies were conducted in the United States (62%), and most had sample sizes in the range of 25 to 99 participants (60%), with a relatively small number of studies enrolling more than 200 participants (9%). More studies enrolled participants from a community population (55%) than from a military, veteran, or other population, and the majority of studies were conducted in the outpatient setting (72%). Studies typically enrolled participants with a mix of trauma types (53%), followed by studies of participants with combat-related trauma (18%). Sixty percent of all studies included in the PTSD-Repository were rated as having a medium ROB, and only 6 percent were rated as having a low ROB. Our exploration and pilot testing of an expanded ROB assessment system emphasized more detailed assessment of elements relevant to PTSD studies including: (1) assessment of methods for managing missing data, including both drop out from treatment and missing measurements (i.e., loss to followup), (2) differential assessment of subjective and objective outcomes, and (3) consideration of a 5-category overall rating system.



Limitations

Many data elements were not reported or were reported in an inconsistent manner across the available body of literature. For example, less than half of the included studies reported loss of PTSD diagnosis or clinically meaningful response/remission of symptoms. Several other 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. As part of this PTSD-Repository update, we abstracted additional details about many of these important variables (e.g., suicide-related inclusion/exclusion criteria as well as outcomes), and also documented when these data were not reported in primary studies so that users of the PTSD-Repository are aware of the source of missing data.



Implications and Conclusions

The PTSD-Repository is a comprehensive database of detailed data compiled from trials of PTSD interventions in adults. The PTSD-Repository will allow clinical, research, education, and policy stakeholders to understand current research on treatment effectiveness and harms, and enable these stakeholders to more quickly and accurately make informed decisions about future research, mental health policy, and clinical care priorities.

This report updates the studies and variables included in the PTSD-Repository to include recently published trials of interventions for PTSD (47 RCTs), interventions targeting comorbid PTSD/SUD (21 RCTs), variables related to comorbidities such as suicidal ideation/behavior and SUDs, and risk of bias assessment. Data abstraction and ROB assessment for all 389 included RCTs are being used by NCPTSD to update the Web-based, interactive PTSD-Repository, a publicly available trials database available at <https://www.ptsd.va.gov/ptsdrepository/index.asp>.

The PTSD-Repository may be expanded in the future by including new studies or additional outcomes and by using an expanded ROB system. Conversion of the abstracted data into an interactive and searchable Web-based dissemination of the PTSD-Repository was recently completed by the NCPTSD and includes key data summaries of the trials included in the PTSD-Repository.



References

1. 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. www.effectivehealthcare.ahrq.gov/reports/final.cfm. Posted final reports are located on the Effective Health Care Program search page: <https://effectivehealthcare.ahrq.gov/>. PMID: 31145565.
2. 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. *Journal of Traumatic Stress*. [Epub ahead of print 15 July 2020] doi: 10.1002/jts.22520.
3. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication No. 10(14)-EHC063-EF. Rockville, MD: Agency for Healthcare Research and Quality; January 2014. Chapters available at: <https://effectivehealthcare.ahrq.gov/topics/ceer-methods-guide/overview>.
4. Hoffman V, Middleton JC, Feltner C, et al. Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder: A Systematic Review Update. Comparative Effectiveness Review No. 207. (Prepared by the RTI International–University of North Carolina at Chapel Hill Evidence-based Practice Center under Contract No. 290-2015-00011-I for AHRQ and PCORI.) AHRQ Publication No. 18-EHC011-EF. PCORI Publication No. 2018-SR-01. Rockville, MD: Agency for Healthcare Research and Quality; May 2018. doi: 10.23970/AHRQEPCCER207.

Full Report

O'Neil ME, Cheney TP, Hsu FC, Carlson KF, Hart EL, Holmes RS, Murphy KM, Graham E, Cameron DC, Kahler J, Lewis M, Kaplan J, McDonagh MS. 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: <https://doi.org/10.23970/AHRQEPCCER235>. Posted final reports are located on the Effective Health Care Program [search page](#).

