

Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: 2024 Update of the Evidence Base for the PTSD Trials Standardized Data Repository

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None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

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The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. The U.S. Department of Veterans Affairs requested this report from the EPC Program at AHRQ. AHRQ assigned this report to the following EPC: Pacific Northwest Evidence-based Practice Center (Contract Number: 75Q80120D00006).

The reports and assessments provide organizations with comprehensive, evidence-based information on common medical conditions, and new healthcare technologies and strategies. This evidence report provides an overview of key issues related to the interventions included—for example, current indications, relevant patient populations and subgroups of interest, outcomes measured, and contextual factors that may affect decisions regarding the intervention. The report includes data abstracted from published randomized controlled trials on interventions for posttraumatic stress disorder. These data were adapted to support the development of a publicly available repository by the National Center for Posttraumatic Stress Disorder (NCPTSD).

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for healthcare quality improvement projects throughout the Nation. The reports undergo peer review and public comment prior to their release as a final report.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform individual health plans, providers, and purchasers as well as the healthcare system as a whole by providing important information to help improve healthcare quality.

If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

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

Abstract

Objectives. Identify and abstract data from randomized controlled trials (RCTs) examining treatment for posttraumatic stress disorder (PTSD) and comorbid PTSD/substance use disorder to update the previous Agency for Healthcare Research and Quality (AHRQ) report on this topic and the National Center for PTSD (NCPTSD) PTSD Trials Standardized Data Repository (PTSD Repository) with newly included trials.

Data sources. We searched PTSDpubs, Ovid® MEDLINE®, Cochrane CENTRAL, PsycINFO®, Embase®, CINAHL®, and Scopus® for eligible RCTs published from March 1, 2023, to April 1, 2024

Review methods. In consultation with AHRQ and NCPTSD, we updated the evidence tables for the PTSD Repository by including evidence published after publication of the last update and studies that met updated inclusion criteria for the database (e.g., interventions that do not require a provider). Evidence tables were also updated with calculated standardized effect sizes for continuous PTSD outcomes for all included studies. We assessed risk of bias (RoB) for all included studies using the Revised Cochrane Risk of Bias 2 (RoB 2) tool for randomized trials.

Results. We added 54 RCTs examining treatments for PTSD, for a total of 550 included trials published from 1988 to April 1, 2024. Among all 550 included RCTs, studies of psychotherapy interventions were the most common (47%), followed by pharmacologic interventions (17%). Most studies were conducted in the United States (58%) and had sample sizes ranging from 25 to 99 participants (59%). Approximately half of the studies enrolled community (i.e., not specifically military) participants (54%), and most were conducted in outpatient settings (78%). Studies typically enrolled participants with a mix of trauma types (52%). Among all 550 included RCTs, RoB was rated as low for 18 percent of studies, 27 percent were rated as having some concerns, and the remaining 54 percent were rated as high RoB.

Among the 54 newly added RCTs, psychotherapy interventions were the most commonly employed (44%), followed by pharmacotherapy (13%) and nonpharmacologic cognitive interventions (11%). Approximately half of the studies were conducted in the United States (48%), and enrolled community participants (54%) and participants with a mix of trauma types (56%). Studies typically had sample sizes ranging from 25 to 99 participants (61%). Of the newly added RCTs, RoB was rated as low for 39 percent of studies, 17 percent were rated as having some concerns, and the remaining 44 percent were rated as high RoB.

Conclusions. This report updates the previous AHRQ report to add 54 RCTs, for a total of 550 trials. This update adds comprehensive data and RoB assessment for the newly included RCTs, and standardized effect sizes for continuous PTSD outcomes for all included studies. As with the

previous AHRQ update, this report will serve as the updated evidence base for the PTSD Repository, a comprehensive database of PTSD trials.

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Comparative Effectiveness Review Number xxx

Pharmacologic and Nonpharmacologic Treatments for Posttraumatic Stress Disorder: 2024 Update of the Evidence Base for the PTSD Trials Standardized Data Repository

Executive Summary



Main Points

- This update adds 54 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 topic¹ and the National Center for PTSD (NCPTSD) PTSD Trials Standardized Data Repository (PTSD Repository);² the new total of included RCTs is 550.
- Across all 550 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 (58%) and had sample sizes in the range of 25 to 99 participants (59%), with a relatively small number of studies enrolling more than 200 participants (8%).
 - Just under a third of studies (32%) provided data on race and ethnicity, and another 25 percent provided data on race only; data were not provided for race or ethnicity in 42 percent of studies.
 - Almost a third of studies (30%) targeted specific types of trauma: combat-related trauma was the most commonly targeted (14% of all studies); 52 percent allowed a mix of trauma types, and 18 percent did not provide information on trauma types.
 - Risk of bias (RoB) was rated as low for 18 percent, some concerns for 27 percent, and high for the remaining 54 percent of studies.





Main Points, continued

- Across the 54 newly added RCTs:
 - The most commonly studied intervention was psychotherapy (44%), followed by pharmacotherapy (13%) and nonpharmacologic cognitive interventions (11%); 6 percent of studies used both pharmacologic and psychotherapeutic interventions.
 - About half of the newly added RCTs were conducted in the United States (48%), and enrolled community (not specifically military) participants (54%); sample sizes were in the range of 25 to 99 participants in most studies (61%).
 - RoB was rated as low for 39 percent, some concerns for 17 percent, and high for the remaining 44 percent of studies.

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 overarching purpose of this project is to identify randomized controlled trials (RCTs) of PTSD interventions for adults and abstract detailed, standardized data into evidence tables. This work is designed to provide a broad range of stakeholders with up-to-date, comprehensive data on PTSD treatment research. The evidence tables created for this project form the basis of the PTSD Repository, a publicly accessible clinical trials database maintained by the NCPTSD (accessible at <https://www.ptsd.va.gov/ptsdrepository/index.asp>).² We initiated this work in 2018, and regular updates coordinated with NCPTSD have included adding newly published RCTs, some additional data elements, and risk of bias (ROB) assessment for all included studies. This current report updates the previous AHRQ report¹ by identifying and abstracting data from newly published RCTs examining treatment for PTSD and comorbid PTSD/SUD, building upon our previous work.^{1,3,4,5,6} These data will continue to inform the subsequent update and expansion of the PTSD Repository.²



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.⁷ For this update, we searched PTSDpubs (formerly PILOTS), Ovid® MEDLINE®, Cochrane CENTRAL, PsycINFO®, Embase®, CINAHL®, and Scopus® for eligible RCTs published from March 1, 2023, to April 1, 2024. We also reviewed previously excluded studies for interventions that meet the updated eligibility criteria, to include self-help or internet-based interventions (those that do not require a provider). We dually reviewed citations from the literature search and potentially

includable full-text articles for eligibility. One team member assessed RoB using Cochrane's RoB 2: A Revised Tool for Assessing Risk of Bias in Randomized Trials,⁸ and a second reviewer checked for accuracy. Disagreements on eligibility or RoB were resolved through consensus. We developed evidence tables for the prior updates^{1,3,4} 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. Standardized effect sizes for continuous PTSD outcomes were calculated by study biostatisticians.



Results

In this update, we added 54 RCTs examining treatments for PTSD for a total of 550 included RCTs overall. The updated report now includes 147 pharmacologic studies (trials with at least one medication arm) and 403 nonpharmacologic studies (trials with no medication arms). The 550 trials were published from 1988 to 2024. Across all 550 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. Interventions targeting comorbid PTSD/SUD or SUD were studied in 6% of included RCTs. Overall, most studies were conducted in the United States (58%), and enrolled community (i.e., not specifically military) populations (54%). A total of 48,177 participants are represented; sample sizes ranged from 8 to 1,001 with most studies (59%) enrolling 25 to 99 participants. The Clinician-Administered PTSD Scale (CAPS) and the PTSD CheckList (PCL) were measures most frequently used to assess continuous PTSD outcomes, used in 57 percent and 42 percent of studies, respectively. PTSD diagnostic change or clinically meaningful response were assessed in 55 percent of studies. Among non-PTSD outcomes, depression was the most commonly assessed (69%), followed by anxiety (33%). Across all 550 RCTs, RoB was rated as low RoB for 18 percent, some concerns for 27 percent, and high for the remaining studies (54%).

Among the 54 newly added RCTs, psychotherapy interventions were the most commonly employed (44%), followed by pharmacotherapy (13%) and nonpharmacologic cognitive interventions (11%). Interventions targeting comorbid PTSD/SUD were studied in 3% of newly added RCTs. About half of studies were conducted in the United States (48%), enrolled community participants (54%), and enrolled participants with a mix of trauma types (56%). The newly added studies had sample sizes ranging from 22 to 1,001, with most studies (61%) having a sample size between 25 and 99 participants. The Clinician-Administered PTSD Scale (CAPS) and the PTSD CheckList (PCL) were measures most frequently used to assess continuous PTSD outcomes, used in 57 percent and 63 percent of studies, respectively. PTSD diagnostic change or clinically meaningful response were assessed in 61 percent of studies. Among non-PTSD outcomes, depression was the most commonly assessed (59% of the newly added studies). Of the 54 newly added RCTs, 44 percent were rated as high RoB, 17 percent were rated as some concerns, and 39 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 duration of PTSD diagnosis or symptoms, number of treatment-naïve participants, mean number of trauma types per participant, number of participants with a history of traumatic brain injuries, SUD, and other psychiatric comorbidities, and suicidal ideation/behavior.



Implications and Conclusions

This report updates the previous AHRQ report on this topic¹ with comprehensive data, calculated standardized effect sizes for continuous PTSD outcomes, and RoB assessment from 54 newly included trials. This update also includes calculated standardized effect sizes for continuous PTSD outcomes for all 550 included trials. As with the previous AHRQ reports on this topic,^{1,3,4,5} 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. Inclusion of RoB assessment using the same scale for all studies and standardized effect sizes allows for more efficient and accurate comparisons across PTSD trials.



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1. Introduction

1.1 Background

Posttraumatic stress disorder (PTSD) is a prevalent disorder with significant negative impacts on health, quality of life, and healthcare utilization.¹ Lifetime prevalence of PTSD is estimated to be between 3.4 and 8.0 percent in U.S. civilians and 7.7 to 13.4 percent in U.S. military veterans.²⁻⁵ Individuals with PTSD are more likely to experience other mental health comorbidities compared to those without, particularly substance use and mood disorders such as depression.^{3,6,7}

Since PTSD was first included by the Diagnostic and Statistical Manual of Mental Disorders, third edition (DSM-III) in 1980, there have been over 500 published randomized controlled trials (RCTs) evaluating a wide range of treatments and treatment modalities (e.g., psychotherapy, psychopharmacotherapy, complementary and integrative approaches, etc.). Many systematic reviews also aim to include nonrandomized comparative studies, which likely number in the thousands. Given the large and varied body of evidence, to make reviews on this topic feasible, even some of the most comprehensive systematic reviews on PTSD have excluded some intervention types (e.g., complementary and integrative approaches) due to the prohibitively large number of studies that would have to be reviewed.⁸ Without a comprehensive database containing all published RCTs on PTSD, clinicians and researchers may need to consult multiple reviews in order to synthesize evidence across studies and evaluate the effectiveness and comparative effectiveness of treatments. In addition, heterogeneity of review methods, scope, and data presentation make it difficult to synthesize across reviews and have led to variation in conclusions.^{9,10} Methodological differences, such as data coding approaches and combining treatment categories for analysis, further limit the comparability of findings.

1.2 Purpose and Scope

Answering important clinical questions about PTSD treatments requires the examination of all available data, yet existing systematic reviews do not make this logistically easy, and they may intentionally exclude important treatments due to resource constraints. It is also important to be able to understand limitations or potential bias in studies when synthesizing information about what types of interventions work for whom. Furthermore, even when abstracted data are made publicly available, they may be presented in a format that does not readily lend itself to re-analysis without reformatting or re-entry. Hence, there is a need for a single source that provides up-to-date, detailed, comprehensive data and risk of bias assessment on existing PTSD trials to better address current clinical, research, and policy stakeholders' needs. To address this need, the PTSD Trials Standardized Data Repository or "PTSD Repository" was created to: (1) serve as a data source for future systematic reviews, meta-analyses, or other cross-study comparisons; (2) help identify research gaps to determine future research priorities; (3) encourage researchers to adopt standard data elements in research and reporting; (4) serve as a source for clinicians seeking information on effectiveness of interventions for patients with particular demographics or exposures; (5) provide the public a source to search for evidence on interventions they or their loved ones are considering; (6) provide policymakers with an up-to-date accounting of evidence to respond to inquiries; and (7) augment and inform the use of patient education tools or decision aids such as the online PTSD Treatment Decision Aid.¹¹ The Department of Veterans Affairs'

1. Introduction

National Center for PTSD (NCPTSD) partnered with the Agency for Healthcare Research and Quality (AHRQ) to develop the evidence tables that form the basis of the PTSD Repository.

The initial development of the evidence tables and subsequent update have been detailed elsewhere.¹²⁻¹⁶ The purpose of this update review, and the four earlier AHRQ reviews, is to search the literature to identify and abstract data from RCTs examining treatment for PTSD and comorbid PTSD/substance use disorder (SUD) to inform the PTSD Repository.¹⁷ This publicly accessible clinical trials database is maintained by NCPTSD and available at <https://www.ptsd.va.gov/ptsdrepository/index.asp>. The initial 2018 report¹² identified 318 studies. Previous updates¹⁴⁻¹⁶ have included: 1) addition of 178 RCTs through extension of the search dates to include newly published studies and expansion of the inclusion criteria to include studies focused on treating comorbid PTSD/SUD; 2) revised evidence tables to include more detailed and discrete data elements and facilitate integration with the online PTSD Repository; 3) abstraction of additional data elements (for example, information on comorbidities and suicide and self-harm related outcomes); 4) expanded abstraction of results data for PTSD outcomes; 5) calculation of standardized effect sizes for continuous PTSD outcomes; 6) RoB assessment using the Cochrane RoB 2 tool. This current update builds on the prior AHRQ reports by adding 54 RCTs (for a total of 550 trials in the database) with complete evidence tables and risk of bias assessment, updating inclusion criteria to include self-help or internet-based interventions (those that do not require a provider, on the recommendation of the Technical Expert Panel and NCPTSD), and providing calculated standardized effect sizes for all included studies.

1.3 Key Question

Key Question 1. What interventions have been studied for the treatment of PTSD alone or with comorbid SUD?

The Key Question is based on updating the same body of literature included in the initial report¹² and expanded to include interventions targeting comorbid PTSD/SUD, as examined in the 2020 update.¹⁴ The PICOTS (populations, interventions, comparators, outcomes, timing, settings, study design) criteria are:

- **Population(s):**
 - Adults (≥ 18 years old) diagnosed with PTSD by a clinician or through a patient-reported assessment tool
- **Interventions:**
 - Pharmacologic and nonpharmacologic interventions, including complementary and integrative approaches, for treatment of PTSD or comorbid PTSD/SUD
- **Comparators:**
 - Any comparator, including another intervention, waitlist/minimal attention, usual care, or placebo
- **Outcomes:**
 - Overall PTSD outcome, PTSD diagnostic change, PTSD clinically meaningful change
 - Other outcomes – Anxiety, anger, depression, function, quality of life, sleep, substance use, suicide- and self-directed violence, withdrawal due to adverse events, serious adverse events

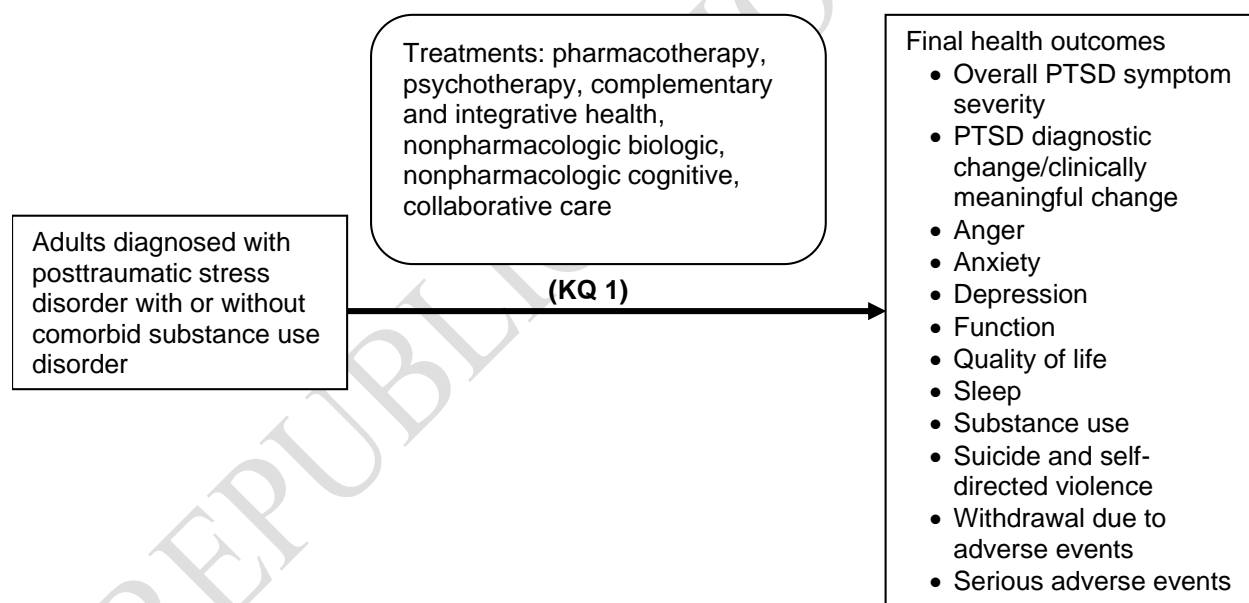
1. Introduction

- **Timing:**
 - No limitation on study duration or length of followup
- **Settings:**
 - No limitation on study setting
- **Study Design:**
 - RCTs

1.4 Analytic Framework

Figure 1 depicts the Key Question within the context of the PICOTS inclusion and exclusion criteria presented in Table 1 in the Methods chapter. Figure 1 illustrates how PTSD treatments – including pharmacotherapy, psychotherapy, nonpharmacologic biologic treatments (e.g., biofeedback, vagal nerve stimulation), and complementary and integrative approaches – may be associated with health and functional outcomes (such as PTSD symptoms and diagnosis, substance use, anxiety, depression, and quality of life), as well as how these interventions may be associated with harms.

Figure 1. Analytic framework for treatments of posttraumatic stress disorder



Abbreviations: KQ = Key Question; PTSD = posttraumatic stress disorder

2. Methods

This report follows the methods suggested in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews¹⁸ where applicable to creating a systematic data repository. Methods were determined *a priori* after discussion with AHRQ and the National Center for PTSD (NCPTSD), and are consistent with methods utilized in our first report¹² and the last update.¹⁶ A protocol was published on the AHRQ website (<https://effectivehealthcare.ahrq.gov/products/ptsd-pharm-non-pharm-treatment-update/protocol>).

2.1 Criteria for Inclusion/Exclusion of Studies in the Review

Detailed inclusion and exclusion criteria for the Key Question are listed in Table 1 following the PICOTS (populations, interventions, comparators, outcomes, timing, settings, study design) criteria identified above (see Key Question). We included treatments for posttraumatic stress disorder (PTSD) and comorbid PTSD/substance use disorder (SUD). Treatments targeting PTSD and a comorbid condition other than SUD were included as long as the treatment could be used for PTSD alone (i.e., without the presence of the comorbid condition). For example, treatments for PTSD and insomnia were included because sleep difficulties are often part of a standalone PTSD diagnosis, and therefore these treatments could be used for PTSD without the presence of another diagnosis. Similarly, treatments for comorbid PTSD and depression were included if they were appropriate for individuals with a standalone PTSD diagnosis because of the frequency of mood-related impacts of PTSD even without a comorbid diagnosis of depression. These inclusion and exclusion criteria were updated from the previous update report¹⁶ to include interventions that do not require a provider (e.g., mobile apps, attention bias modification).

2. Methods

Table 1. PICOTS: Inclusion and exclusion criteria

PICOTS	Include	Exclude
Populations	<ul style="list-style-type: none"> Adults (mean age ≥ 18 years old) with PTSD diagnosed by a clinician or through the administration of a validated clinician-administered or patient-reported assessment tool 	<ul style="list-style-type: none"> Children (mean age < 18 years old) Diagnosis of acute stress disorder Studies that do not specify criteria used to diagnose PTSD Sample population with $< 80\%$ of participants diagnosed with PTSD (i.e., $> 20\%$ with study-defined subthreshold PTSD), or if include comorbid SUD, $< 80\%$ of participants diagnosed with comorbid PTSD/SUD
Interventions	<ul style="list-style-type: none"> Pharmacologic and/or nonpharmacologic interventions for PTSD or comorbid PTSD/SUD in adults Interventions can include any pharmacologic component, whether singly, in combination with other treatment categories, or compared with another intervention category, or complementary and integrative approaches, nonpharmacologic biologic treatments, and psychotherapeutic treatments Interventions targeting core symptoms of PTSD (e.g., insomnia and nightmares related to PTSD) are included No limitation on delivery format or provider type; provider involvement not required (e.g., self-help or internet-based interventions are included) 	<ul style="list-style-type: none"> Interventions designed to simultaneously target PTSD and comorbid conditions other than SUD if they cannot be standalone PTSD interventions (i.e., interventions targeting PTSD and a comorbidity such as depression are included if the intervention can be a treatment for PTSD alone). Interventions designed to prevent PTSD, treat self-stigma, or facilitate posttraumatic growth are excluded unless they are designed to treat PTSD directly as well.
Comparators	<ul style="list-style-type: none"> No limitations applied. Direct head-to-head comparison of PTSD interventions are included. Interventions such as waitlist/minimal attention, usual care, placebo, or other minimally-active treatment (e.g., education or attention control) are categorized as "Controls" 	None
Outcomes	<ul style="list-style-type: none"> Any overall PTSD outcome 	<ul style="list-style-type: none"> Studies reporting only individual symptoms or symptom clusters without overall PTSD outcome Studies that did not perform formal statistical test for between-group comparison of a PTSD outcome
Timing	<ul style="list-style-type: none"> Any study duration and length of followup 	None
Setting	<ul style="list-style-type: none"> All study settings 	None
Study Design	<ul style="list-style-type: none"> RCTs 	<ul style="list-style-type: none"> Non-RCTs Selected systematic reviews will be considered as reference check sources of studies to be reviewed for possible inclusion (data will be abstracted from individual studies rather than from systematic reviews)

Abbreviations: PICOTS = populations, interventions, comparators, outcomes, timing, settings, study design; PTSD = posttraumatic stress disorder; RCTs = randomized controlled trials; SUD = substance use disorder

2. Methods

2.2 Literature Search

Electronic databases were searched for evidence from March 1, 2023, to April 1, 2024. Literature databases searched included PTSDpubs (formerly PILOTS), Ovid® MEDLINE®, Cochrane CENTRAL, Embase®, the Cumulative Index to Nursing and Allied Health Literature (CINAHL®), SCOPUS, and PsycINFO®. Search strategies are provided in Appendix A. The search strategies were developed and conducted by the Pacific Northwest Evidence-based Practice Center (EPC) librarian and peer reviewed by a NCPTSD librarian. We also reviewed previously excluded studies for interventions that meet the updated inclusion criterion. A gray literature search was not conducted. Due to the nature of the project, a portal for submission of Supplemental Evidence And Data for Systematic review (SEADS) was not opened for this project.

PICOTS (Table 1) were used to determine eligibility for inclusion and exclusion of abstracts. One reviewer determined eligibility at the title/abstract review stage and a second investigator reviewed excluded records. For records included at the title/abstract review stage, full-text articles were retrieved and reviewed independently for eligibility by two reviewers. Studies may have met more than one exclusion criterion, but for efficiency, only one reason was coded (the first reason identified by reviewer). Disagreements were resolved by consensus of the team of investigators. A record of included studies is available in Appendix B and studies excluded at the full-text level with reasons for exclusion appear in Appendix C.

2.3 Data Abstraction

After studies were screened and deemed to meet inclusion criteria, study data were abstracted, including study design, year, setting, country, sample size, eligibility criteria, source(s) of funding, study characteristics, population characteristics, intervention characteristics, and study results (see Appendix D for a complete list of data elements abstracted). The Technical Expert Panel and NCPTSD provided guidance about important variables to include. Data were abstracted into detailed evidence tables in Microsoft® Excel developed for the first report¹² and revised for the subsequent update reports¹⁴⁻¹⁶ to include additional data elements such as detailed study inclusion/exclusion criteria and specific data elements for inclusion criteria related to suicide and psychosis, proportion of participants with comorbidities at baseline (e.g., suicidal ideation/behavior, psychotic, personality, and anxiety disorder, and prior hospitalization), results for secondary PTSD outcomes at treatment arm-level, and results for suicide- or self-directed violence-related outcomes including suicidal ideation/behavior. These data elements were abstracted for all included studies and were provided in the evidence tables of the prior reports. Secondary publications were reviewed for potentially relevant data in addition to the primary publication. The citation and an indication of whether the publication provided additional data were abstracted for all secondary publications. Data abstracted from all publications (primary and secondary) were entered under the same study identifier in the data tables. Authors' studies included in previous updates were contacted via email and provided with the opportunity to review abstracted data as well as provide unpublished data. Unpublished data are included in the evidence tables as a separate data table (Appendix E-13). i

For the 2022 update,¹⁵ the evidence tables were restructured to ensure that future updates to the PTSD Repository no longer required any hand searching and editing when transforming data from the Microsoft® Excel data tables into the PTSD Repository online database, and that data

2. Methods

integration processes could be automated using replicable syntax. The 2022 update also added calculation of standardized effect sizes for continuous PTSD outcomes for newly included studies, provided the study reported the necessary data. Both between and within group effect sizes were calculated, allowing users to examine and compare effectiveness of interventions. These updated processes were maintained in subsequent updates. This 2024 update adds calculated standardized effect size data for continuous PTSD outcomes for all 550 included trials (496 previously included trials and the 54 newly included trials). All abstracted data were dual reviewed for accuracy and completeness.

A separate evidence table was constructed to record risk of bias (RoB) assessments, described below. All studies were incorporated in the summarized results presented below, regardless of overall RoB rating.

All data from the evidence tables were combined into a single excel file for usability, organized with separate data tables as worksheets (tabs) within the file (Appendix E). The Contents tab lists all data tables as well as the most recent literature search end date, and the date of the most recent change to the file. A data dictionary is also included for additional information on the included variables.

2.4 Evidence Synthesis

The evidence tables are designed to enable a variety of syntheses that would be of interest to different stakeholders. Results from studies were not synthesized, but characteristics of included studies including number of publications by year, study sample size, proportion of studies enrolling community versus military/veteran populations, and distribution of studies by PTSD assessment method, were summarized using simple counts and proportions.

2.5 Standardized Effect Size Calculation

Meta-analysis was not performed. To facilitate quantitative syntheses by users of the evidence tables, standardized effect sizes were calculated for continuous PTSD outcomes, provided the necessary data was reported in the study. This update includes calculated standardized effect sizes for continuous PTSD outcomes for all 550 included RCTs.

To facilitate comparison across studies and across outcomes, a within-arm effect size was calculated using the formula in Figure 2, as an analog of Cohen's *d*. Hedge's *g* was used as the standardized effect size for between-arm comparisons. The following data are required to calculate a between-arm effect size: 1) N analyzed at followup; 2) mean score at followup, mean change score, or mean difference between arms (adjusted or unadjusted); and 3) measure of variance for item 2 (i.e., standard deviation, standard error, or confidence interval). Hedge's *g* was calculated based on adjusted mean difference, if reported. Otherwise, it was calculated based on followup scores or change scores, with followup scores preferred. We preferred followup scores because they have been shown to be more conservative when combining randomized controlled trials (RCTs) compared to placebo when baseline scores show some evidence of imbalance. When baseline scores are balanced, the followup score and change score provide similar results.¹⁹ For studies not reporting standard deviation, it was calculated from 95 percent confidence interval whenever reported. All analyses were performed using R (version 4.2.3).

2. Methods

Figure 2. Within-arm effect size formula

$$d = \frac{Mean_{followup} - Mean_{baseline}}{s}$$

$$\text{Where, } s = \sqrt{s_{baseline}^2 + s_{followup}^2 - 2 \times corr \times s_{baseline} \times s_{followup}}$$

$$\text{Assuming correlation} = 0.5 \text{ and } N_{baseline} = N_{followup}$$

Abbreviations: d = analog of Cohen's d; s = standard deviation; corr = correlation

2.6 Assessment of Methodological Risk of Bias of Individual Studies

Because previously-included studies from prior reports¹⁴ were assessed with an earlier version of Cochrane's RoB assessment tool based on the AHRQ Methods Guide for Effectiveness and Comparative Effectiveness Review,²⁰ we updated RoB assessments for all included RCTs using Cochrane's RoB 2 system. The updated RoB assessments were completed for all included studies in the previous update report,¹⁶ ensuring that all studies in the database now use the same, gold standard RoB 2 assessment. To clarify aspects of the RoB assessments, and to ensure transparency and ease of future updating, we included detailed definitions related to how RoB was assessed and clearly described cutoff values (e.g., for attrition) applied when implementing the Cochrane RoB 2 system. We also abstracted RoB-related data into additional columns to document the overall percent of primary PTSD outcome assessment data that was missing (i.e., overall attrition from measurement) and the percent primary PTSD outcome data in each arm of the study of missing that was missing (i.e., differential attrition from measurement). We assessed RoB for all reported continuous outcomes; because three studies did not report a continuous PTSD outcome, we instead assessed RoB for the PTSD dichotomous outcome in these three studies. As many studies assessed multiple outcome measures that differed in assessor blinding, we have included a second subset of RoB domain 4 questions, domain 4 ratings, and overall study ratings for these studies, which correspond to ratings based on these additional outcome measure(s). The variable names (headers) for these are appended with the title, "Rating for additional outcome(s)". For newly included studies, RoB was assessed using the same assessment tool for RoB 2.

2.7 Grading the Strength of Evidence for Major Comparisons and Outcomes

Strength of evidence was not assessed for this review.

2.8 Assessing Applicability

Applicability was not assessed for this review.

2. Methods

2.9 Peer Review and Public Commentary

Experts in the field of PTSD were invited to provide external peer review of this review and evidence tables. Comments and editorial review were also sought from the AHRQ Task Order Officer, an associate editor, and partners at NCPTSD. The draft report was posted on the AHRQ website for 4 weeks to elicit public comment. In response to reviewers' comments, we revised text as needed and addressed all relevant reviewer comments in an associated disposition of comments report with the authors' individual responses. This report will be posted after the publication of the final evidence report on the AHRQ website.

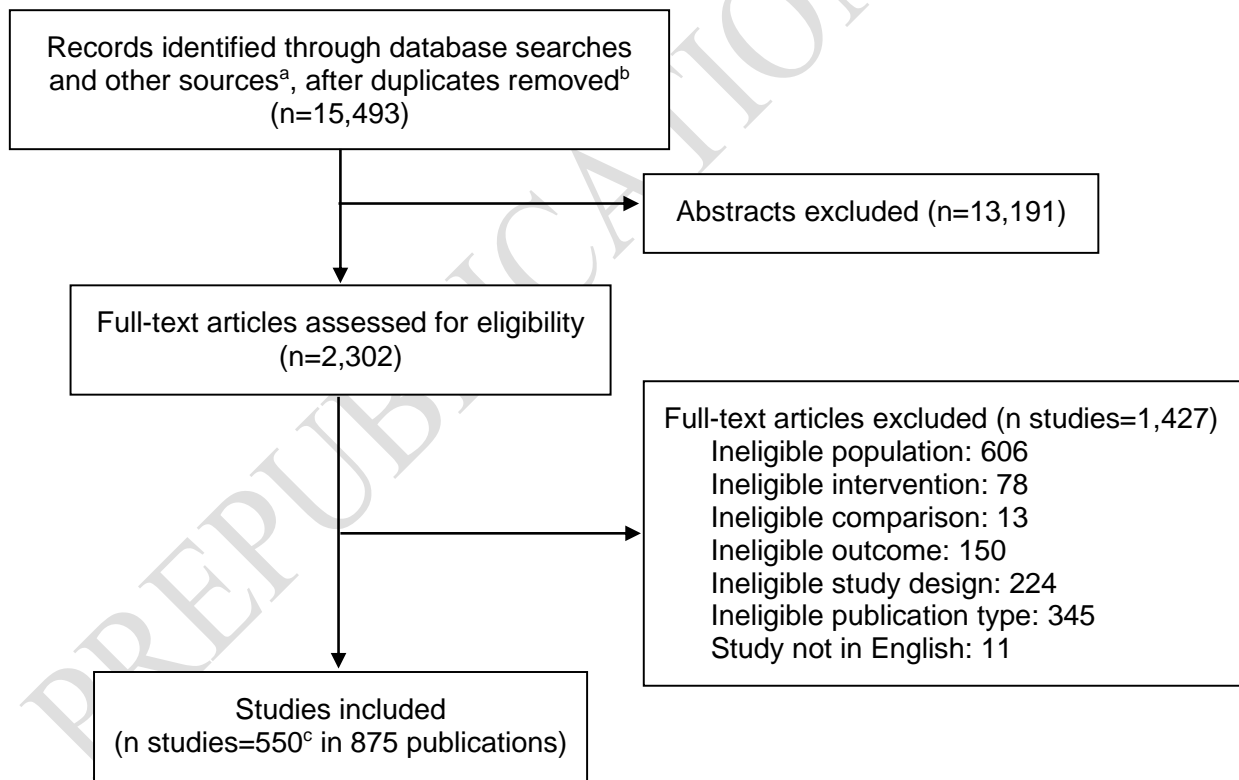
PREPUBLICATION FINAL

3. Results

3.1 Results of Literature Search

In this update we included 54 new trials²¹⁻⁷⁴ published through April 1, 2024, bringing the total number of included trials in this report to 550 (in 875 publications). The literature flow diagram (Figure 3) summarizes the search and selection of articles performed previously in prior reports in addition to this update to provide a comprehensive overview of all included studies. Combining all database searches and other sources yielded 15,493 unique records. After review of abstracts and titles, 2,302 articles were selected for full-text review, and 550 trials were determined to meet inclusion criteria and were designated for data abstraction. Reasons for exclusion of studies were ineligible population, intervention, comparison, outcome, study design, publication type, and foreign language articles. Appendix B contains the list of studies that met inclusion criteria; Appendix C lists studies excluded upon full-text review and reasons for exclusion.

Figure 3. Literature flow diagram (summary of all included studies)



^aOther sources include prior reports, reference lists of relevant articles, systematic reviews, etc.

^bMultiple update searches were performed with overlapping search dates; reported is number of unique records across searches.

^cIn this update report, there are 54 new trials.²¹⁻⁷⁴ There are 550 total studies in 548 records (Appendix B).

3.2 Results, Characteristics of Included Studies

3.2 Characteristics of Included Studies

Interventions were first classified by treatment focus: posttraumatic stress disorder (PTSD), PTSD and substance use disorder (SUD), SUD, active control, or inactive control. In this classification, each arm was classified into a single category. Control arms were categorized based on the intervention and study design. Interventions without an active treatment component, such as waitlist or placebo, are coded as inactive control. Intervention arms being used to control for active components of another treatment are coded as active control if there is expected to be some active effect but less than the main treatment (e.g., superiority trials). For example, for a trial comparing prolonged exposure versus psychoeducation, with a superiority design hypothesizing larger effect with prolonged exposure, the psychoeducation arm would be coded as active control. In trials with a noninferiority design both intervention arms will have PTSD coded as the treatment focus.

Treatments were also classified by the intervention categories described in Table 2. These categories included pharmacologic treatments and five nonpharmacologic treatment categories (psychotherapy, nonpharmacologic biologic, nonpharmacologic cognitive, complementary and integrative health, and collaborative care), plus control. Study arms coded as active control for treatment focus above, are categorized as control and additionally categorized corresponding to the actual components of the treatment for intervention category. Using the same example as above, the prolonged exposure arm (coded as PTSD for treatment focus above) would be categorized as psychotherapy, and the psychoeducation arm (coded as active control for treatment focus) would be categorized as control and also as psychotherapy. Each treatment arm was classified; an arm could have more than one intervention category because a treatment could include interventions falling into different categories. For example, a study that evaluated a combined psychotherapy and pharmacotherapy intervention versus waitlist would have the first arm classified as both psychotherapy and pharmacotherapy, and the second arm as inactive control.

3.2 Results, Characteristics of Included Studies

Table 2. Intervention categories with examples^a

Category	Definition	Examples
Pharmacotherapy	Medication	Antiadrenergic drugs Antidepressants Antipsychotics Benzodiazepines Cannabinoids Mood Stabilizers
Nonpharmacologic Biologic	Interventions that use a medical device or procedure of some kind.	Electroconvulsive therapy Hyperbaric oxygen therapy Repetitive transcranial magnetic stimulation Stellate ganglion block Vagal nerve stimulation Neurofeedback
Complementary and Integrative Health	Wide category of approaches that are considered to be outside the standard in the current practice of Western medicine.	Acupuncture Clinical hypnosis Meditation Massage therapy Natural products Tai chi/qi gong Yoga
Psychotherapy	Talk therapy with a licensed provider	Cognitive Processing Therapy Eye Movement Desensitization and Reprocessing Cognitive Behavioral Therapy Narrative Exposure Therapy Present-centered therapy Prolonged Exposure
Nonpharmacologic Cognitive	Interventions that teach cognitive skills to improve attention.	Attention bias modification Attention control training
Collaborative Care	Interventions in which integrated medical and mental health treatment is delivered in primary care, often by nurse managers.	Centrally assisted collaborative telecare Three component model Trauma-informed collaborative care
Other	Treatments that don't fit into another category	Animal-assisted Other physical activity and recreational therapies Digital interventions not delivered by a licensed provider
Inactive Control	Interventions which are essentially inactive or are not presumed to have an effect on mental health symptoms	Waitlist Placebo Assessment only

^aTable 2 intervention lists and categories adapted from the 2017 Department of Veterans Affairs/Department of Defense clinical practice guideline.⁷⁵

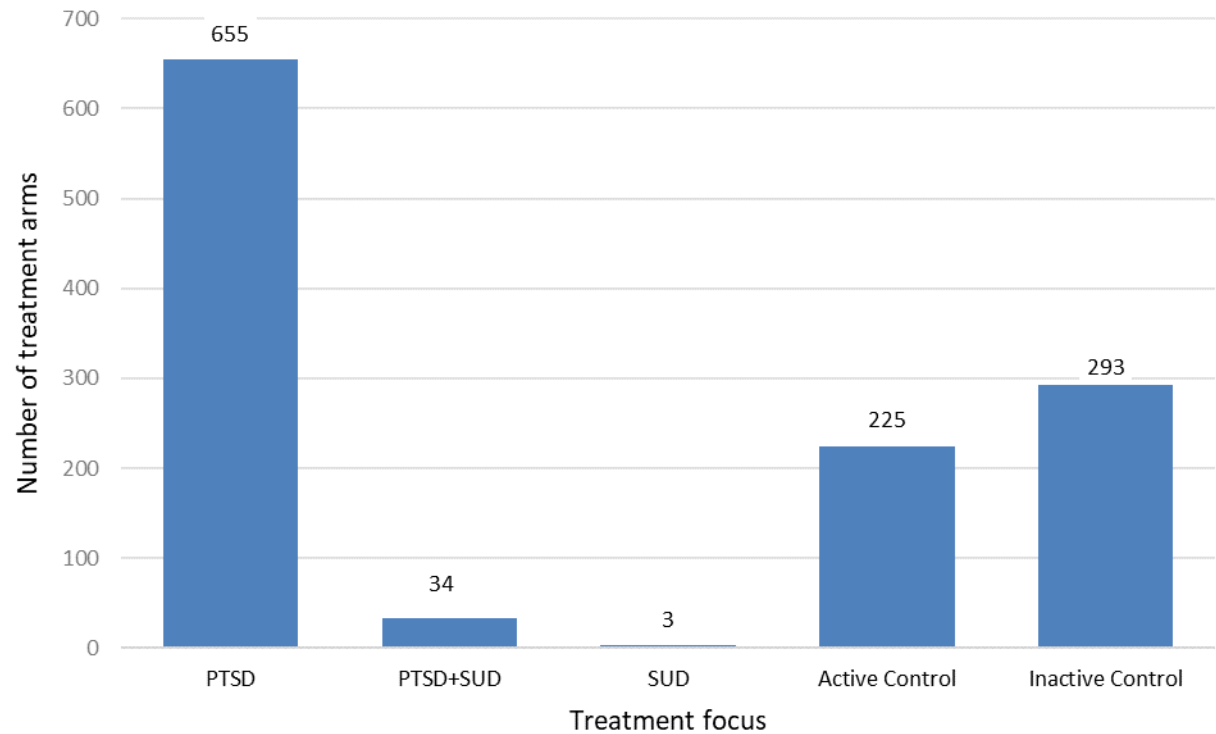
3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

3.2.1 Overall Studies Included in the Evidence Tables

The data abstraction evidence tables (Appendix E) for this report present detailed information on study and population characteristics for the 550 total included trials.

Across included studies, comorbid PTSD/SUD was the focus for 3 percent of treatment arms and less than 1 percent focused on SUD (Figure 4). Fifty-four percent of treatment arms addressed PTSD, 19 percent were active controls, and 24 percent were inactive control arms.

Figure 4. Summary of all included studies: distribution of treatment arms by treatment focus^a

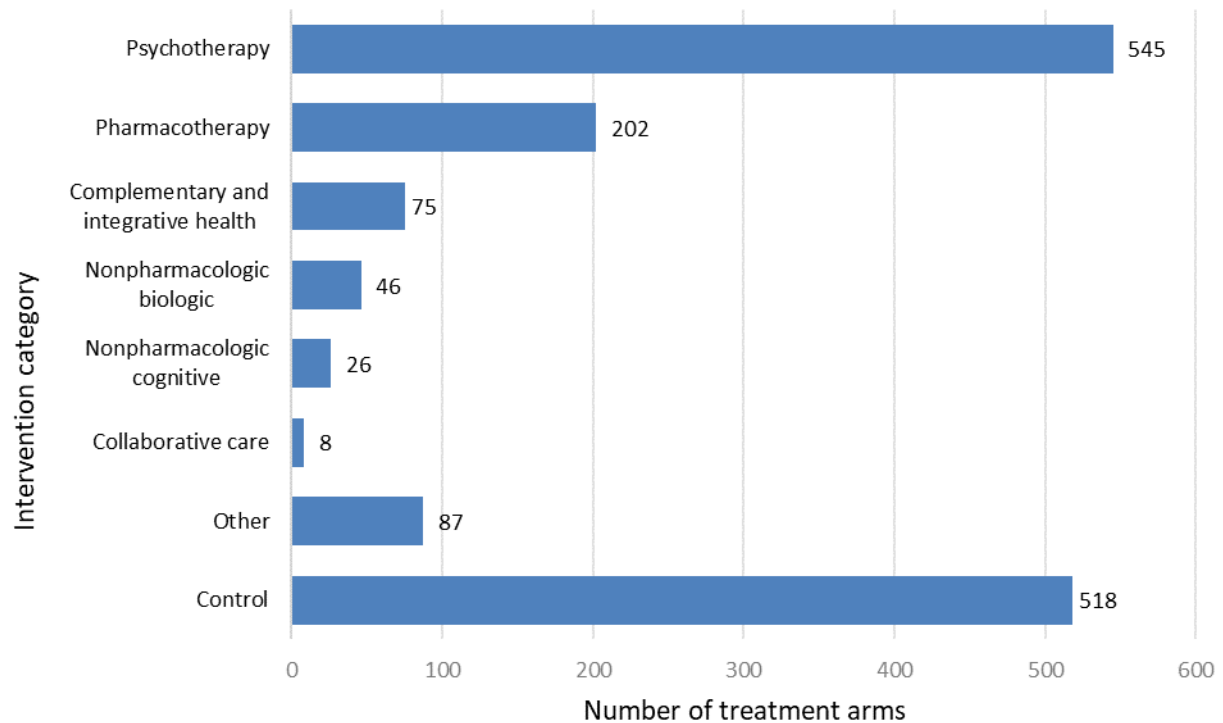


^aStudies have more than one treatment arm.
Abbreviations: PTSD = posttraumatic stress disorder; SUD = substance use disorder

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

The distribution of treatment arms by intervention category is shown in Figure 5. Psychotherapy was the most frequently studied treatment, employed in 47 percent of total treatment arms, followed by pharmacotherapy in 17 percent of treatment arms. Control arms comprised 45 percent of treatment arms (either inactive or active).

Figure 5. Summary of all included studies: distribution of treatment arms by intervention category^a



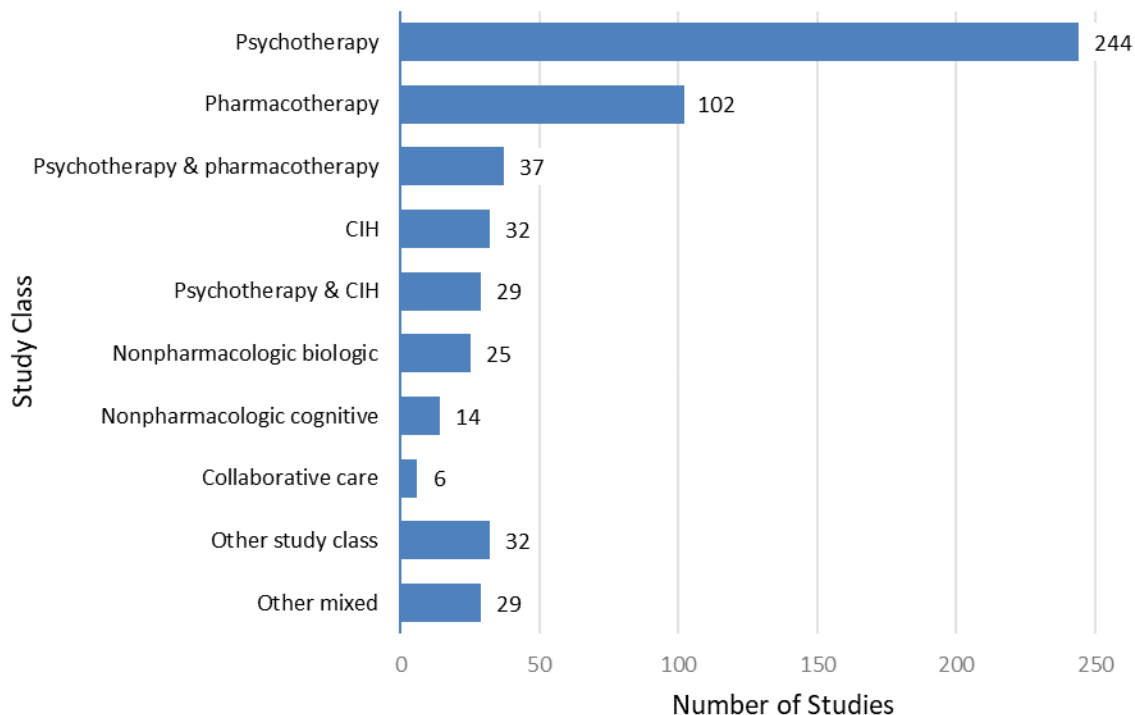
^aStudies have more than one treatment arm. Counts for these categories sum to greater than the total of 1,210 treatment arms in the included studies since some treatment arms combine multiple interventions of different categories. For example, one treatment arm could combine a psychotherapy treatment with a pharmacotherapy treatment. Thus each category would count for one within this single arm.

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

Studies were grouped into ten study classes based on interventions studied. For studies in which the treatment arms were all the same category, or compared with a treatment arm categorized as inactive control, the study was categorized as the study class of the active treatment(s). For example, a study of prolonged exposure (psychotherapy) versus waitlist (inactive control) would be categorized as psychotherapy for the study class. The category Other study class includes studies in which all interventions are classified as Other for intervention category. Studies in which the treatment arms were of different intervention categories were classified into a combination category for study class, for the most common combinations (i.e., psychotherapy and pharmacotherapy, and psychotherapy and complementary and integrative health [CIH]). Other combinations were grouped in the Other mixed study class.

Psychotherapy was the most commonly studied intervention (44% of studies), followed by pharmacotherapy interventions (19%), and combined psychotherapy and pharmacotherapy (7%) (Figure 6).

Figure 6. Summary of all included studies: distribution of included publications by study class



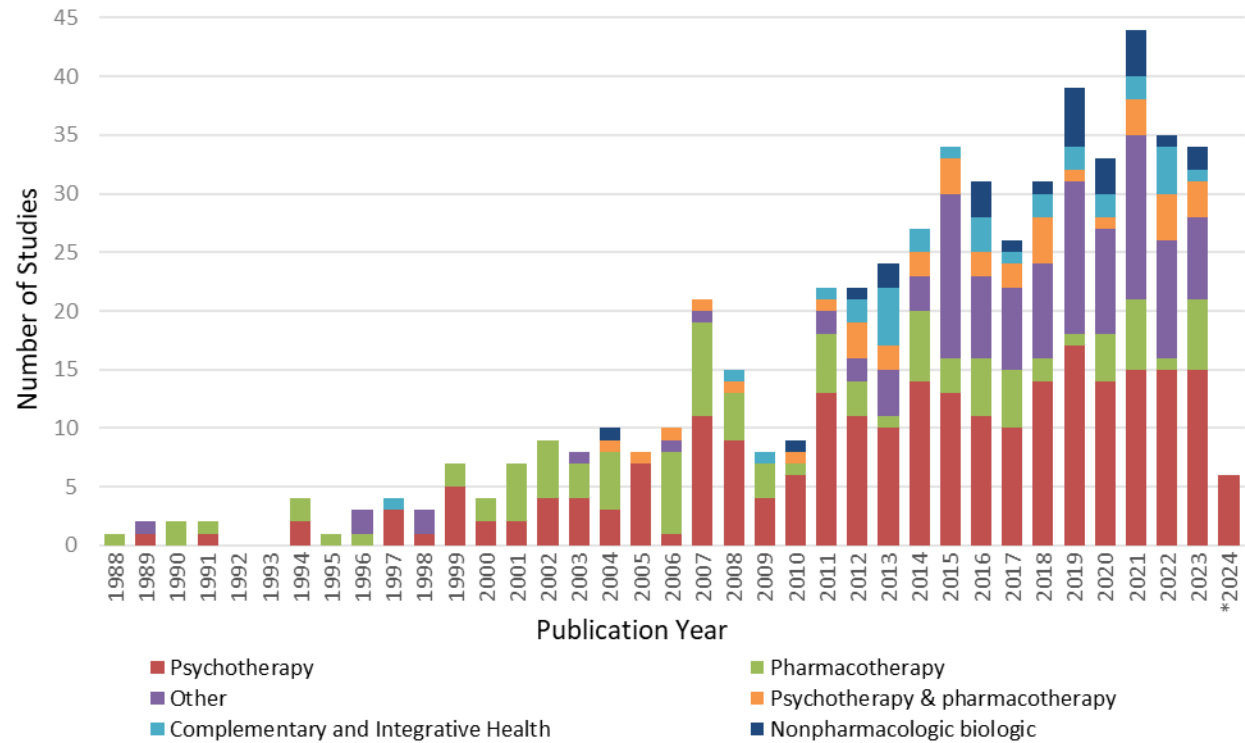
Other mixed includes studies in which the interventions studied were a combination other than psychotherapy & pharmacotherapy or psychotherapy & CIH (e.g., nonpharmacologic biologic & psychotherapy). Other study class includes studies of interventions classified as Other for intervention category.

Abbreviations: CIH = complementary and integrative health

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

The publication dates of the included studies ranged from 1988 to partway through 2024 (Figure 7). Forty-four studies were published in 2021, the highest amount of any year. The number of studies published per year increased in the 2000s then again in the 2010s. Most studies of CIH interventions were published after 2010, a trend also observed with studies of nonpharmacologic biologic treatments.

Figure 7. Summary of all included studies: distribution of included publications by year^a

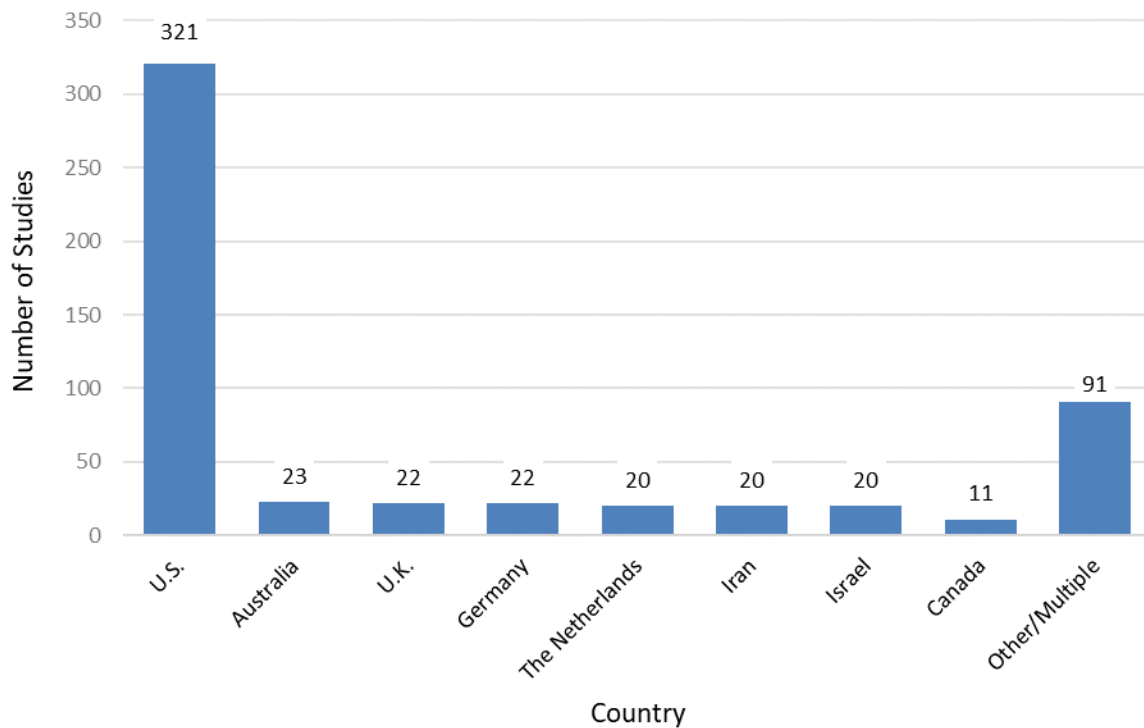


^a2024 is a partial year (search date was through April 2024).

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

The majority of studies (58%) were conducted in the United States (Figure 8), though it is important to note that inclusion eligibility required that the study was published in English.

Figure 8. Summary of all included studies: distribution of included studies by country



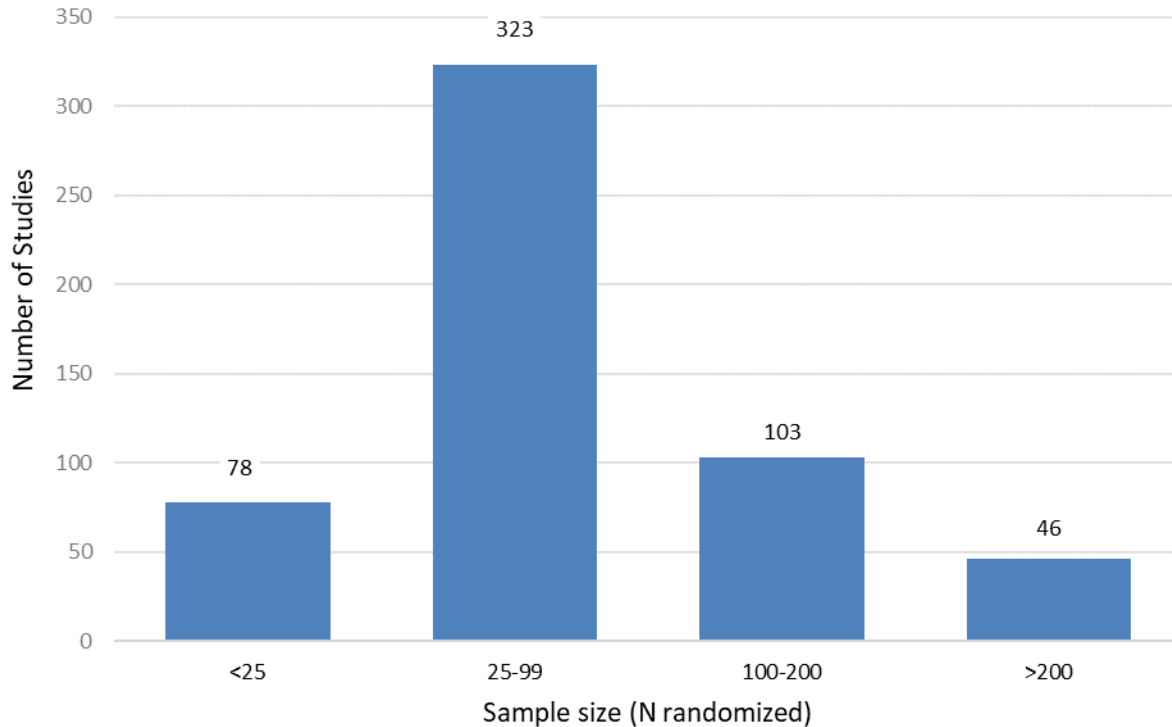
Multiple = study conducted in multiple countries. Only the eight countries with largest number of studies were included in this graph, studies conducted in the remaining countries are counted in “Other/Multiple”.

Abbreviations: U.K. = United Kingdom; U.S. = United States

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

There was no restriction on sample size for study inclusion. Sample sizes across included studies ranged from 8 to 1,001 participants, with a total of 48,177 participants included in the database. The median sample size was 58 (interquartile range [IQR] 32 to 103). A little over half of studies (59%) had sample sizes in the range of 25 to 99 participants and a relatively small number of studies (14%) enrolled fewer than 25 participants (Figure 9).

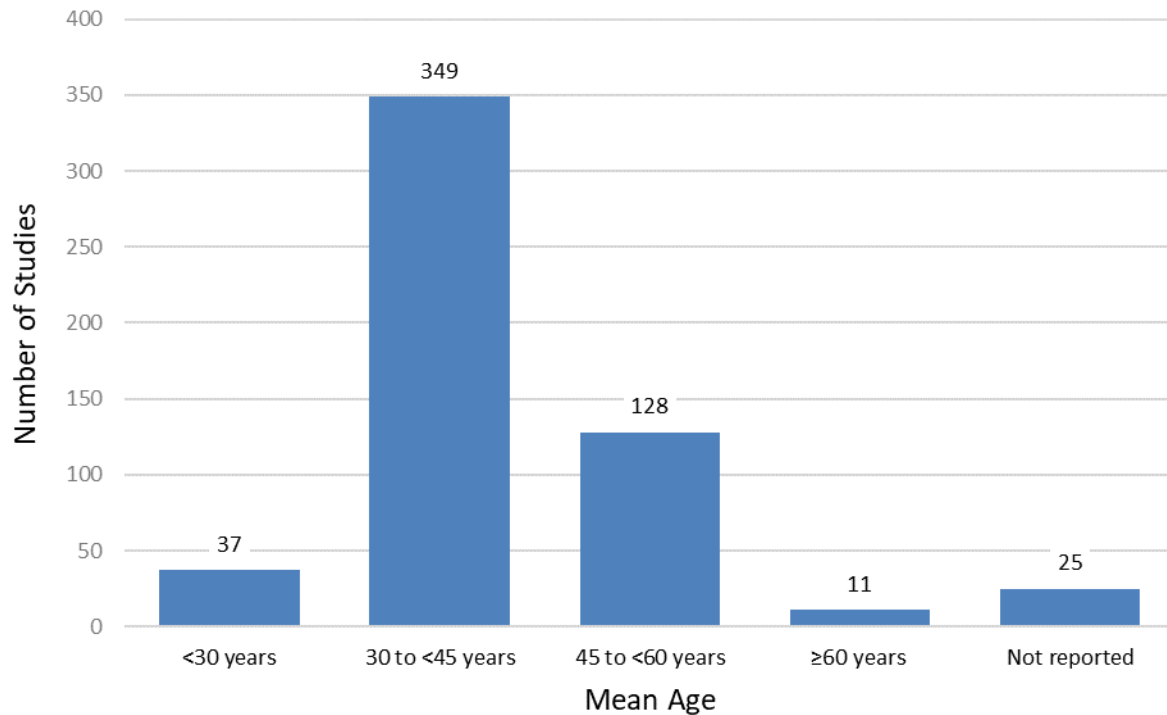
Figure 9. Summary of all included studies: studies by sample size



3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

The sample mean age ranged from 18 to 71 years (median 40 years). Most studies were conducted in younger populations (Figure 10). The sample mean age was 30 to <45 years for 63 percent of studies, while about a quarter of studies had sample mean age from 45 to <60 years (23%); five percent of studies did not provide mean age for the sample.

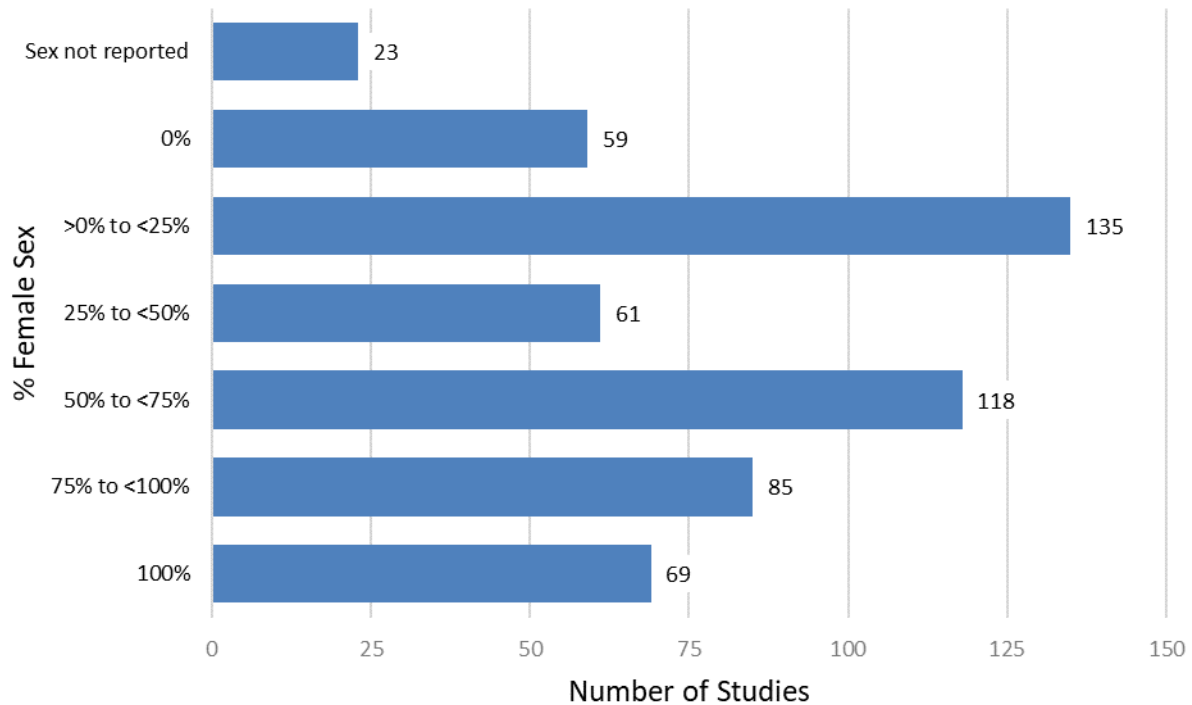
Figure 10. Summary of all included studies: studies by mean age



3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

Most studies enrolled both female and male participants, at varying proportions (Figure 11). About a quarter of studies included only one sex: 13 percent (69 studies) included only female participants and 11 percent (59 studies) included only male participants. A small number (23 studies, 4%) did not report sex of the participants. Seventeen studies (3%) reported data for gender identity and/or sexual orientation of the sample.

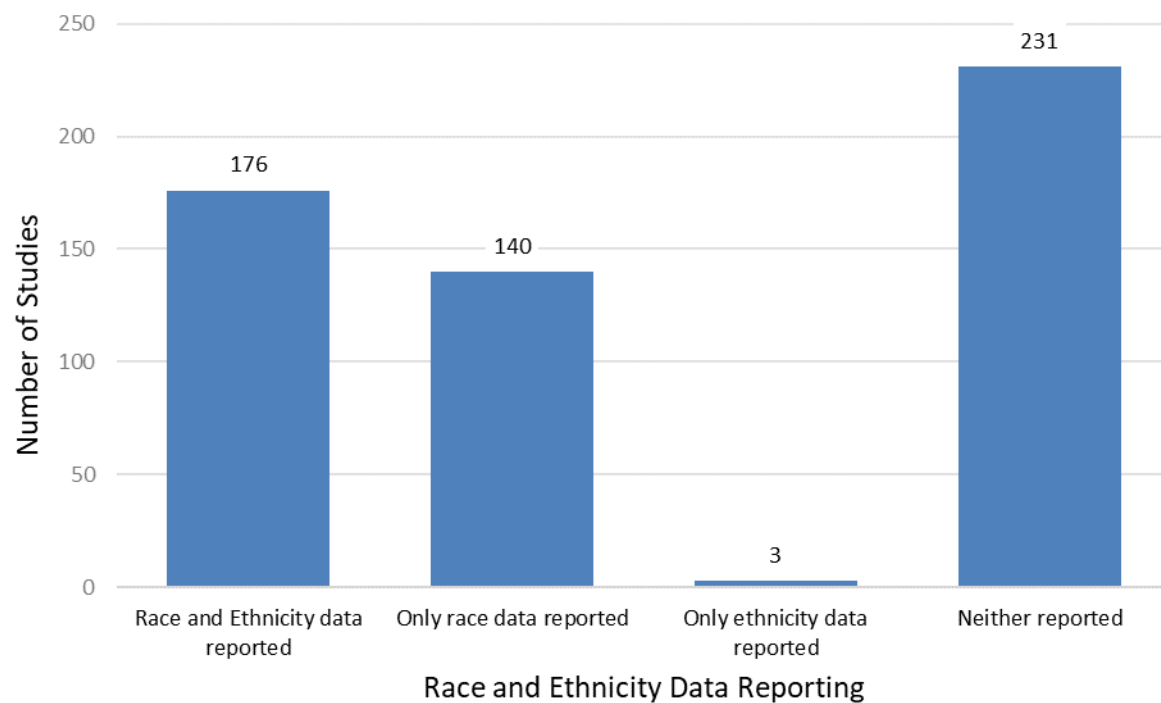
Figure 11. Summary of all included studies: studies by participant sex (% female)



3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

Race and ethnicity data were abstracted according to U.S. Census categories. Because race and ethnicity data were reported in different ways (i.e., grouped into different, non-U.S. Census categories) across many studies, some data were not able to be abstracted because they could not be accurately grouped into U.S. Census categories. Additionally, race and ethnicity data were sometimes reported inconsistently or not reported across some studies. Just under a third of studies (32%) provided data on both race and ethnicity that could be grouped into U.S. Census categories; another 25 percent provided data on race only and 3 studies (<1%) provided data on ethnicity only (Figure 12). Data were not provided for race or ethnicity corresponding to U.S. Census categories in 42 percent of studies.

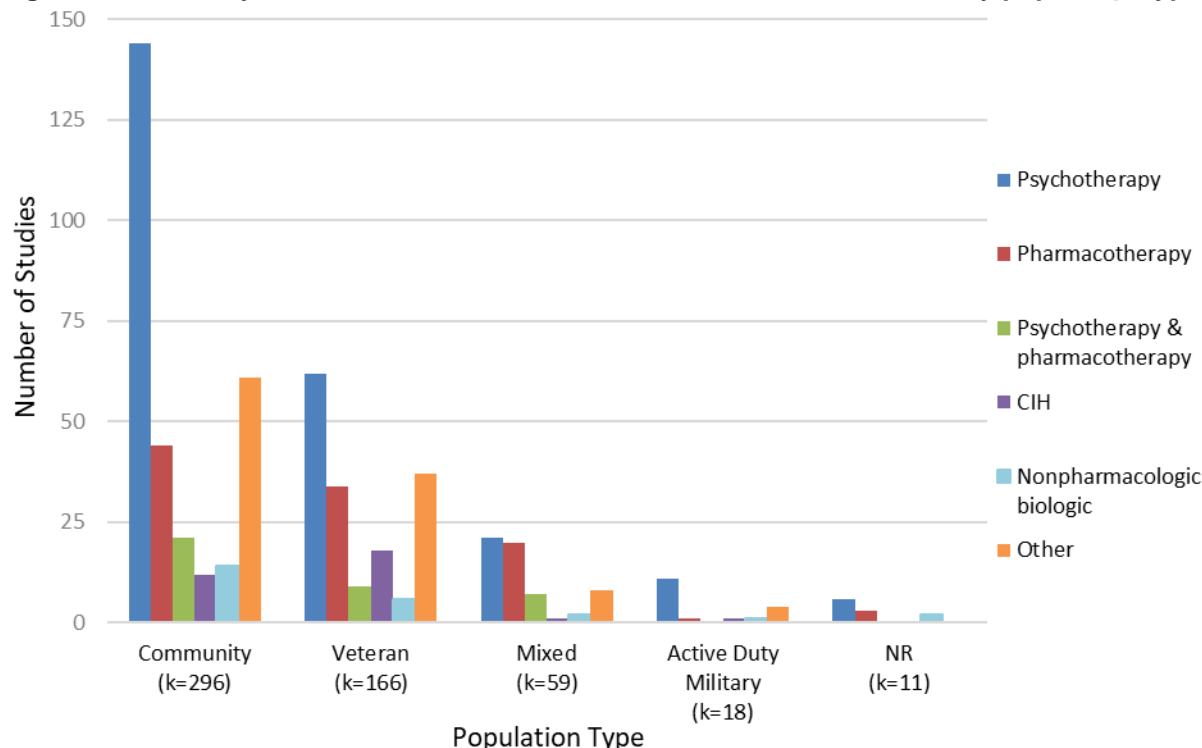
Figure 12. Summary of all included studies: studies reporting on race and ethnicity



3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

Slightly more studies enrolled participants from a community population (54% of studies) than from a military, veteran, or mixed population (Figure 13). Community samples may or may not include Active Duty Military or veteran participants, as many studies did not clarify these variables when describing community samples. The community population was predominant across trials of most treatment types (psychotherapy, pharmacologic, and nonpharmacologic biologic RCTs); however, for CIH, most studies (56%; 18 of 32 studies) were among veterans.

Figure 13. Summary of all included studies: distribution of included studies by population type



Mixed = Any combination of active duty military, veteran, and community-based samples.

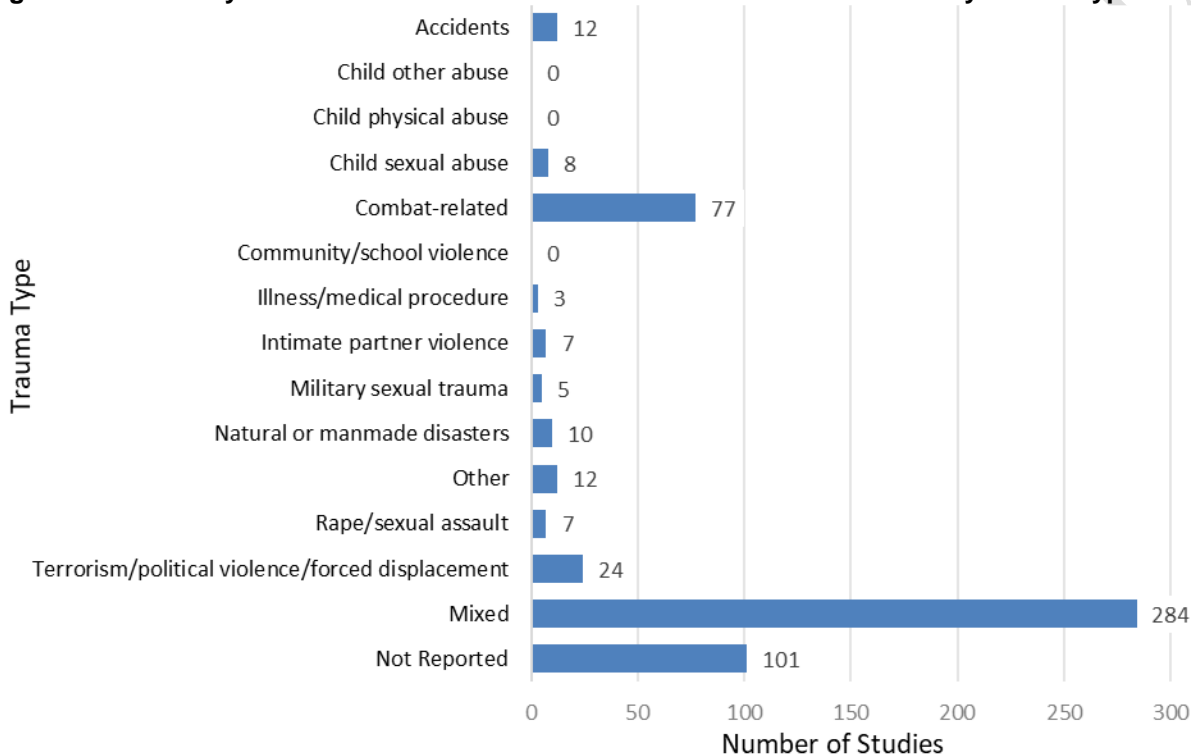
Abbreviations: CIH = complementary and integrative health; k = number of studies; NR = not reported

Only a small proportion of studies (8%, 42 studies) included any participants with subthreshold PTSD. However, studies including more than 20 percent of participants with subthreshold PTSD were excluded from the database according to inclusion/exclusion criteria (i.e., only those with more than 80% of participants with PTSD were included in the database and in this calculation). Most studies (78%) were conducted in the outpatient setting.

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

Some studies targeted specific types of trauma (e.g., required participants to have experienced combat-related trauma or sexual assault), though in most cases other additional trauma types were allowed (i.e., most studies did not target specific types of trauma and included participants with a mix of trauma types). The distribution of included studies by trauma type are shown in Figure 14, with mixed trauma types being most prevalent among these study populations (52%), followed by combat-related trauma (14%). Almost one-fifth of studies (18%) did not provide information on trauma type.

Figure 14. Summary of all included studies: distribution of included studies by trauma type



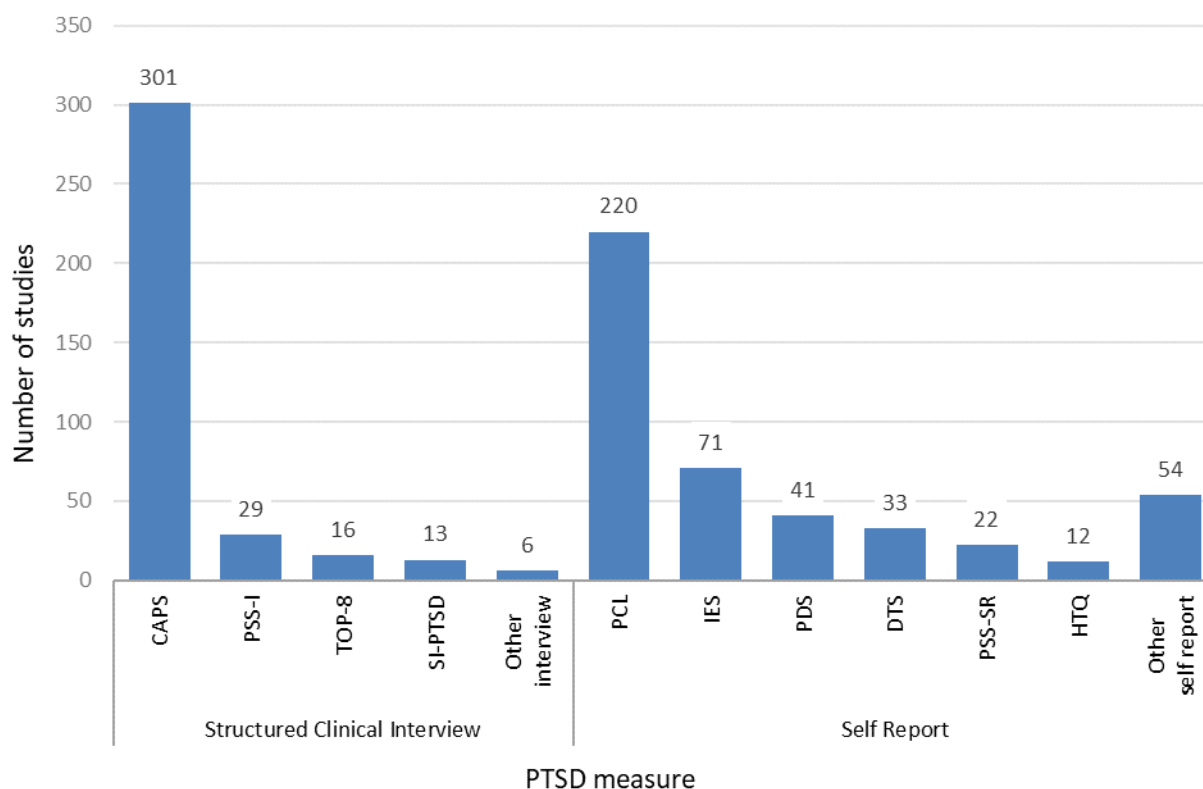
Notes: Active Duty member reporting sexual assault outside of military was categorized as rape/sexual assault. Intimate partner violence includes domestic violence. Accidents includes motor vehicle accidents, transportation-related accidents, and accidents due to construction. Natural or manmade disasters includes tornadoes, hurricanes, wildfires, earthquake, drought, and chemical spills. Mixed indicates multiple trauma types were targeted/included (e.g., a study which included participants with either child sexual abuse or rape/sexual assault would be classified as mixed).

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

The measure most frequently used to assess continuous PTSD outcomes was the Clinician-Administered PTSD Scale (CAPS), used in 57 percent of studies (Figure 15). Other structured clinical interview measures were used in another 11 percent of studies (some studies used both CAPS and another interview measure); 36 percent of studies did not use any interview measure. A larger number of studies used a self report measure (415 studies, 75%). The self report measures most frequently used were the PTSD Checklist (PCL) (42%), Impact of Event Scale (IES) (13%), and Posttraumatic Diagnostic Scale (PDS) (8%).

Most studies (461 studies, 84%) provided data allowing calculation of a standardized effect size for between-group comparison of a continuous PTSD outcome.

Figure 15. Summary of all included studies: PTSD measures used to assess continuous PTSD outcomes^a



^aStudies may have used more than one measure to assess PTSD outcomes. Measures used in 10 or fewer studies are grouped as categories within the measure type ("Other interview" and "Other self report").

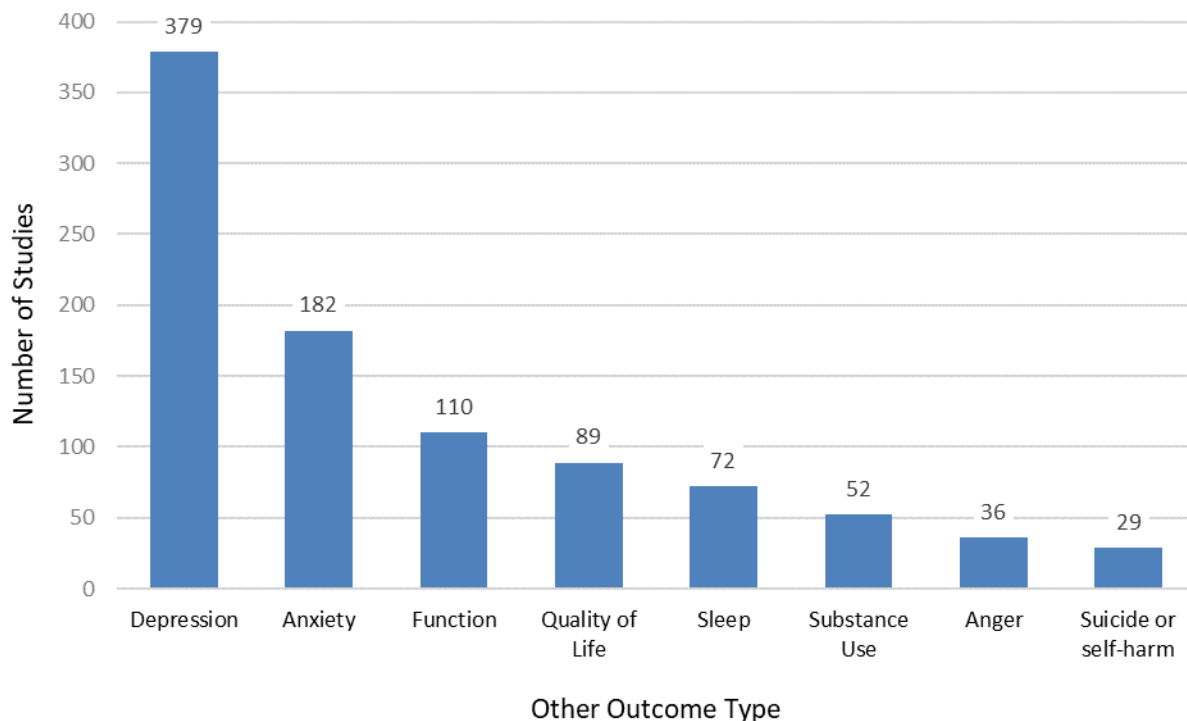
Abbreviations: CAPS = Clinician-Administered PTSD Scale; IES = Impact of Event Scale; PCL = PTSD Checklist; PDS = Posttraumatic Diagnostic Scale; PSS-I = PTSD Symptom Scale - Interview; PSS-SR = PTSD Symptom Scale – Self-Report; PTSD = posttraumatic stress disorder; SI-PTSD = Structured Interview for PTSD; TOP-8 = Treatment-Outcome Posttraumatic Stress Disorder Scale.

PTSD diagnostic change and clinically meaningful response were included as dichotomous outcomes, with just over half of studies (55%) reporting at least one of these outcomes. Slightly more studies reported clinically meaningful response (39%) than diagnostic change (35%); 19 percent of studies reported both outcomes.

3.2.1 Results, Characteristics of Included Studies, Overall Studies Included in the Evidence Tables

Among other (non-PTSD) outcomes (Figure 16), depression was the most commonly assessed (69% of studies), followed by anxiety (33%), function (20%), and quality of life (16%). Suicide outcomes, which included continuous and dichotomous measures related to suicide or self-directed violence (e.g., Columbia Suicide Severity Rating Scale score, proportion of participants with endorsement of item 4 and/or item 5 on Beck Scale for Suicide Ideation) were infrequently reported. Note that data for suicide death and suicide attempt are entered as harms and not reflected here.

Figure 16. Summary of all included studies: non-PTSD outcomes reported^a



^aStudies may have reported more than one other outcome type.
Abbreviations: PTSD = posttraumatic stress disorder

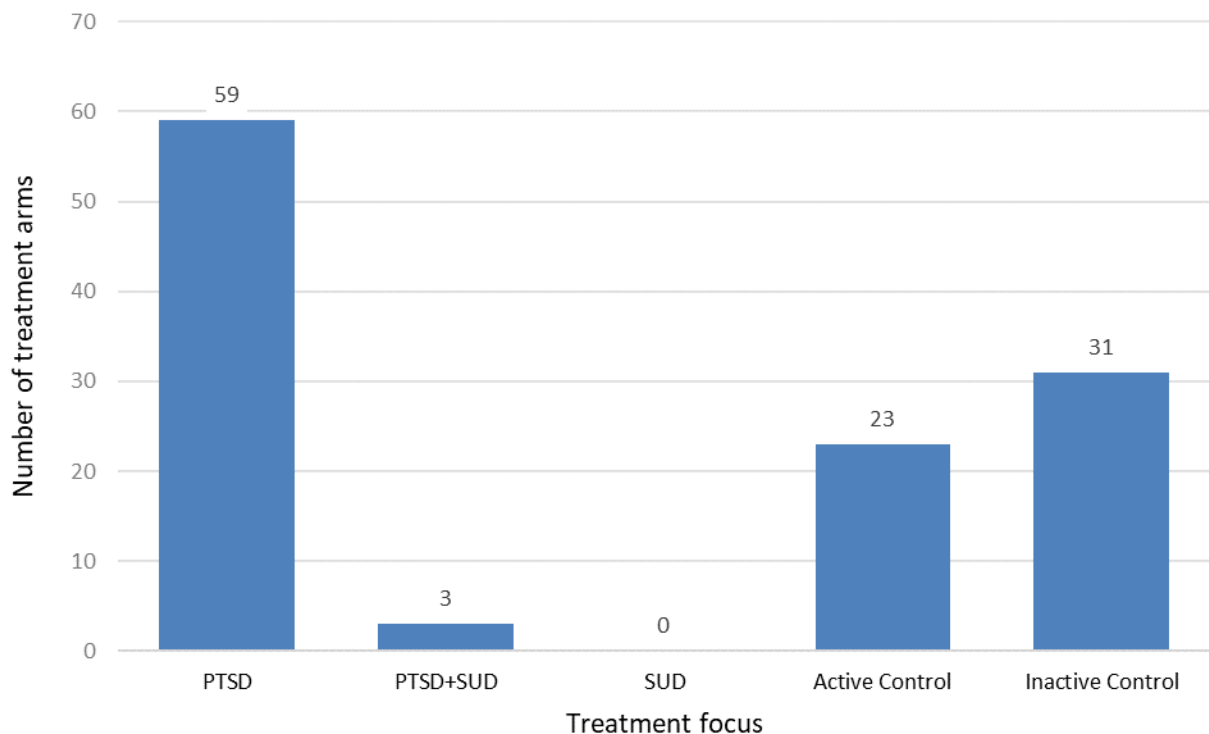
3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

3.2.2 Studies Added in This Update

Key characteristics for the 54 trials added in this update are described in Tables 3-5. Table 3 provides study and sample characteristics. Table 4 details characteristics of the interventions. Table 5 provides a list of outcomes for each of the studies. Additional information about these studies is included in the detailed data abstraction evidence tables in Appendix E.

Among the 54 newly included trials, the treatment focus of the interventions was mostly PTSD (51% of treatment arms); 3 arms (3%) focused on comorbid PTSD/SUD, and none focused on SUD alone. The remaining arms were control arms, with slightly fewer active control arms than inactive control arms (20% versus 27%) (Figure 17).

Figure 17. Summary of newly included studies: distribution of treatment arms by treatment focus^a



^aStudies have more than one treatment arm.

Abbreviations: PTSD = posttraumatic stress disorder; SUD = substance use disorder.

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Table 3. Summary of newly included studies: study and sample characteristics

Author, Year	Study Class	Sample Size	Countries	Clinical Setting	Military Status	Race/Ethnicity Reported	Trauma Type
Allen, 2022 ³⁵	Psychotherapy	49	Australia	Other	Community	Neither reported	Mixed
Astill-Wright, 2023 ⁶³	Psychotherapy	40	U.K.	Outpatient clinic	Community	Only race data reported	Mixed
Back, 2023 ³⁶	Pharmacotherapy	141	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	NR
Bizouerne, 2023 ⁶⁴	Psychotherapy	110	Iraq	Outpatient clinic	Community	Neither reported	NR
Brocker, 2024 ⁶⁵	Other study class	62	South Africa	Mixed	Community	Only race data reported	Mixed
Cloitre, 2024 ⁶⁶	Psychotherapy	161	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	Military sexual trauma
Darvish, 2019 ²⁶	Other study class	66	Iran	Outpatient clinic	Veteran	Neither reported	NR
de Kleine, 2019 ²⁸	Nonpharmacologic cognitive	107	The Netherlands	Outpatient clinic	Community	Neither reported	Mixed
Duek, 2023 ³⁸	Psychotherapy & pharmacotherapy	28	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	Mixed
Dunn, 2007 ³⁸	Psychotherapy	101	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	Combat-related
Ehlers, 2023 ⁴⁴	Psychotherapy	217	U.K.	Other	Community	Only race data reported	Mixed
Every-Palmer, 2024 ⁶⁷	Psychotherapy	24	New Zealand	Mixed	Community	Only race data reported	Mixed
Feder, 2023 ⁴⁵	Pharmacotherapy	30	U.S.	Outpatient clinic	Community	Race and Ethnicity data reported	Mixed
Fine, 2023 ⁶²	Other mixed	55	Israel	Outpatient clinic	Community	Neither reported	Child sexual abuse
Fonzo, 2019 ²⁷	Other study class	84	U.S.	Outpatient clinic	Mixed	Only race data reported	NR
Golier, 2023 ³⁹	Pharmacotherapy	80	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	Mixed
Haller, 2023 ⁴⁰	Psychotherapy & CIH	74	Germany	Outpatient clinic	Community	Neither reported	NR
Himmerich, 2016 ²⁵	Psychotherapy	38	Germany	Mixed	Active Duty Military	Neither reported	Combat-related
Hollifield, 2024 ⁶⁸	CIH	93	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	Mixed
Kanaan, 2023 ⁴⁶	Pharmacotherapy	104	Australia	Other	Community	Neither reported	NR
Kearney, 2023 ⁵²	Psychotherapy	59	Canada	Outpatient clinic	Community	Race and Ethnicity data reported	Mixed

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Study Class	Sample Size	Countries	Clinical Setting	Military Status	Race/Ethnicity Reported	Trauma Type
Kuhn, 2017 ²²	Other study class	120	U.S.	Other	Community	Race and Ethnicity data reported	Mixed
Larsen, 2019 ³⁰	Nonpharmacologic cognitive	29	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	NR
Lazarov, 2019 ²⁹	Nonpharmacologic cognitive	50	U.S.	Outpatient clinic	Community	Neither reported	NR
Litz, 2007 ²⁴	Psychotherapy	45	U.S.	Outpatient clinic	Mixed	Neither reported	Mixed
Litz, 2024 ⁶⁹	Psychotherapy	174	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	NR
McLean, 2024 ⁷⁰	Psychotherapy	124	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	NR
Miller-Graff, 2021 ³⁴	Other study class	105	Egypt	Other	Community	Neither reported	NR
Miner, 2016 ²³	Other study class	49	U.S.	Other	Community	Race and Ethnicity data reported	NR
Mitchell, 2023 ⁵³	Psychotherapy & pharmacotherapy	104	Israel; U.S.	Outpatient clinic	Mixed	Race and Ethnicity data reported	Mixed
Monga, 2023 ⁵⁴	Pharmacotherapy	72	U.S.	Outpatient clinic	Community	Only race data reported	NR
Müller-Engelmann, 2024 ⁷¹	Psychotherapy	32	Germany	Outpatient clinic	Community	Neither reported	Mixed
Niles, 2020 ³³	Nonpharmacologic cognitive	1,001	U.S.	Other	Community	Race and Ethnicity data reported	Mixed
Parmenter, 2024 ⁷²	Pharmacotherapy	358	U.S.	Outpatient clinic	NR	Race and Ethnicity data reported	Mixed
Peck, 2023 ³⁷	Psychotherapy & pharmacotherapy	30	U.S.	Mixed	Community	Only race data reported	Mixed
Possemato, 2024 ⁷⁴	Psychotherapy	63	U.S.	Primary care clinic	Veteran	Race and Ethnicity data reported	NR
Prguda, 2023 ⁴⁸	Psychotherapy	31	Australia	Outpatient clinic	Veteran	Only race data reported	NR
Rajabi, 2023 ⁴⁷	Pharmacotherapy	26	Iran	Outpatient clinic	Active Duty Military	Neither reported	Combat-related
Schoofs, 2024 ⁷³	Other study class	40	Germany	Outpatient clinic	Mixed	Neither reported	Mixed
Segal, 2020 ³¹	Nonpharmacologic cognitive	60	Israel	Outpatient clinic	Community	Neither reported	Mixed
Sele, 2023 ⁵⁵	Psychotherapy	99	Norway	Residential inpatient	Community	Race and Ethnicity data reported	Mixed
Shea, 2023 ⁵⁶	Psychotherapy	115	U.S.	Outpatient clinic	Veteran	Race and Ethnicity data reported	Mixed

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Study Class	Sample Size	Countries	Clinical Setting	Military Status	Race/Ethnicity Reported	Trauma Type
Sloan, 2023 ⁶¹	Psychotherapy	178	U.S.	Mixed	Veteran	Race and Ethnicity data reported	Mixed
Smaik, 2023 ⁵⁷	Psychotherapy	40	Jordan	Outpatient clinic	Community	Neither reported	Mixed
Stein, 2023 ⁵⁸	Psychotherapy	365	Egypt; Germany; Jordan; Saudi Arabia; Other ("Middle East" and "North Africa", countries not specified)	Other	Community	Neither reported	Mixed
Sturt, 2023 ⁵⁹	Psychotherapy	60	U.K.	Outpatient clinic	Veteran	Only race data reported	NR
Taylor, 2023 ⁴¹	Psychotherapy	93	U.S.	Outpatient clinic	Mixed	Race and Ethnicity data reported	NR
Voorendonk, 2023 ⁵¹	Other mixed	119	The Netherlands	Outpatient clinic	Community	Neither reported	Mixed
Wakusawa, 2023 ⁵⁰	Other mixed	22	Japan	Outpatient clinic	Community	Neither reported	Mixed
Walter, 2023 ⁴⁹	Psychotherapy	94	U.S.	Outpatient clinic	Active Duty Military	Race and Ethnicity data reported	Mixed
Watkins, 2023 ⁴²	Psychotherapy	112	U.S.	Outpatient clinic	Mixed	Only race data reported	Mixed
Woud, 2021 ³²	Nonpharmacologic cognitive	80	Germany	Residential inpatient	Community	Neither reported	Mixed
Yuan, 2023 ⁶⁰	Nonpharmacologic biologic	75	China	Outpatient clinic	Community	Neither reported	NR
Zhao, 2023 ⁴³	Nonpharmacologic biologic	27	U.S.	Outpatient clinic	Community	Race and Ethnicity data reported	NR

Abbreviations: CIH = complementary and integrative health; NR = not reported; U.K. = United Kingdom; U.S. = United States.

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Table 4. Summary of newly included studies: intervention characteristics

Author, Year	Intervention Group ^a	Treatment Name	Treatment Focus	Intervention Categorization	Intervention Format	Intervention Delivery Method
Allen, 2022 ³⁵	A	Internet-based CBT	PTSD	Other	Individual	Technology assisted
Allen, 2022 ³⁵	B	WL	Inactive Control	Control	NA	NA
Astill-Wright, 2023 ⁶³	A	Rewind psychotherapy protocol	PTSD	Psychotherapy	Individual	Video
Astill-Wright, 2023 ⁶³	B	WL	Inactive Control	Control	Individual	NA
Back, 2023 ³⁶	A	Doxazosin	PTSD+SUD	Pharmacotherapy	Individual	In Person
Back, 2023 ³⁶	B	Placebo	Inactive Control	Control	Individual	In Person
Bizouerne, 2023 ⁶⁴	A	Group traumatic episode protocol	PTSD	Psychotherapy	Group	In Person
Bizouerne, 2023 ⁶⁴	B	Trauma-focused CBT	PTSD	Psychotherapy	Group	In Person
Brocker, 2024 ⁶⁵	A	Counsellor-supported PTSD Coach	PTSD	Other	Individual	Mixed
Brocker, 2024 ⁶⁵	B	Enhanced TAU	Inactive Control	Control	Individual	In Person
Cloitre, 2024 ⁶⁶	A	STAIR	PTSD	Psychotherapy	Individual	Video
Cloitre, 2024 ⁶⁶	B	PCT	Active Control	Psychotherapy	Individual	Video
Darvish, 2019 ²⁶	A	Text messaging-based psychiatric nursing program	PTSD	Other	Individual	Technology Alone
Darvish, 2019 ²⁶	B	TAU	Inactive Control	Control	Individual	NA
de Kleine, 2019 ²⁸	A	Cognitive Bias Modification	PTSD	Nonpharmacologic cognitive	Individual	Technology Alone
de Kleine, 2019 ²⁸	B	Control Training	Inactive Control	Control	Individual	Technology Alone
Duek, 2023 ³⁸	A	Ketamine + PE	PTSD	Psychotherapy & pharmacotherapy	Individual	In Person
Duek, 2023 ³⁸	B	Midazolam + PE	Active Control	Psychotherapy & pharmacotherapy	Individual	In Person
Dunn, 2007 ²¹	A	Self-management group therapy	PTSD	Psychotherapy	Group	In Person
Dunn, 2007 ²¹	B	Psychoeducational group therapy	Active Control	Psychotherapy	Group	In Person
Ehlers, 2023 ⁴⁴	A	Internet-delivered cognitive therapy for PTSD	PTSD	Other	Individual	Technology assisted
Ehlers, 2023 ⁴⁴	B	Internet-delivered stress management therapy for PTSD	Active Control	Other	Individual	Technology assisted
Ehlers, 2023 ⁴⁴	C	WL with TAU	Inactive Control	Control	NA	NA

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Intervention Group ^a	Treatment Name	Treatment Focus	Intervention Categorization	Intervention Format	Intervention Delivery Method
Every-Palmer, 2024 ⁶⁷	A	EMDR + TAU	PTSD	Psychotherapy	Individual	In Person
Every-Palmer, 2024 ⁶⁷	B	TAU	Inactive Control	Control	Individual	In Person
Feder, 2023 ⁴⁵	A	Ketamine	PTSD	Pharmacotherapy	Individual	In Person
Feder, 2023 ⁴⁵	B	Midazolam	Active Control	Pharmacotherapy	Individual	In Person
Fine, 2023 ⁶²	A	Trauma-focused intensive therapy + amygdala electrical finger print neurofeedback	PTSD	Psychotherapy & nonpharmacologic biologic	Mixed	In Person
Fine, 2023 ⁶²	B	Trauma-focused intensive therapy	Active Control	Pharmacotherapy	Mixed	In Person
Fonzo, 2019 ²⁷	A	Cognitive/affective remediation training	PTSD	Other	Individual	Technology Alone
Fonzo, 2019 ²⁷	B	Attention Control	Inactive Control	Control	Individual	Technology Alone
Golier, 2023 ³⁹	A	Mifepristone	PTSD	Pharmacotherapy	Individual	In Person
Golier, 2023 ³⁹	B	Placebo	Inactive Control	Control	Individual	In Person
Haller, 2023 ⁴⁰	A	Pranayama-assisted trauma-focused CBT	PTSD	Psychotherapy & CIH	Individual	In Person
Haller, 2023 ⁴⁰	B	Trauma-focused CBT	Active Control	Psychotherapy	Individual	In Person
Himmerich, 2016 ²⁵	A	Inpatient psychotherapy	PTSD	Psychotherapy & other	Mixed	In Person
Himmerich, 2016 ²⁵	B	Outpatient clinical management	Active Control	Psychotherapy	Mixed	In Person
Hollifield, 2024 ⁶⁸	A	Verum acupuncture	PTSD	CIH	Individual	In Person
Hollifield, 2024 ⁶⁸	B	Sham acupuncture	Inactive Control	Control	Individual	In Person
Kanaan, 2023 ⁴⁶	A	N-acetylcysteine + TAU	PTSD	Pharmacotherapy	Individual	Mixed
Kanaan, 2023 ⁴⁶	B	Placebo + TAU	Inactive Control	Control	Individual	Mixed
Kearney, 2023 ⁵²	A	Deep-brain reorienting	PTSD	Psychotherapy	Individual	Video
Kearney, 2023 ⁵²	B	WL	Inactive Control	Control	NA	NA
Kuhn, 2017 ²²	A	PTSD Coach smartphone application	PTSD	Other	Individual	Technology Alone
Kuhn, 2017 ²²	B	WL	Inactive Control	Control	NA	NA
Larsen, 2019 ³⁰	A	Adaptive computerized working memory training (n-back)	PTSD	Nonpharmacologic cognitive	Individual	Technology Alone

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Intervention Group ^a	Treatment Name	Treatment Focus	Intervention Categorization	Intervention Format	Intervention Delivery Method
Larsen, 2019 ³⁰	B	Non-adaptive computerized working memory training (1-back)	Active Control	Nonpharmacologic cognitive	Individual	Technology Alone
Lazarov, 2019 ²⁹	A	Bias-contingent attention bias modification	PTSD	Nonpharmacologic cognitive	Individual	Technology Alone
Lazarov, 2019 ²⁹	B	Attention control training	PTSD	Nonpharmacologic cognitive	Individual	Technology Alone
Litz, 2007 ²⁴	A	Internet-delivered self-management CBT	Active Control	Other	Individual	Mixed
Litz, 2007 ²⁴	B	Internet-delivered supportive counseling	PTSD	Other	Individual	Mixed
Litz, 2024 ⁶⁹	A	Adaptive Disclosure-Enhanced	PTSD	Psychotherapy	Individual	In Person
Litz, 2024 ⁶⁹	B	PCT	Active Control	Psychotherapy	Individual	In Person
McLean, 2024 ⁷⁰	A	Written exposure therapy	PTSD	Other	Individual	Technology Alone
McLean, 2024 ⁷⁰	B	Verbal exposure therapy	PTSD	Other	Individual	Technology Alone
Miller-Graff, 2021 ³⁴	A	PTSD Coach Online-Arabic	PTSD	Other	Individual	Technology Alone
Miller-Graff, 2021 ³⁴	B	WL	Inactive Control	Control	NA	NA
Miner, 2016 ²³	A	PTSD Coach smartphone application	PTSD	Other	Individual	Technology Alone
Miner, 2016 ²³	B	WL	Inactive Control	Control	NA	NA
Mitchell, 2023 ⁵³	A	MDMA-assisted therapy	PTSD	Psychotherapy & pharmacotherapy	Individual	In Person
Mitchell, 2023 ⁵³	B	Placebo + therapy	Active Control	Psychotherapy	Individual	In Person
Monga, 2023 ⁵⁴	A	Topiramate	PTSD	Pharmacotherapy	Individual	In Person
Monga, 2023 ⁵⁴	B	Placebo	Inactive Control	Control	Individual	In Person
Müller-Engelmann, 2024 ⁷¹	A	C-METTA (cognitive techniques + loving-kindness meditations)	PTSD	Psychotherapy	Individual	In Person
Müller-Engelmann, 2024 ⁷¹	B	Waitlist	Inactive Control	Control	NA	NA
Niles, 2020 ³³	A	Personalized attention bias modification	PTSD	Nonpharmacologic cognitive	Individual	Technology Alone

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Intervention Group ^a	Treatment Name	Treatment Focus	Intervention Categorization	Intervention Format	Intervention Delivery Method
Niles, 2020 ³³	B	Non-personalized attention bias modification	Active Control	Nonpharmacologic cognitive	Individual	Technology Alone
Niles, 2020 ³³	C	Placebo training	Inactive Control	Control	Individual	Technology Alone
Parmenter, 2024 ⁷²	A	TNX-102 SL (cyclobenzaprine sublingual)	PTSD	Pharmacotherapy	Individual	In Person
Parmenter, 2024 ⁷²	B	Placebo	Inactive Control	Control	Individual	In Person
Peck, 2023 ³⁷	A	PE + financial incentives + TAU for OUD	PTSD+SUD	Psychotherapy & pharmacotherapy	Individual	Mixed
Peck, 2023 ³⁷	B	PE + TAU for OUD	Active Control	Psychotherapy & pharmacotherapy	Individual	Mixed
Peck, 2023 ³⁷	C	TAU for OUD	Active Control	Pharmacotherapy	Individual	Mixed
Possemato, 2024 ⁷⁴	A	Primary care treatment integrating motivation and exposure (PC-TIME)	PTSD+SUD	Psychotherapy	Individual	Mixed
Possemato, 2024 ⁷⁴	B	Primary care TAU	Inactive Control	Control	Individual	Mixed
Prguda, 2023 ⁴⁸	A	CBT for insomnia + imagery rehearsal therapy for nightmares	PTSD	Psychotherapy	Group	In Person
Prguda, 2023 ⁴⁸	B	CBT for insomnia	Active Control	Psychotherapy	Group	In Person
Rajabi, 2023 ⁴⁷	A	Memantine	PTSD	Pharmacotherapy	Individual	In Person
Rajabi, 2023 ⁴⁷	B	Placebo	Inactive Control	Control	Individual	In Person
Schoofs, 2024 ⁷³	A	High intensity interval exercise training	PTSD	Other	Individual	In Person
Schoofs, 2024 ⁷³	B	Low intensity exercise training	Active Control	Other	Individual	In Person
Segal, 2020 ³¹	A	Personalized Attention Control Therapy	PTSD	Nonpharmacologic cognitive	Individual	In Person
Segal, 2020 ³¹	B	Non-Personalized Attention Control Therapy	Active Control	Nonpharmacologic cognitive	Individual	In Person
Segal, 2020 ³¹	C	Control	Inactive Control	Control	Individual	In Person
Sele, 2023 ⁵⁵	A	STAIR Narrative Therapy	PTSD	Psychotherapy	Mixed	In Person
Sele, 2023 ⁵⁵	B	STAIR	Active Control	Psychotherapy	Mixed	In Person
Sele, 2023 ⁵⁵	C	PE	Active Control	Psychotherapy	Individual	In Person
Shea, 2023 ⁵⁶	A	Interpersonal psychotherapy	PTSD	Psychotherapy	Individual	In Person
Shea, 2023 ⁵⁶	B	PE	PTSD	Psychotherapy	Individual	In Person

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Intervention Group ^a	Treatment Name	Treatment Focus	Intervention Categorization	Intervention Format	Intervention Delivery Method
Sloan, 2023 ⁶¹	A	Written exposure therapy	PTSD	Psychotherapy	Individual	Mixed
Sloan, 2023 ⁶¹	B	PE	PTSD	Psychotherapy	Individual	Mixed
Smaik, 2023 ⁵⁷	A	Narrative exposure therapy	PTSD	Psychotherapy	Individual	In Person
Smaik, 2023 ⁵⁷	B	WL	Inactive Control	Control	Individual	In Person
Stein, 2023 ⁵⁸	A	Cognitive restructuring	PTSD	Other	Individual	Technology Alone
Stein, 2023 ⁵⁸	B	Exposure treatment	PTSD	Other	Individual	Technology Alone
Stein, 2023 ⁵⁸	C	WL	Inactive Control	Control	Individual	Technology Alone
Sturt, 2023 ⁵⁹	A	Reconsolidation of Traumatic Memories	PTSD	Psychotherapy	Individual	Video
Sturt, 2023 ⁵⁹	B	Trauma-focused CBT	PTSD	Psychotherapy	Individual	Video
Taylor, 2023 ⁴¹	A	CBT for insomnia and nightmares followed by CPT	PTSD	Psychotherapy	Individual	In Person
Taylor, 2023 ⁴¹	B	CPT followed by CBT for insomnia and nightmares	Active Control	Psychotherapy	Individual	In Person
Taylor, 2023 ⁴¹	C	CPT	Active Control	Psychotherapy	Individual	In Person
Voorendonk, 2023 ⁵¹	A	Intensive trauma-focused treatment for PTSD + Physical activity	PTSD	Psychotherapy & other	Mixed	Mixed
Voorendonk, 2023 ⁵¹	B	Intensive trauma-focused treatment for PTSD + Non-physical activity	Active Control	Psychotherapy & CIH	Mixed	Mixed
Wakusawa, 2023 ⁵⁰	A	Traumatic stress protocol	PTSD	Psychotherapy & pharmacotherapy & CIH	Individual	In Person
Wakusawa, 2023 ⁵⁰	B	WL	Inactive Control	Control	NA	NA
Walter, 2023 ⁴⁹	A	Behavioral activation + CPT	PTSD	Psychotherapy	Individual	In Person
Walter, 2023 ⁴⁹	B	CPT	Active Control	Psychotherapy	Individual	In Person
Watkins, 2023 ⁴²	A	CPT	PTSD	Psychotherapy	Individual	In Person
Watkins, 2023 ⁴²	B	WL	Inactive Control	Control	Individual	Phone
Woud, 2021 ³²	A	Cognitive Bias Modification - Appraisal + TAU	PTSD	Nonpharmacologic cognitive	Individual	Technology Alone
Woud, 2021 ³²	B	Peripheral Vision Task+ TAU	Inactive Control	Control	Individual	Technology Alone

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	Intervention Group ^a	Treatment Name	Treatment Focus	Intervention Categorization	Intervention Format	Intervention Delivery Method
Yuan, 2023 ⁶⁰	A	Intermittent theta burst stimulation	PTSD	Nonpharmacologic biologic	Individual	In Person
Yuan, 2023 ⁶⁰	B	rTMS	PTSD	Nonpharmacologic biologic	Individual	In Person
Yuan, 2023 ⁶⁰	C	Sham intermittent theta burst stimulation	Inactive Control	Control	Individual	In Person
Zhao, 2023 ⁴³	A	Personalized neurofeedback	PTSD	Nonpharmacologic biologic	Individual	In Person
Zhao, 2023 ⁴³	B	Sham neurofeedback	Inactive Control	Nonpharmacologic biologic	Individual	In Person

^aEach intervention group (study arm) is labeled with a letter (A, B, C) and listed in a separate row, therefore studies are listed in multiple rows.

Abbreviations: CBT = cognitive behavioral therapy; CIH = complementary and integrative health; CPT = cognitive processing therapy; EMDR = eye movement desensitization and reprocessing; NA = not applicable; OUD = opiate use disorder; PCT = present-centered therapy; PC-TIME = primary care treatment integrating motivation and exposure; PE = prolonged exposure; PTSD = posttraumatic stress disorder; rTMS = repetitive transcranial magnetic stimulation; STAIR = skill training in affective regulation; SUD = substance use disorder; TAU = treatment as usual; TNX-102 SL = cyclobenzaprine sublingual; WL = waitlist

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Table 5. Newly included studies: type of PTSD outcomes and other reported outcomes

Author, Year	PTSD Continuous Outcome Measure(s)	PTSD Diagnostic Change	PTSD Clinically Meaningful Response	Anger	Anxiety	Depression	Function	Quality of Life	Sleep	Substance Use	Suicide/ Self-directed violence
Allen, 2022 ³⁵	PCL	Y	Y	N	Y	Y	N	N	N	N	N
Astill-Wright, 2023 ⁶³	CAPS, PCL	Y	N	N	Y	Y	Y	N	Y	Y	N
Back, 2023 ³⁶	CAPS, PCL	N	N	N	N	N	N	N	N	Y	N
Bizouerne, 2023 ⁶⁴	IES	N	N	N	N	N	N	N	N	N	N
Brocker, 2024 ⁶⁵	CAPS, PCL	Y	Y	N	Y	Y	N	N	N	N	N
Cloitre, 2024 ⁶⁶	CAPS, ITQ, PCL	Y	Y	N	N	Y	Y	N	N	Y	Y
Darvish, 2019 ²⁶	Self-rating scale for PTSD	Y	N	N	N	N	N	N	N	N	N
de Kleine, 2019 ²⁸	PSS-SR	N	N	N	N	Y	N	N	N	N	N
Duek, 2023 ³⁸	PCL	N	N	N	N	Y	N	N	N	N	N
Dunn, 2007 ³⁸	CAPS, DTS	N	N	N	N	Y	N	N	N	N	N
Ehlers, 2023 ⁴⁴	CAPS, IES, PCL	Y	Y	N	Y	Y	Y	Y	Y	N	N
Every-Palmer, 2024 ⁶⁷	CAPS, PSS-SR	Y	N	N	N	Y	Y	N	N	N	N
Feder, 2023 ⁴⁵	CAPS	N	Y	N	N	Y	N	N	N	N	Y
Fine, 2023 ⁶²	CAPS, PCL	Y	N	N	N	N	N	N	N	N	N
Fonzo, 2019 ²⁷	CAPS	N	N	N	N	N	N	N	N	N	N
Golier, 2023 ³⁹	CAPS, PCL	N	Y	Y	N	Y	N	N	Y	N	N
Haller, 2023 ⁴⁰	PCL	N	N	N	Y	Y	N	Y	N	N	N
Himmerich, 2016 ²⁵	PDS	N	N	N	N	N	N	N	N	N	N
Hollifield, 2024 ⁶⁸	CAPS	Y	N	N	N	N	N	N	N	N	N
Kanaan, 2023 ⁴⁶	CAPS, PCL	Y	N	N	Y	Y	N	Y	N	Y	N
Kearney, 2023 ⁵²	CAPS	Y	N	N	N	N	N	N	N	N	N
Kuhn, 2017 ²²	PCL	N	Y	N	N	Y	Y	N	N	N	N
Larsen, 2019 ³⁰	PCL	N	Y	N	Y	Y	N	N	N	N	N

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	PTSD Continuous Outcome Measure(s)	PTSD Diagnostic Change	PTSD Clinically Meaningful Response	Anger	Anxiety	Depression	Function	Quality of Life	Sleep	Substance Use	Suicide/ Self-directed violence
Lazarov, 2019 ²⁹	CAPS, PCL	N	Y	N	N	Y	N	N	N	N	N
Litz, 2007 ²⁴	PSS-I	Y	Y	Y	Y	Y	N	N	N	N	N
Litz, 2024 ⁶⁹	CAPS	Y	Y	N	N	N	Y	N	N	Y	N
McLean, 2024 ⁷⁰	PCL	N	N	N	N	N	N	N	N	N	N
Miller-Graff, 2021 ³⁴	PCL	N	N	N	Y	Y	N	N	N	N	N
Miner, 2016 ²³	PCL	N	Y	N	N	N	N	N	N	N	N
Mitchell, 2023 ⁵³	CAPS	Y	Y	N	N	N	Y	N	N	N	Y
Monga, 2023 ⁵⁴	CAPS, TOP	N	Y	N	Y	Y	N	N	N	N	N
Müller-Engelmann, 2024 ⁷¹	CAPS, PCL	Y	Y	N	N	Y	N	Y	N	N	N
Niles, 2020 ³³	PCL	N	N	N	Y	Y	N	N	N	N	N
Parmenter, 2024 ⁷²	CAPS	N	N	N	N	N	N	N	Y	N	N
Peck, 2023 ³⁷	CAPS, PCL	Y	N	N	Y	Y	N	N	N	N	N
Possemato, 2024 ⁷⁴	PCL	Y	N	N	N	N	N	N	N	Y	N
Prguda, 2023 ⁴⁸	PCL	N	N	N	Y	Y	N	N	Y	N	N
Rajabi, 2023 ⁴⁷	CAPS	N	N	N	N	N	N	N	N	N	N
Schoofs, 2024 ⁷³	CAPS, PCL	N	N	N	N	Y	N	N	N	N	N
Segal, 2020 ³¹	CAPS, PCL	Y	N	N	N	Y	N	N	N	N	N
Sele, 2023 ⁵⁵	CAPS, ITQ, PCL	Y	Y	N	N	Y	N	N	N	N	N
Shea, 2023 ⁵⁶	CAPS	Y	Y	N	Y	Y	Y	Y	N	N	Y
Sloan, 2023 ⁶¹	CAPS	Y	N	N	N	N	N	N	N	N	N
Smaik, 2023 ⁵⁷	HTQ	N	N	N	Y	Y	N	N	N	N	N
Stein, 2023 ⁵⁸	PCL	Y	Y	N	Y	Y	N	Y	N	N	N
Sturt, 2023 ⁵⁹	PCL	N	Y	N	N	N	N	N	N	N	N
Taylor, 2023 ⁴¹	PCL	Y	Y	N	N	N	N	N	Y	N	N

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Author, Year	PTSD Continuous Outcome Measure(s)	PTSD Diagnostic Change	PTSD Clinically Meaningful Response	Anger	Anxiety	Depression	Function	Quality of Life	Sleep	Substance Use	Suicide/ Self-directed violence
Voorendonk, 2023 ⁵¹	CAPS, PCL	Y	N	N	Y	Y	N	Y	Y	N	N
Wakusawa, 2023 ⁵⁰	IES	N	N	N	N	N	N	N	N	N	N
Walter, 2023 ⁴⁹	CAPS, PCL	Y	Y	N	N	Y	N	N	N	N	N
Watkins, 2023 ⁴²	CAPS, PCL	N	N	N	Y	Y	N	N	Y	N	N
Woud, 2021 ³²	PCL	N	N	N	N	N	N	N	N	N	Y
Yuan, 2023 ⁶⁰	PCL	N	N	N	N	N	N	N	N	N	N
Zhao, 2023 ⁴³	CAPS, PCL	N	N	N	N	N	N	N	N	N	N

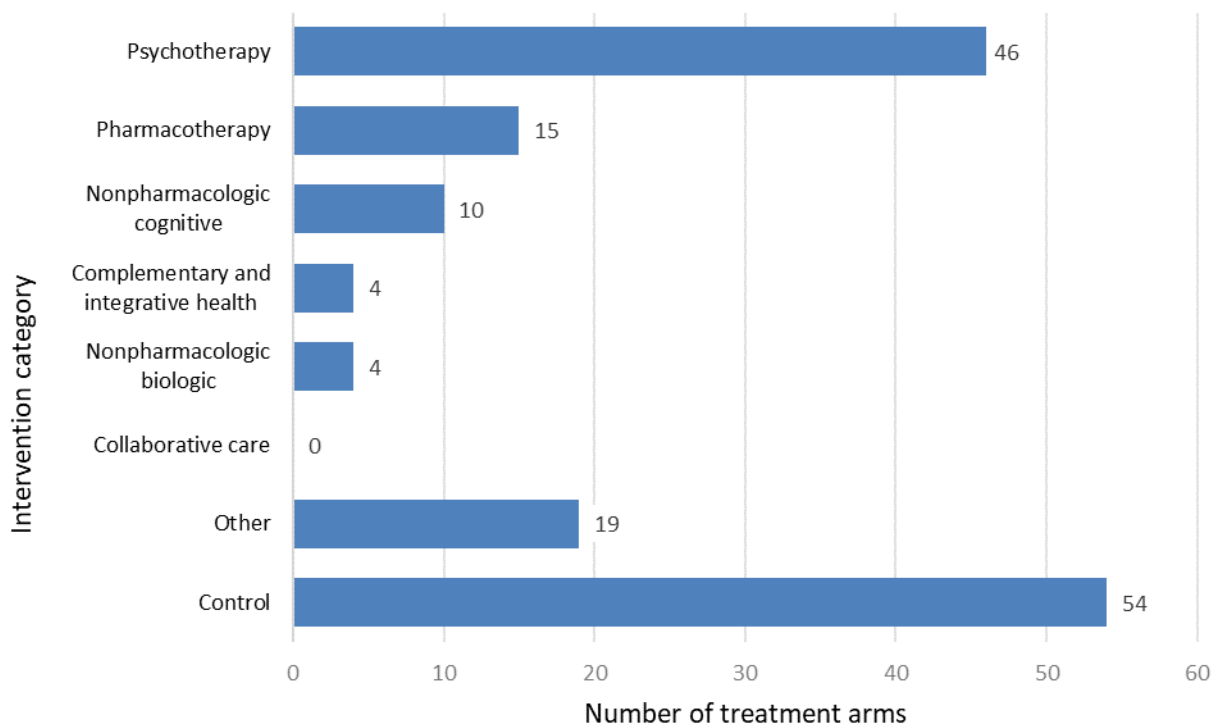
Abbreviations: CAPS = Clinician-Administered PTSD Scale; DTS = Davidson Trauma Scale; HTQ = Harvard Trauma Questionnaire; IES = Impact of Event Scale; ITQ = International Trauma Questionnaire; N = No, data element was not reported for the study; PCL = PTSD Checklist; PDS = Posttraumatic Diagnostic Scale; PSS-I = PTSD Symptom Scale-Interview; PSS-SR = PTSD Symptom Scale-Self-Report; PTSD = posttraumatic stress disorder; TOP = Treatment-Outcome Post Traumatic Stress Disorder Scale; Y = Yes, outcome was reported for the study.

Note: cells containing “Y” are shaded green

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

The distribution of treatment arms by intervention category is shown in Figure 18. Psychotherapy was the most frequently employed (67% of treatment arms); other treatments commonly employed included pharmacotherapy (22%), nonpharmacologic cognitive interventions (14%), CIH (6%), and nonpharmacologic biologic (6%). Because inclusion criteria were expanded during this update to include interventions that do not require a provider, there are relatively higher numbers of studies employing nonpharmacologic cognitive and other intervention category treatments compared to the rates of these intervention categories in previously included studies.

Figure 18. Summary of newly included studies: distribution of treatment arms by intervention category^a

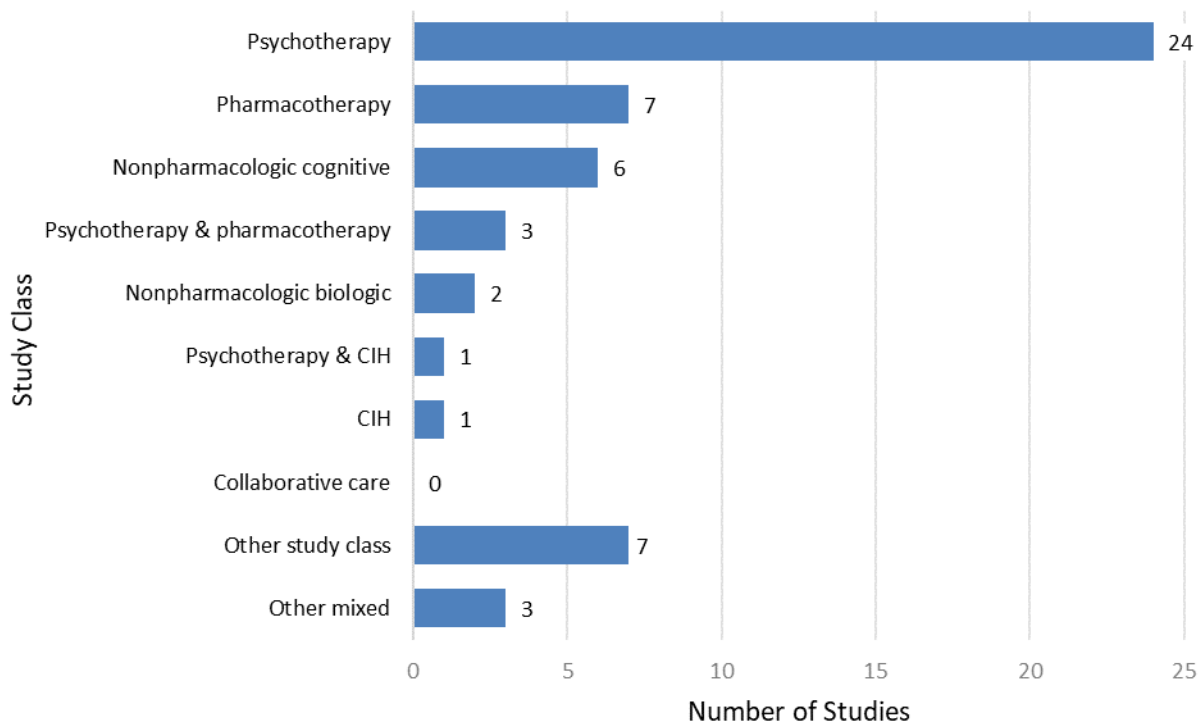


^aStudies have more than one treatment arm. Counts for these categories sum to greater than the total number of treatment arms in the included studies since some treatment arms combine multiple interventions of different categories. For example, one treatment arm could combine a psychotherapy treatment with a pharmacotherapy treatment. Thus each category would count for one within this single arm.

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Almost all the trials (47/54, 87%) examined interventions within a single category versus a control. The predominant intervention studied was psychotherapy treatments (44%), with the remainder of studies classified as pharmacotherapy (13%), nonpharmacologic cognitive (11%), psychotherapy & pharmacotherapy (6%), nonpharmacologic biologic (4%), psychotherapy & CIH (2%), CIH (2%), other study class (13%) and other mixed (6%) (Figure 19).

Figure 19. Summary of newly included studies: distribution by study class^a



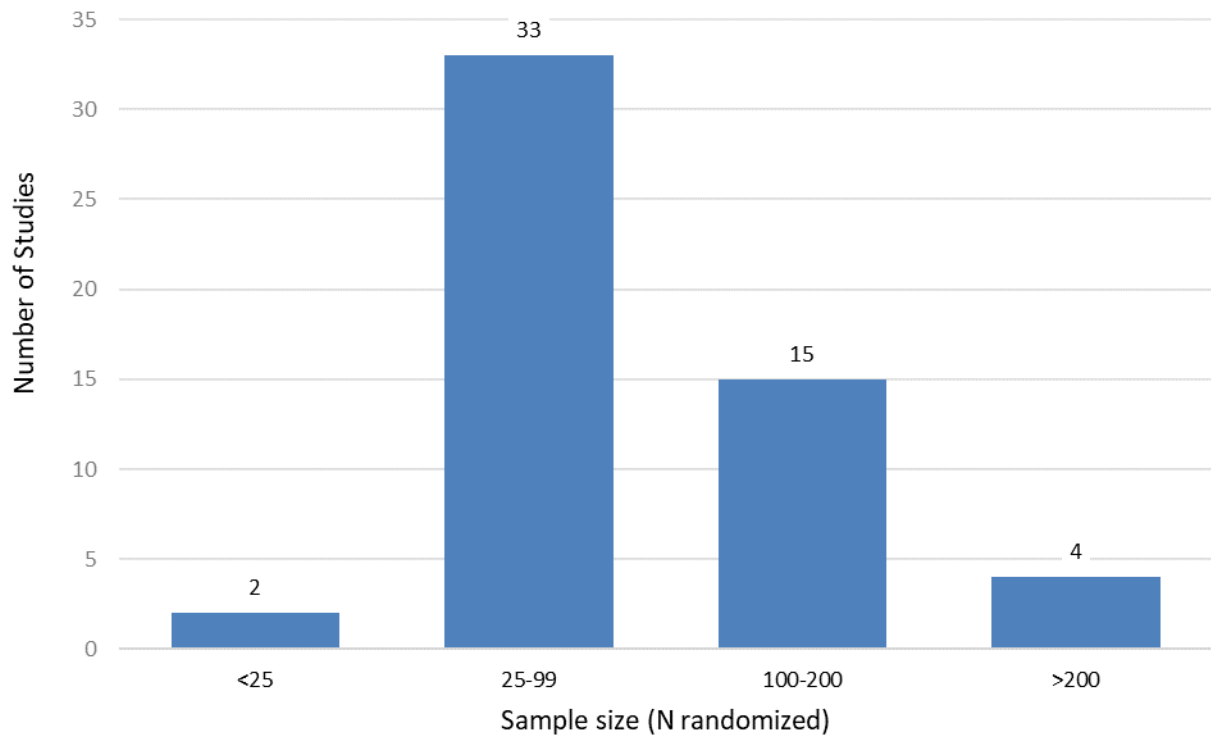
^aOther mixed includes studies in which the interventions studied were a combination other than psychotherapy & pharmacotherapy or psychotherapy & CIH (e.g., nonpharmacologic biologic & psychotherapy). Other study class includes studies of interventions classified as Other for intervention category.

Abbreviations: CIH = complementary and integrative health.

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

A total of 5,715 participants were enrolled in the newly included studies, with sample sizes ranging from 22 to 1,001. Most studies (61%) had sample sizes between 25 and 99 participants (Figure 20). There were four studies with over 200 participants.

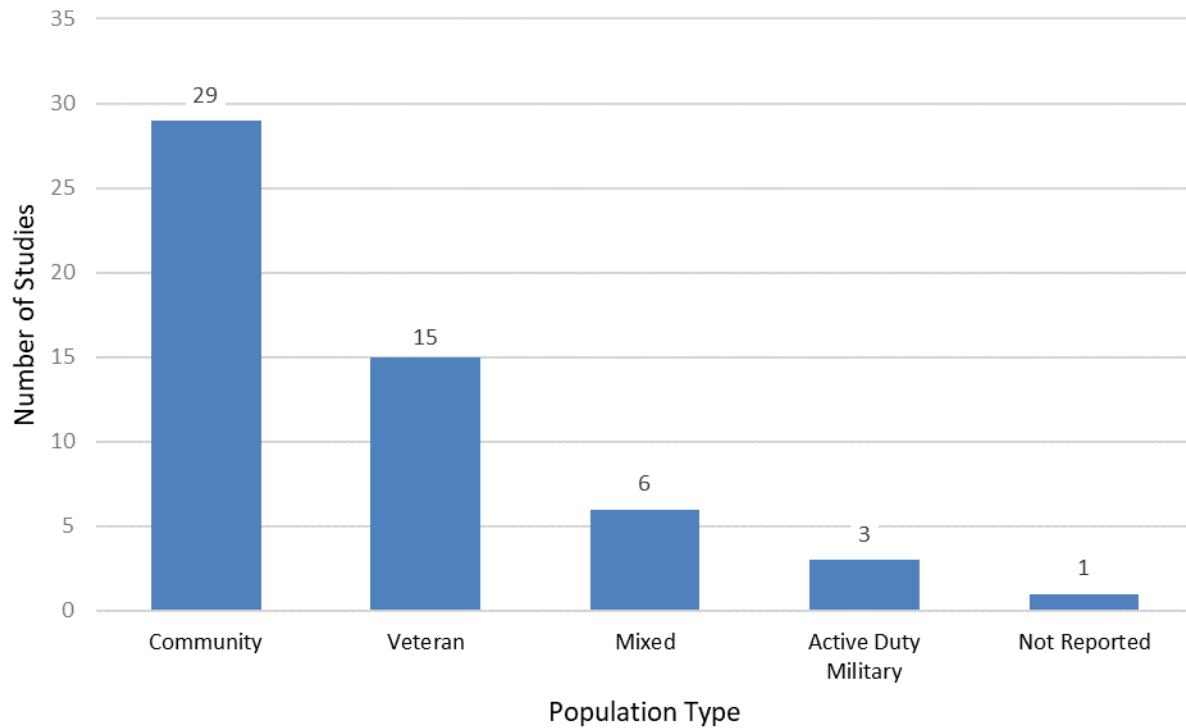
Figure 20. Summary of newly included studies: distribution of studies by sample size



3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Participants were drawn from the community population in 54 percent of studies, veterans in 28 percent of studies, and Active Duty Military in 6 percent of studies; 6 studies (11%) were in a mixed population; one study (2%) did not provide information on population (Figure 21).

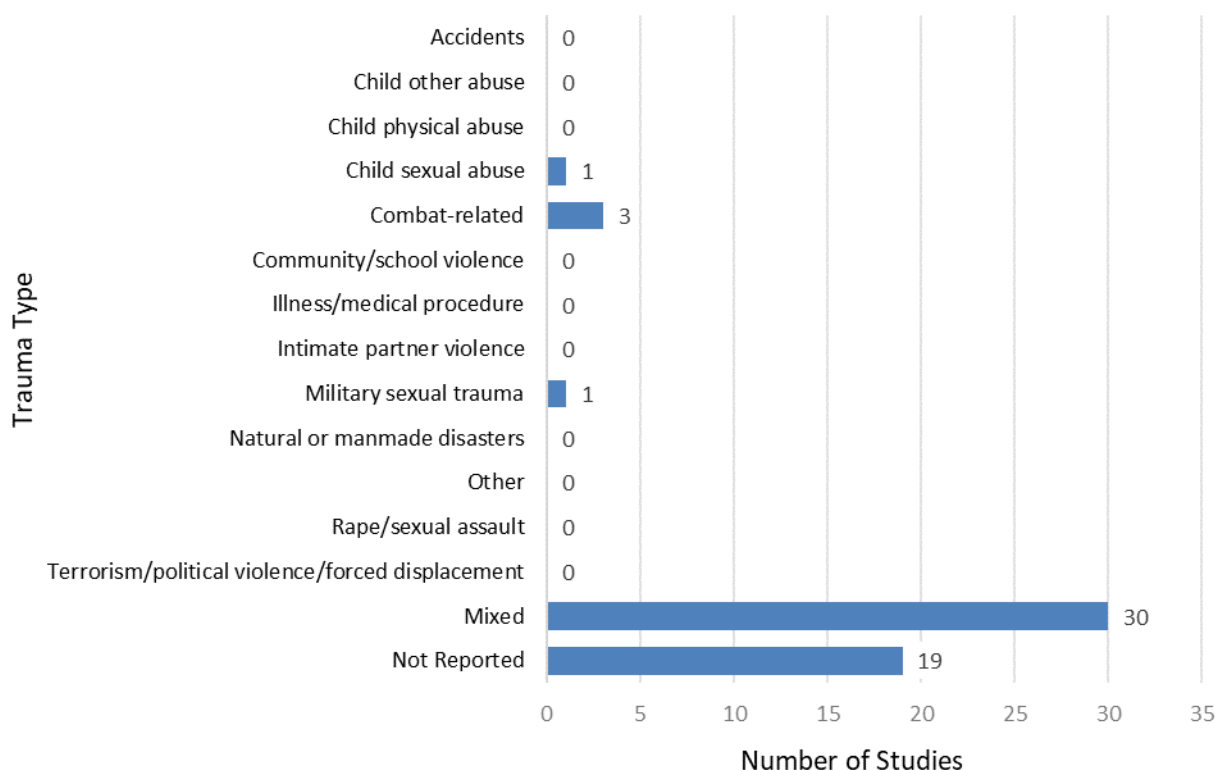
Figure 21. Summary of newly included studies: distribution of studies by population type



3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Five studies limited inclusion to participants who had experienced specific trauma types, and 19 studies (35%) did not provide information on trauma types (Figure 22). The largest number of studies allowed a mix of trauma types (30 studies, 56%).

Figure 22. Summary of newly included studies: distribution of studies by trauma type



Notes: Active Duty member reporting sexual assault outside of military was categorized as rape/sexual assault. Accidents include motor vehicle accidents, transportation-related accidents, and accidents due to construction. Mixed indicates multiple trauma types were targeted/included (e.g., a study which included participants with either child sexual abuse or rape/sexual assault would be classified as mixed).

Additional study and sample characteristics for studies added in this update are summarized in Table 6. Most studies were conducted in younger populations: the sample mean age was 30 to <45 years for 69 percent of studies, and no studies had a sample mean age 60 years or higher. Most studies enrolled both female and male participants, at varying proportions. Two studies (4%) included only female participants, and 6 percent of studies included only male participants. Six studies (11%) reported data for gender identity, and one (2%) reported data for both gender identity and sexual orientation of the sample. Over half of studies reported data on race that could be grouped into U.S. Census categories (61%), and 43 percent provided both race and ethnicity data. Data were not provided for race or ethnicity corresponding to U.S. Census categories in 39 percent of the studies.

Just under half of the studies (48%) were conducted in the U.S. Other countries in which at least three studies were conducted are Germany, United Kingdom and Australia. The majority of studies were conducted in the outpatient setting (70%).

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

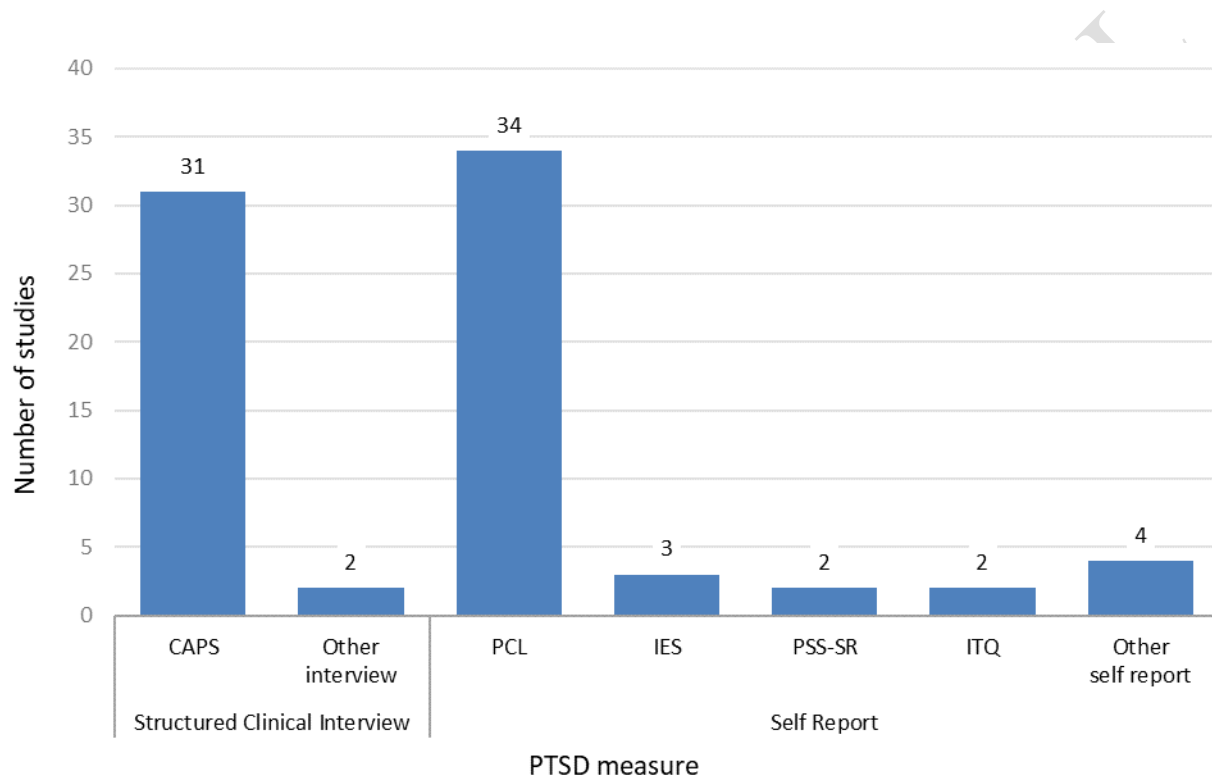
Table 6. Summary of sample and study characteristics for newly included studies

Characteristics	Categories	N studies	% of total studies
Age, sample mean	<30 years	5	9%
	30 to <45 years	37	69%
	45 to <60 years	12	22%
	≥60 years	0	0%
	Not reported	0	0%
Sex, % Female	100%	2	4%
	75% to <100%	17	31%
	50% to <75%	14	26%
	25% to <50%	5	9%
	>0% to <25%	12	22%
	0%	3	6%
	Sex not reported	1	2%
Gender and sexual orientation	Both gender and sexual orientation reported	1	2%
	Only gender data reported	6	11%
	Only sexual orientation data reported	0	0%
	Neither reported	47	87%
Race and ethnicity	Both race and ethnicity data reported	23	43%
	Only race data reported	10	19%
	Only ethnicity data reported	0	0%
	Neither reported	21	39%
Country	U.S.	26	48%
	Germany	5	9%
	Australia	3	6%
	U.K.	3	6%
	Other/Multiple	17	31%
Setting	Outpatient clinic	38	70%
	Inpatient/intensive outpatient	2	4%
	Primary care clinic	1	2%
	Other/Mixed	13	24%

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Most studies (78%, 42 studies) used a self-report measure to assess continuous PTSD outcomes; the PCL was used in 63 percent of studies (Figure 23). An interview measure was used in over half of studies (59%, 32 studies); 31 of these used the CAPS (57%) and 2 studies used another interview measure (one study used both CAPS and another interview measure).

Figure 23. Summary of newly included studies: PTSD measures used to assess continuous PTSD outcomes^a



^aStudies may have used more than one measure to assess PTSD outcomes.

Abbreviations: CAPS = Clinician-Administered PTSD Scale; DTS = Davidson Trauma Scale; IES = Impact of Event Scale; PCL = PTSD Checklist; PDS = Posttraumatic Diagnostic Scale; PSS-I = PTSD Symptom Scale - Interview; PSS-SR = PTSD Symptom Scale - Self-Report; PTSD = posttraumatic stress disorder.

3.2.2 Results, Characteristics of Included Studies, Studies Added in This Update

Over half of studies (61%) reported at least one dichotomous PTSD outcome. PTSD diagnostic change was reported in 46 percent and clinically meaningful response in 39 percent; both outcomes were reported in 13 studies (24%) (Table 7). Among other (non-PTSD) outcomes, depression was the most commonly assessed (59% of studies), followed by anxiety (33%), function (15%) and sleep (15%).

Table 7. Summary of PTSD and other outcomes for newly included studies

Outcome	N studies	% of studies
PTSD clinically meaningful response	21	39%
PTSD diagnostic change	25	46%
Anger	2	4%
Anxiety	18	33%
Depression	32	59%
Function	8	15%
Quality of Life	7	13%
Sleep	8	15%
Substance Use	6	11%
Suicide/Self-directed violence	5	9%

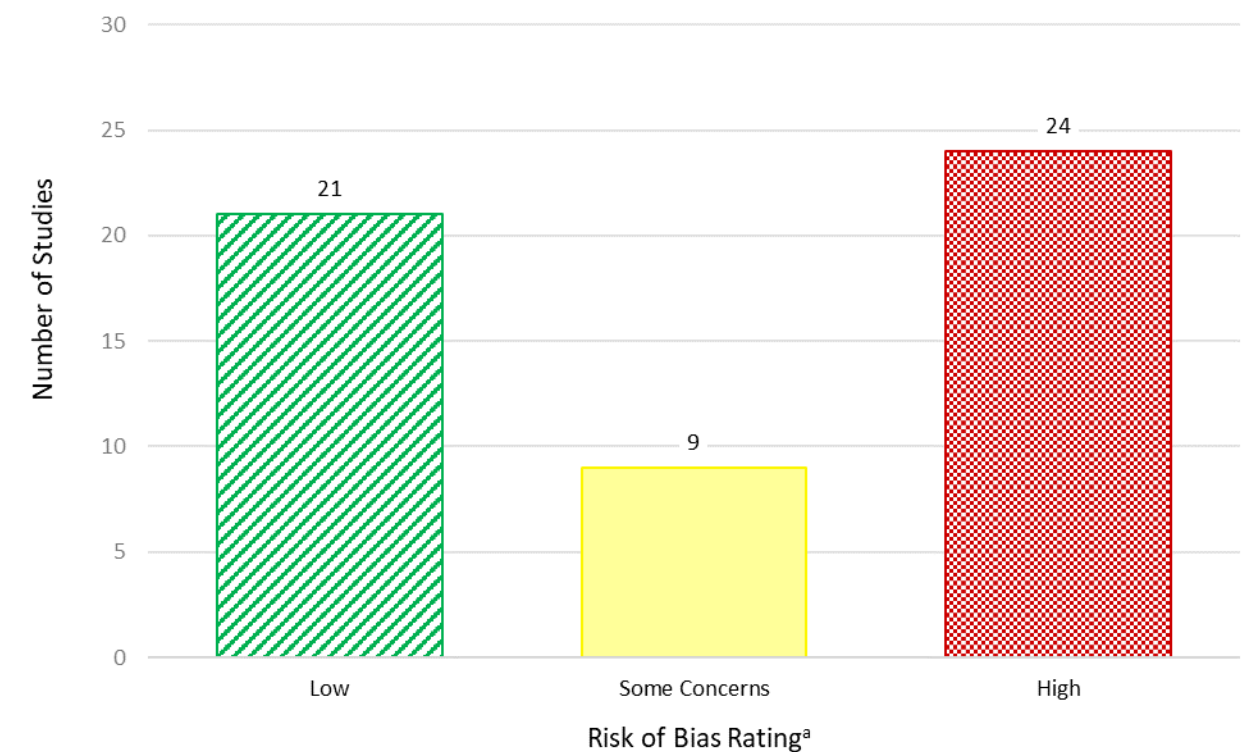
Abbreviations: PTSD = posttraumatic stress disorder.

3.3 Risk of Bias Assessment

Risk of bias (RoB) was assessed using Cochrane’s RoB 2 tool, as described in the Methods section. Detailed RoB ratings are presented in the evidence tables (Appendix E). In this section, we present the overall RoB rating; if multiple outcome measures were used, we present the data corresponding to the lowest risk of bias across all outcomes reported in the study. Ratings for additional outcome measures are available in the evidence table.

In this update, 54 newly included trials were assessed using Cochrane’s RoB 2 tool for trials (Table 8). The overall risk of bias was assessed as high for 44 percent of studies, some concerns for 17 percent of studies, and low for 39 percent (Figure 24). Studies were rated as high risk of bias mainly in the domains assessing deviations from intended interventions, missing outcome data or measurement of the outcome (Table 8).

Figure 24. Risk of bias rating^a for newly included studies (RoB 2 methods)



^aOverall RoB rating; if multiple outcome measures were used, we present the data corresponding to the with lowest risk of bias across all outcomes reported in the study.

Table 8. Newly included trials: risk of bias ratings by domain using Cochrane RoB 2 methods (k=54)

Author, Year	Bias Due to Randomization	Bias Due to Deviations From Intended Interventions	Bias Due to Missing Outcome Data	Risk of Bias in Measurement of the Outcome ^a	Bias in Selection of Reported Result	Overall RoB Assessment ^a
Allen, 2022 ³⁵	Low	High	High	High	Low	High
Astill-Wright, 2023 ⁶³	Low	High	Low	Low	Low	High
Back, 2023 ³⁶	Low	Low	Some Concerns	Low	Low	Some Concerns
Bizouerne, 2023 ⁶⁴	Some Concerns	High	Some Concerns	Some Concerns	Low	High
Brocker, 2024 ⁶⁵	Low	Low	Low	Low	Low	Low
Cloitre, 2024 ⁶⁶	Low	Low	Low	Low	Low	Low
Darvish, 2019 ²⁶	Low	High	Low	High	Low	High
de Kleine, 2019 ²⁸	Low	Low	Low	Low	Low	Low
Duek, 2023 ³⁸	Low	Low	Low	Low	Low	Low
Dunn, 2007 ³⁸	Low	High	High	Low	Low	High
Ehlers, 2023 ⁴⁴	Low	Low	Low	Low	Low	Low
Every-Palmer, 2024 ⁶⁷	Low	Low	Low	Low	Low	Low
Feder, 2023 ⁴⁵	Low	Low	Low	Low	Low	Low
Fine, 2023 ⁶²	Some Concerns	Low	Low	Low	Low	Some Concerns
Fonzo, 2019 ²⁷	Low	Low	High	Low	Low	High
Golier, 2023 ³⁹	Low	Low	Low	Low	Low	Low
Haller, 2023 ⁴⁰	Low	Low	Low	Some Concerns	Low	Some Concerns
Himmerich, 2016 ²⁵	Some Concerns	High	High	High	Low	High
Hollifield, 2024 ⁶⁸	Low	Low	Low	Low	Low	Low
Kanaan, 2023 ⁴⁶	Low	Low	Low	Low	Low	Low
Kearney, 2023 ⁵²	Some Concerns	High	Low	Low	Low	High
Kuhn, 2017 ²²	Low	Low	Low	High	Low	High
Larsen, 2019 ³⁰	Some Concerns	Low	Some Concerns	Some Concerns	Low	High
Lazarov, 2019 ²⁹	Low	Low	Low	Low	Low	Low
Litz, 2007 ²⁴	Some Concerns	Low	Some Concerns	Low	Low	Some Concerns
Litz, 2024 ⁶⁹	Low	Low	Low	Low	Low	Low
McLean, 2024 ⁷⁰	Low	High	High	Some Concerns	Low	High
Miller-Graff, 2021 ³⁴	Low	High	Some Concerns	High	Low	High
Miner, 2016 ²³	Some Concerns	Low	Low	High	Low	High
Mitchell, 2023 ⁵³	Low	Low	Low	Low	Low	Low
Monga, 2023 ⁵⁴	Some Concerns	Low	High	Low	Low	High
Müller-Engelmann, 2024 ⁷¹	Some Concerns	Low	Low	Low	Low	Some Concerns
Niles, 2020 ³³	Low	Low	Some Concerns	Low	Low	Some Concerns

Parmenter, 2024 ⁷²	Some Concerns	Low	Low	Low	Low	Some Concerns
Peck, 2023 ³⁷	Some Concerns	Low	Low	High	Low	High
Possemato, 2024 ⁷⁴	Low	Low	Low	High	Low	High
Prguda, 2023 ⁴⁸	Some Concerns	Low	Low	Some Concerns	Low	Some Concerns
Rajabi, 2023 ⁴⁷	Low	Low	Low	Low	Low	Low
Schoofs, 2024 ⁷³	Low	Low	Low	Low	Low	Low
Segal, 2020 ³¹	Low	Low	Low	Low	Low	Low
Sele, 2023 ⁵⁵	Low	Low	Low	Low	Low	Low
Shea, 2023 ⁵⁶	Low	High	High	Low	Low	High
Sloan, 2023 ⁶¹	Low	Low	Low	Low	Low	Low
Smaik, 2023 ⁵⁷	Low	Low	Low	High	Low	High
Stein, 2023 ⁵⁸	Low	Low	High	High	Low	High
Sturt, 2023 ⁵⁹	Low	High	High	High	Low	High
Taylor, 2023 ⁴¹	Some Concerns	Low	High	Some Concerns	Low	High
Voorendonk, 2023 ⁵¹	Low	Low	Low	Some Concerns	Low	Some Concerns
Wakusawa, 2023 ⁵⁰	Some Concerns	Low	Low	High	Low	High
Walter, 2023 ⁴⁹	Low	Low	Low	Low	Low	Low
Watkins, 2023 ⁴²	Low	Low	Low	Low	Low	Low
Woud, 2021 ³²	Low	Low	Low	Low	Low	Low
Yuan, 2023 ⁶⁰	Low	High	Low	Low	Low	High
Zhao, 2023 ⁴³	Some Concerns	High	Low	Low	Low	High

^aIf multiple outcome measures were used, we present the data corresponding to the with lowest risk of bias across all outcomes reported in the study.

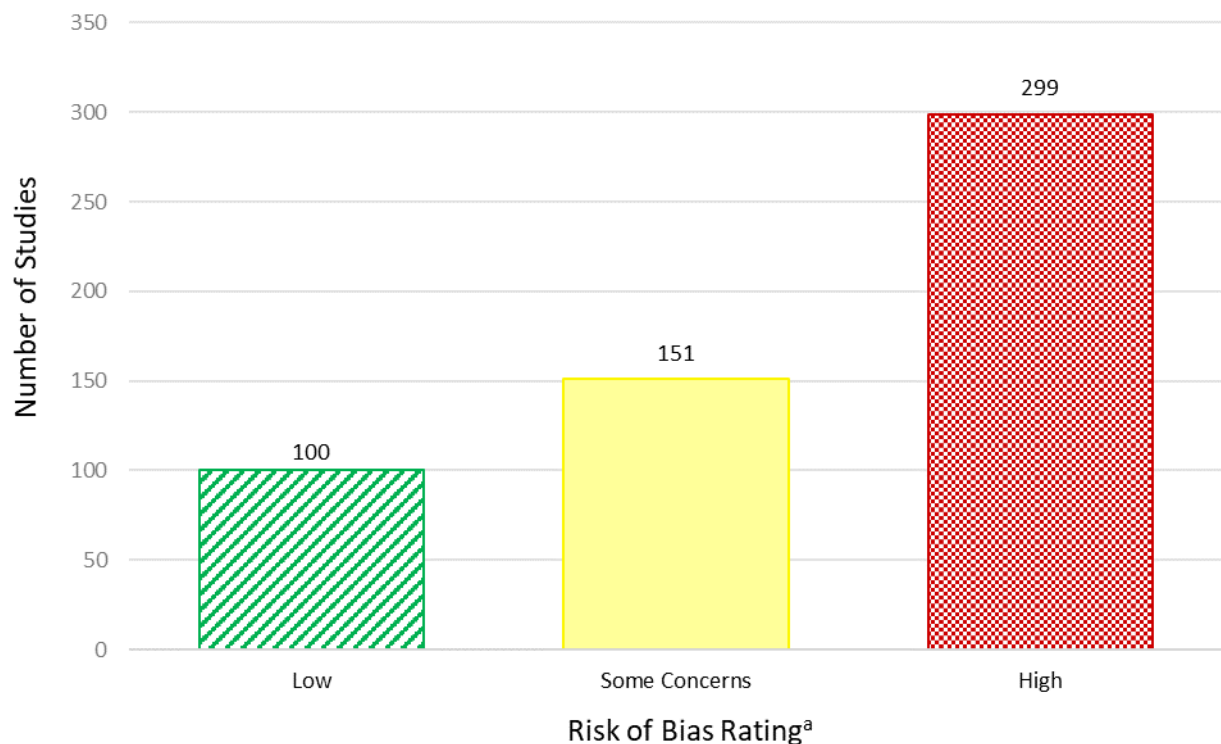
Note: cells are shaded corresponding to the value: “High” shaded in red, “Some Concerns” in yellow, and “Low” in green.

Abbreviations: AHRQ = Agency for Healthcare Research and Quality; ROB = risk of bias

3.3 Results, Risk of Bias Assessment

Across all 550 included trials, RoB was rated as high for 54 percent, some concerns for 27 percent, and low for 18 percent (Figure 25). Figure 26 shows the risk of bias ratings as a percentage of the total studies within each study class. The majority of studies were rated as high risk of bias in all study classes, except the psychotherapy & pharmacotherapy combined class which had an approximately equal proportion of studies for all ratings (32% rated as low, 35% rated as some concerns, and 32% rated as high risk of bias). Complementary and integrative health had the highest proportion of studies rated as high risk of bias (63%). Slightly lower proportions of studies were rated as high risk of bias in psychotherapy (58%), pharmacotherapy (53%), and other (55%) study classes. Most study classes had between 25 and 35 percent of studies rated as some concerns (range 22% to 35%). About a third of studies (32%) in the psychotherapy and pharmacotherapy study class were rated as low risk of bias, followed by nonpharmacologic biologic (20%), psychotherapy (18%) and pharmacotherapy (18%). For studies in all other study classes, 15 to 16 percent were rated as low risk of bias.

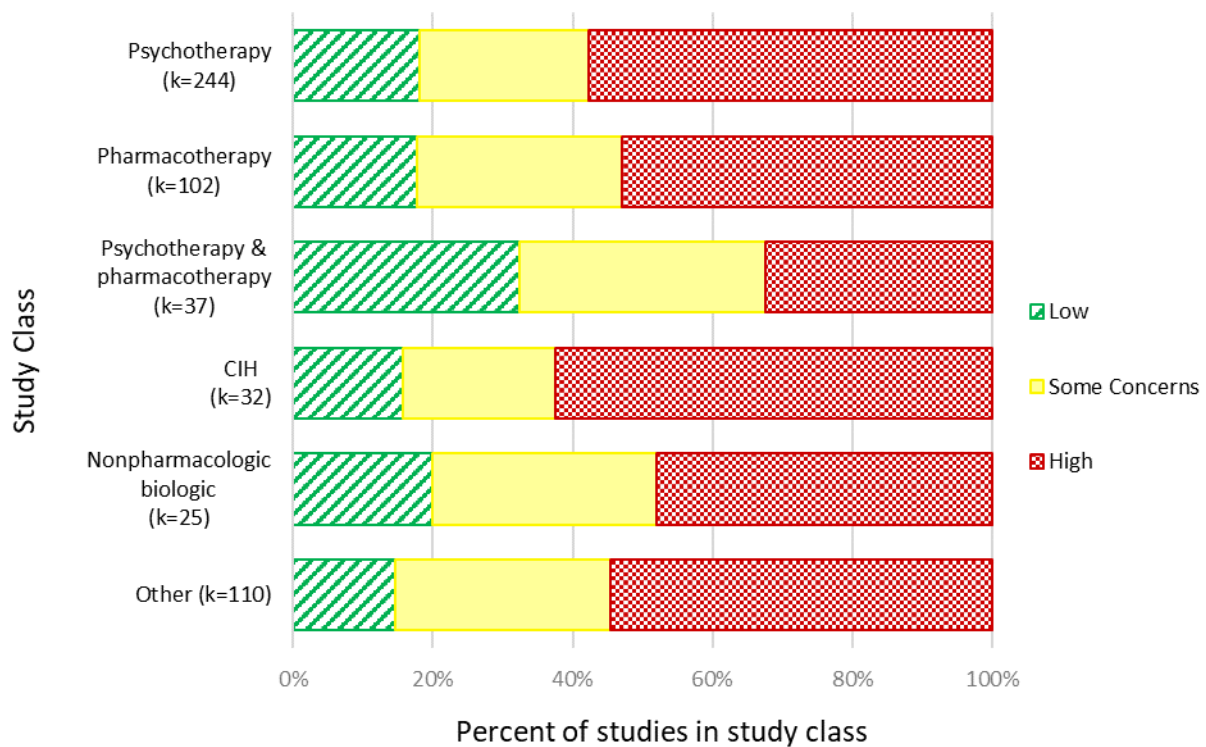
Figure 25. Risk of bias rating^a for all included studies assessed using Cochrane RoB 2 methods



^aOverall RoB rating; if multiple outcome measures were used, we present the data corresponding to the with lowest risk of bias across all outcomes reported in the study.

3.3 Results, Risk of Bias Assessment

Figure 26. Risk of bias ratings^a for all included studies using Cochrane RoB 2 methods by study class



^aOverall RoB rating; if multiple outcome measures were used, we present the data corresponding to the with lowest risk of bias across all outcomes reported in the study.

Abbreviations: CIH = complementary and integrative health; k = number of studies

4. Discussion

4.1 Summary and Implications

This report is updated to include detailed data extraction and risk of bias (RoB) assessments for 54 newly included randomized controlled trials (RCTs) of posttraumatic stress disorder (PTSD) treatments for those with PTSD and comorbid PTSD/substance use disorder (SUD). The updated evidence tables are being used by the National Center for PTSD (NCPTSD) to update the PTSD Repository, a publicly available trials database accessible at <https://ptsd-va.data.socrata.com/> and from the NCPTSD homepage (<https://www.ptsd.va.gov/ptsdrepository/index.asp>). A total of 550 RCTs are now included with detailed data abstraction, calculated standardized effect sizes for continuous PTSD outcomes, and RoB assessment using Cochrane's RoB 2 tool for trials.⁷⁶

The PTSD Repository serves a variety of clinical, research, and policy purposes, and its recent expansion and release as a Web-based, interactive database is designed to serve a broad range of stakeholders including patients, providers, researchers, and policymakers. As part of these dissemination efforts to a broad range of stakeholders, data visualizations and data stories are available as curated, accessible summaries of key findings from PTSD Repository trials. These summaries explain how to use the PTSD Repository data and focus on topics such as "Who Has Been Studied?"⁷⁷ Additionally, in an effort to assist a range of stakeholders use the data more quickly and accurately, data from the PTSD Repository evidence tables were recently incorporated into the Metapsy project,⁷⁸ a meta-analysis web resource focused on mental health trial data (<https://www.metapsy.org/database/ptsd>). The data have also been used to augment other data sources for recent guideline development groups.^{79,80}

These resources provide an accurate, standardized, and up-to-date source for PTSD trial data that can be used in a variety of contexts such as serving as source data for systematic reviews and meta-analyses to examine the efficacy of various treatments, quickly informing mental health or government organizations when they are asked to respond to media requests about the state of research on a particular intervention, providing a source of reliable information for researchers identifying research gaps or writing background/rationale sections of grants, and many other purposes. Other such databases in related fields of traumatic brain injury⁸¹ and depression^{82,83} have served these and other purposes and have been used as the basis for numerous publications and grant-funded studies.

While most meta-analytic comparisons are beyond the scope of this database development project, summary data from the evidence tables provide insight into population, intervention, and study characteristics that are more or less common (and more or less commonly reported in publications) in PTSD RCTs. For example, while limiting our inclusion to English-language publications means that only a subset of international research is included, we found that 42% of English-language RCTs were conducted outside the United States (U.S.). Because we focused on U.S. Census categories to classify race/ethnicity reported in the studies, and countries other than the U.S. commonly categorize race/ethnicity in other ways, we found that many of the studies reported race/ethnicity data that did not correspond to U.S. Census categories. Overall, we found that 84% of RCTs conducted outside the U.S. or in multiple countries didn't report race or ethnicity in ways that could be applied to U.S. Census category groups. Of those that did, most were conducted in Europe or Canada (see Table 9 for a summary). Additionally, changing political and social norms related to asking about nonbinary gender categories or about sexual orientation are slow to appear in the RCT literature, and can reflect views common to the

4. Discussion

countries and regions in which the trials were conducted. For example, only 8 studies reported data on participant sexual orientation, and 12 studies reported nonbinary gender categories; all were conducted in the U.S., Europe, or Australia. The summary data also suggest studies focus on different types of trauma depending on where the trial is conducted. For example, 20 of 24 studies targeting terrorism/political violence/forced displacement, 10 of 10 studies targeting natural or manmade disasters, and 8 of 12 targeting accidents were conducted outside the U.S.

Table 9. Non-U.S. trials reporting race and ethnicity data

Country	Both race and ethnicity data reported	Only race data reported
Australia	7	0
Brazil	1	0
Canada	2	2
China	1	0
Germany	2	0
Iran	1	0
Multiple	4	3
New Zealand	1	0
Norway	0	1
South Africa	1	0
Sweden	1	0
The Netherlands	1	0
U.K.	8	0

Abbreviations: U.K. = United Kingdom; U.S. = United States

Estimated standardized effect sizes for continuous PTSD outcomes were added in this update for newly included studies and studies included prior to the 2022 update.¹⁵ These data are now provided for all 550 included trials, facilitating comparison across trials. However, users of these data are cautioned to carefully consider which studies are appropriate to compare, as the PTSD Repository includes a diverse group of trials in terms of populations, interventions, comparators, outcomes, timing, and settings studied. In addition, the RoB should be considered in comparisons and interpretation of findings.

This work developing and updating the evidence tables was undertaken with guidance from NCPTSD and Technical Expert Panels (TEPs). In earlier phases of this project, these discussions emphasized how to scope the project, which data elements and studies to abstract and include in future updates, how to maintain data accuracy and relevance in large evidence tables, how to update and conduct RoB assessments, and potential next steps for the PTSD Repository. The TEPs and NCPTSD recommended regular updates to keep the PTSD Repository updated with the most current trial data. Ongoing discussions with the TEPs and NCPTSD have also highlighted the importance of developing a process to refine variable definitions, add variables, adjust the scope (e.g., add studies targeting comorbidities or those including participants meeting a broader definition of PTSD or subthreshold PTSD), and revise data management processes to ensure fluid integration into the Web-based database. Examples of these revisions include recent updates to the ways that suicide-related variables were abstracted and coded, the addition of detailed inclusion/exclusion criteria for each study, and the current process of updating RoB

4. Discussion

assessments using the newly available, pilot-tested Cochrane RoB 2 tool for randomized trials. In the current update, the TEP guidance emphasized the importance of including interventions that do not require a provider interaction, such as computer-based nonpharmacologic cognitive interventions, online support tools or apps, etc. These recommendations informed expansion of the inclusion criteria during this update.

This update added RCTs published through April 1, 2024. Combined with the first four reports, this overarching project includes evidence from over a 35-year span, with the earliest studies dating back to 1988.^{12,14-16}

The evidence tables (Appendix E) for this report are extensive and far more detailed than typical systematic review evidence tables, reflecting the objective of displaying detailed data elements in a data repository that is designed to be formatted for public availability. We devoted considerable time and attention to developing standard conventions for recording data (e.g., abbreviations, data formatting) and data abstraction instructions to ensure consistent and comprehensive reporting of the many elements of study data being abstracted for this repository. This update includes detailed data from 54 newly included trials of treatments for PTSD or comorbid PTSD and SUDs as well as RoB assessment using Cochrane's RoB 2⁷⁶ tool for trials and calculated standardized effect size estimates for continuous PTSD outcomes for all 550 included trials.

Variations in study designs and approaches to reporting presented many challenges to the data abstraction process. For example, some studies reported difference in change from baseline between groups, while others only reported within-group change from baseline or endpoint difference between groups. In some instances, the RCT may have analyzed a primary outcome other than PTSD, such as anxiety or sleep outcomes. However, provided that a study analyzed and reported an overall PTSD outcome, the study was included in the evidence tables. In some instances, distinguishing harms from negative outcomes (e.g., unintended adverse consequences of treatment vs. lack in efficacy of the intervention) was challenging because certain variables (e.g., increased suicidal ideation/behavior) were classified as an outcome in some studies, and as an adverse event in others. To standardize our approach for data entry, suicide behaviors and deaths were always abstracted as harms; where appropriate data was provided, additional information on other suicide-related data and self-harm was abstracted as outcomes. Many studies of both pharmacologic and nonpharmacologic interventions did not report details about adverse events.

For some data elements, standardization was not possible, and our data abstraction was guided by what the study reported and how the study reported the data (e.g., labeling of control interventions as placebo, usual care, minimal intervention, active placebo, etc.; gender categories and/or sexual orientation; race/ethnicity; current or historical substance use disorder or depression; clinically meaningful response; loss of diagnosis as an outcome); we report qualitative details related to study descriptions of such elements in the evidence tables in columns with the 'details' label (Appendix E). Akin to other data elements reported differently across studies, results and effect sizes were inconsistently reported and reported using different statistics in the included studies; therefore, we had to use a variety of methods to calculate comparable, standardized effect sizes depending on data availability across the diverse group of studies, as described in the methods. Lastly, gaps in reporting of certain data elements resulted in many evidence table cells listing 'not reported' (NR). Similar gaps in reporting of RoB-related elements also were apparent, particularly in earlier studies. Recognition of these gaps may help future researchers to report study methods and results more comprehensively.

4. Discussion

Finally, there are also some limitations to the RoB assessment in this report: RoB was assessed by one person and checked for accuracy by another person rather than by a dual independent review and consensus process. This leads to the possibility that systematic differences between raters might be reflected in the ratings. However, we implemented detailed guidance for raters, including definitions related to how RoB was assessed and thresholds (e.g., for attrition), to reduce interrater variability and provide transparency in methodology. We also implemented an automated data validation process to check that RoB ratings were congruent with the Cochrane RoB 2.0 algorithm as an additional check for errors or inconsistencies, and two reviewers checked any discrepancies identified during this process.

4.2 Next Steps

The completion of this project signifies the end of the fifth phase of work and expansion of the PTSD Repository evidence tables. In this phase, we added newly included RCTs, with detailed data abstraction into evidence tables, RoB assessment, and provide calculated standard effect sizes for all 550 included trials. The NCPTSD created the Web-based, searchable, interactive PTSD Repository database, and the current project updates and expands the evidence tables that serve as the foundation for that work.^{16,77,84,85}

In addition to updates to include newly published RCTs, future additions to the evidence tables have been explored and recommended by the TEP. These future additions could include reporting outcomes for PTSD symptom clusters, item-level data, individual participant-level data, subgroup analyses (e.g., to provide data on what works for whom, particularly minoritized groups), participant populations with >20 percent subthreshold PTSD, broader PTSD diagnostic criteria applied for inclusion, interventions designed to prevent PTSD or treat comorbid PTSD and other disorders such as depression, nonrandomized trials that control for important confounders, and qualitative and quantitative synthesis of key outcome data. We base these suggestions on our interaction with the evidence base, the TEP, and NCPTSD.

In summary, the PTSD Repository can (1) serve as a data source for future systematic reviews, meta-analyses, or other cross-study comparisons; (2) help identify research gaps to determine future research priorities; (3) encourage researchers to adopt standard data elements in research and reporting; (4) serve as a source for clinicians seeking information on effectiveness of interventions for patients with particular demographics or exposures; (5) provide the public a source to search for evidence on interventions they or their loved ones are considering; (6) provide policymakers with an up-to-date accounting of evidence to respond to inquiries; and (7) augment and inform the use of existing patient education tools or the online PTSD Treatment Decision Aid.¹¹ The TEP highlighted how adding variables, outcomes, subpopulations, updated RoB 2 assessment, and other studies in the future could help achieve the aforementioned goals of developing this database. This report and future updates aim to aid in the dissemination of the PTSD Repository. We plan to continue to provide data for all types of potential PTSD Repository users, so that content can be developed to support ease and accuracy of use, such as updated data dictionaries and data stories that provide both information on how to use the PTSD Repository as well as summaries of key findings from PTSD Repository data. The TEP comments compiled during the initial and continuation stages of this project provide a guide for future work in updating the evidence tables of the PTSD Repository.

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Abbreviations and Acronyms

Acronym or Abbreviation	Definition
AHRQ	Agency for Healthcare Research and Quality
CAPS	Clinician-Administered PTSD Scale
CBT	cognitive behavioral therapy
CIH	complementary and integrative health
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CPT	Cognitive Processing Therapy
corr	correlation
d	analog of Cohen's d
DSM	Diagnostic and Statistical Manual of Mental Disorders
EPC	evidence-based practice center
IES	Impact of Event Scale
IQR	Interquartile range
k	number of studies
KQ	Key Question
N	No, data element was not reported for the study
NA	not applicable
NCPTSD	National Center for Posttraumatic Stress Disorder
NR	not reported
PCL	PTSD Checklist
PDS	Posttraumatic Diagnostic Scale
PE	Prolonged Exposure
PICOTS	populations, interventions, comparators, outcomes, timing, settings, study design
PSS-I	PTSD Symptom Scale-Interview
PSS-SR	PTSD Symptom Scale-Self-Report
PTSD	posttraumatic stress disorder
PTSD Repository	PTSD Trials Standardized Data Repository
RCT	randomized controlled trial
RoB	risk of bias
s	standard deviation
SEADS	Supplemental Evidence And Data for Systematic Review
SI-PTSD	Structured Interview for PTSD
SUD	substance use disorder
TAU	treatment as usual
TEP	Technical Expert Panel
TOP-8	Treatment-Outcome Posttraumatic Stress Disorder Scale
U.K.	United Kingdom
U.S.	United States
Y	Yes, outcome was reported for study