Efficacy and acceptability of interventions for co-occurring PTSD and SUD: A meta-analysis

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Abstract

Over the past 20 years, numerous treatments addressing comorbid Posttraumatic Stress Disorder (PTSD) and Substance Use Disorder (SUD) have been developed and tested. The current meta-analysis examined the efficacy and acceptability of the two central treatment types—trauma-focused and non-trauma-focused—compared with all comparators and with cognitive-behavioral manualized SUD treatments immediately post-treatment and at longest follow-up. Twenty-eight randomized clinical trials (N= 3247) were included. There were small to large within-group effects for all forms of active treatment (gs = 0.30–1.11). Trauma-focused but not non-trauma-focused treatments outperformed all comparators on PTSD outcomes at post-treatment. Neither trauma-focused nor non-trauma-focused treatment outperformed all comparators on SUD outcomes at post-treatment. Neither trauma- nor non-trauma-focused treatment outperformed...
manualized SUD treatments on PTSD outcomes at either time point. Manualized SUD treatments outperformed trauma-focused treatments on SUD outcomes at post-treatment and non-trauma-focused treatments on PTSD outcomes at follow-up. Regarding treatment retention, neither trauma-focused nor non-trauma-focused treatments significantly differed from all comparators or from manualized SUD treatments. Between-group results were largely unchanged in trim-and-fill analyses, but were not robust to fail-safe N. Few moderators were detected. Taken together, results suggest that trauma-focused, non-trauma-focused, and manualized SUD interventions are sound options for individuals with comorbid PTSD/SUD.

Keywords
Meta analysis; Posttraumatic stress disorder; Substance use disorder; Randomized controlled trials; Cognitive behavior therapy

1. Introduction
Posttraumatic Stress Disorder (PTSD) is the hallmark psychiatric disorder that can develop following trauma exposure (American Psychiatric Association, 2013). Past-year and lifetime prevalence estimates of PTSD among community-dwelling U.S. adults are 4.7% and 6.1%, respectively (Goldstein et al., 2016). PTSD commonly co-occurs with other psychiatric conditions, including Substance Use Disorders (SUDs). Recent epidemiologic research demonstrates that 57.7% of those with lifetime PTSD have had either a lifetime Alcohol Use Disorder (AUD), Drug Use Disorder (DUD), or both, while the burden of lifetime PTSD among those with lifetime SUD is markedly lower (12.3%; Simpson, Rise, Browne, Lehavot, & Kaysen, 2019; see also Blanco et al., 2013). Among those seeking SUD treatment, PTSD comorbidity is, however, quite common, with estimates of current PTSD generally being just under 40% (Gielen, Havermans, Tekelenburg, & Jansen, 2012; Harrington & Newman, 2007; Reynolds et al., 2005). Critically, individuals with co-occurring PTSD and SUD are at elevated risk relative to their single disorder peers regarding social and functional instability, additional psychiatric comorbidities, and risk of suicidal behaviors (Blanco et al., 2013; Hassan, Le Foll, Intiiaz, & Rehm, 2017; Sells et al., 2016).

Given the level of disease burden and deleterious effects on functioning associated with co-occurring PTSD/SUD, it is not surprising that these individuals are likely to access treatment. A recent nationally representative study estimated that approximately 36% of people with comorbid PTSD/SUD have sought SUD-specific care while 84% have sought care in mental health settings (Simpson et al., 2020; see also Hawn, Cusack, & Amstadter, 2020). However, despite these high rates of treatment engagement, persistence of PTSD is common with over two-thirds of individuals with comorbid PTSD/SUD meeting criteria for a chronic PTSD diagnosis and nearly 40% for a chronic SUD (i.e., positive diagnosis both prior to the past year and in the past year; Simpson et al., 2020).

Such epidemiological data highlight the under- and unmet treatment needs of people with comorbid PTSD/SUD and suggest that many of these individuals do not adequately respond to available treatments at the population level. However, epidemiological data are not
fine-grained enough to provide specific insights regarding the types of care associated with better and worse outcomes, as information regarding dose and type of care (e.g. whether empirically supported) are generally not available. Rather, we must rely on the results of randomized clinical trials (RCTs) and synthesis of these results. Although many RCTs examining PTSD interventions have excluded people with SUDs (Leeman et al., 2017), there is still a substantial body of relevant work pertaining to treatment options for individuals with PTSD/SUD.

Broadly, behavioral interventions that have been evaluated as treatments for PTSD/SUD in RCTs may be classified as either (a) trauma-focused treatments, meaning that systematic trauma-processing occurs in the majority of sessions (Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure; COPE; Back et al., 2018; Norman et al., 2019; Cognitive Processing Therapy [CPT]; Simpson et al., 2021; and Prolonged Exposure therapy [PE]; Foa et al., 2013) or (b) non-trauma-focused treatments that address both SUD and PTSD without explicit discussion of trauma specifics (Integrated Cognitive Behavioral Treatment [ICBT]; McGovern et al., 2015; Seeking Safety: Najavits, Krinsley, Waring, Gallagher, & Skidmore, 2018). All of the extant non-trauma-focused treatments address PTSD symptoms and substance use in various integrated fashions while approximately half of trauma-focused treatments integrate elements aimed at ameliorating SUDs with trauma-exposure elements to address PTSD symptomatology (Back et al., 2019; Ruglass et al., 2017) and half deliver the SUD and PTSD treatments separately (Coffey et al., 2016; Foa et al., 2013).

There have been robust efforts to synthesize the available literature on PTSD/SUD behavioral treatments. Indeed, there are numerous narrative reviews (Bailey, Trevillion, & Gilchrist, 2019; Berenz & Coffey, 2012; van Dam et al., 2012; Flanagan et al., 2016; McCauley, Killeen, Gros, Brady, & Back, 2012; Najavits & Hien, 2013; Ralevski, Olivera-Figueroa, & Petrakis, 2014; Simpson, Lehavot, & Petrakis, 2017) and two meta-analyses (Roberts, Roberts, Jones, & Bisson, 2015; Torchalla, Nosen, Rostam, & Allen, 2012) of this literature. Roberts et al. (2015) included 13 RCTs in the most recent and comprehensive meta-analysis. They found trauma-focused treatments to be significantly more effective than treatment-as-usual and no/minimal treatment for PTSD both at post-treatment and follow-up and for substance use at follow-up, but also associated with significantly poorer treatment retention, again compared to treatment-as-usual and no/minimal treatment. Non-trauma-focused treatments did not differ significantly from comparators on treatment retention and little support was found for them on either PTSD or SUD indicators.

While Roberts et al. (2015) meta-analysis provided a valuable overview of the extant PTSD/SUD behavioral RCT literature, the number of relevant studies has more than doubled in the intervening six years. Given the modest number of studies available for several comparisons tested by Roberts et al. (Ks ranged from 1 to 4 studies), which likely impacted statistical power (Valentine, Pigott, & Rothstein, 2010), the increase in available studies suggests that it is an opportune time for an updated examination. In addition, Roberts et al. did not evaluate potential moderators of treatment response, such as participant drug use involvement or recruitment setting (i.e., SUD treatment clinics vs. community-based recruitment), factors that may be markers of disease severity (Moss, Goldstein, Chen, & Yi,
Thus, we undertook an updated meta-analysis of behavioral treatments for adults with co-occurring PTSD/SUD in RCTs involving outcomes pertaining to PTSD severity, substance use, and treatment retention. Following Roberts et al., we classified studies as testing trauma-focused treatments or non-trauma-focused treatments and examined outcomes at both immediate post-treatment and longest follow-up.

In addition to comparing trauma-focused treatments to all comparators and non-trauma-focused treatments to all comparators (manualized SUD treatment, SUD treatment as usual, and no/minimal treatment), we also included comparisons involving only those trials that included manualized SUD treatments. The latter set of comparisons was undertaken because manualized SUD treatment conditions generally account for time, attention, and therapist training, thus allowing evaluation of the unique contributions of trauma-focused and non-trauma-focused treatments above and beyond common therapeutic elements (Wampold & Imel, 2015). For trauma-focused interventions, unique therapy elements typically include explicit focus on trauma memories to provide an opportunity for new learning and emotional processing (PE; Foa et al., 2013) or to arrive at healthier beliefs about the trauma, oneself, and others (CPT; Resick, Monson, & Chard, 2016). For non-trauma-focused interventions, unique therapy elements typically include strategies to increase patients’ understanding of the relationships between trauma-related triggers and substance use and to build coping skills to enable patients to break this reactive link (ICBT, McGovern et al., 2015; Seeking Safety, Najavits et al., 2018). Also, because manualized SUD treatments are frequently offered in SUD clinical settings (Center for Substance Abuse Treatment, 1999; Hendershot, Witkiewitz, George & Marlatt, 2011; VA/DoD Management of Substance Use Disorders Workgroup, 2015), these interventions are likely received by many with PTSD/SUD who do not have access to care for both aspects of the comorbidity because few community-based clinics offer PTSD/SUD treatment (see Killeen, Back, & Brady, 2015). Although such interventions are likely delivered more rigorously in the context of RCTs than in standard clinical settings, knowledge of the efficacy of manualized SUD treatments for individuals with co-occurring PTSD/SUD is important from a public health standpoint. Specifically, should meta-analytic empirical research suggest that manualized SUD treatments are either comparable or superior to either trauma-focused or non-trauma-focused PTSD/SUD treatments it would support investing in improving the delivery of these already familiar care options.

We hypothesized that trauma-focused treatments would be associated with superior PTSD and substance outcomes relative to all comparators, but would outperform manualized SUD treatment only on PTSD outcomes. Based on Roberts et al. (2015) findings, we anticipated that trauma-focused treatments would be associated with significantly lower treatment retention than all comparators generally and manualized SUD treatments specifically. We did not anticipate differences between non-trauma-focused treatments and all comparators or manualized SUD comparators on PTSD or SUD outcomes or treatment retention (Roberts et al., 2015). In the absence of data explicitly speaking to treatment acceptability, we followed Roberts et al. (2015) and used treatment retention as a proxy for treatment acceptability.

We examined several potential moderators. First, because there is consistent support for the self-medication hypothesis in the context of co-occurring PTSD/SUD such that many
individuals with both disorders report using substances to cope with their PTSD memories and symptoms (Hawn et al., 2020) and those with comorbid PTSD/SUD generally prefer integrated treatment (Back et al., 2014), we evaluated whether integrated trauma-focused treatment that addresses both sides of the comorbidity simultaneously (vs. non-integrated) moderated treatment outcomes. Second, in light of findings suggesting that those with co-occurring PTSD/DUD are at elevated risk of worse social functioning (e.g., greater risk of unemployment and lifetime incarceration; lower educational attainment), greater SUD severity, and greater suicide risk than those with PTSD/AUD-only (Simpson et al., 2019), we evaluated whether the proportion of the samples with reported drug use moderated treatment effects. Third, we explored whether the setting in which the RCTs took place (e.g., SUD treatment clinics vs. community recruitment by university-based investigators) moderated outcomes given epidemiologic evidence that those with PTSD/SUD who receive SUD treatment have markedly more severe SUDs and are more likely to have chronic SUDs than those reporting no treatment or mental health treatment only (Simpson et al., 2020). Fourth, we evaluated whether differential assessment attrition moderated outcomes because study outcomes could be biased if, for example, less severe, more stable study participants are more likely to attend post-treatment assessments than more severe, less stable participants. Finally, we examined whether treatment delivery platform moderated outcomes because individually delivered treatment has been found to be more efficacious in treating PTSD than group delivered treatment (Haagen, Smid, Knipscheer, & Kleber, 2015; Resick et al., 2017).

2. Method

2.1. Protocol and registration

No published protocol exists for this meta-analysis.

2.2. Eligibility criteria

Studies needed to meet the following basic criteria to be included: (1) were available in English, (2) examined the effects of cognitive and/or behavioral treatments (i.e., psychotherapies) with the intention of addressing both PTSD and SUD, (3) included only adults ages 18 and over (4) used an RCT design, and (5) outcomes pertained to both PTSD symptomatology and substance use. Study samples also needed to be comprised of individuals with current comorbid PTSD and SUD such that at least 80% of participants met diagnostic criteria for both disorders or at least 80% had clinical presentations consistent with PTSD and SUD. Specifically, studies involving a mix of participants with threshold and sub-threshold DSM or ICD diagnoses of PTSD were included as were studies with participants who screened positive for PTSD (i.e., if diagnostic interviews were not conducted). Of note, ample evidence suggests that subthreshold PTSD is associated with significant distress and impairment (Pietrzak, Goldstein, Southwick, & Grant, 2011; Zlotnick, Franklin, & Zimmerman, 2002). Similarly, studies were included if they used an accepted alcohol or drug use screen (e.g. the AUDIT; Babor, de la Fuente, Saunders, &

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1This was moot for the non-trauma-focused interventions as they are all integrated.
Grant, 1992) with a cut score indicating likely disordered use AND required recent unsafe use (e.g. alcohol consumption in excess of NIAAA safe drinking guidelines).

No restrictions were placed on publication status (i.e., unpublished data and dissertations were eligible). Studies were excluded if they only assessed ancillary indicators of substance use (e.g. craving), did not assess both outcomes in an outpatient context (e.g. all assessments took place in controlled environments), or reported on subsets of samples from studies not intending to address both aspects of the comorbidity during treatment (e.g., Jason et al., 2011; Park, Cheng, Samet, Winter & Saitz, 2015). We contacted investigators regarding the availability of results from unpublished RCTs identified in trial registries (e.g., Hamblen, personal communication; Vujanovic, personal communication) as well as for information on subsets of participants likely meeting criteria for PTSD/SUD in studies targeting these disorders but allowing a broader spectrum of enrollees (i.e., Brief et al., 2013, personal communication; Haller et al., 2016, personal communication).

2.3. Information sources

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards were followed (Moher, Liberati, Tetzlaff, Altman & PRISMA Group, 2009; see Table A.1 for PRISMA Checklist). With input from the first author (TLS), a medical research librarian (DKNL) systematically searched ten databases: PubMed, Embase, Cochrane Central Register of Controlled Trials, PsycINFO, CINAHL Complete, PTSDpubs, Web of Science, ProQuest Dissertations and Theses Global, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. Databases were searched from inception to July 9, 2021. Five articles were identified for review through review of reference sections.

2.4. Search, study selection, and data collection process

The search strategies incorporated controlled vocabulary terms and keywords appropriate to each database to represent the concepts of PTSD, SUD, and controlled clinical trials (see Table A.2 for full search terms used in each database).

After removing duplicates, each title and/or abstract was independently evaluated by two of three authors (SEH, AL, TLS) based on inclusion/exclusion criteria. The remaining studies underwent full text review by two of the same three authors. Disagreements were settled through discussion until consensus was reached.

Two of three authors independently extracted information on demographics, treatment delivery, and outcome data for each study using standardized spreadsheets (SEH, AL, TLS). There were no substantive errors detected in the coding when the spreadsheets were mechanically compared. Two authors (SMB, TLS) independently extracted risk of bias information with disagreements discussed until consensus was reached.

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2 Roberts et al. (2015) included four studies that did not meet the current study inclusion criteria: 1) Coffey, Stasiewicz, Hughes, and Brimo (2006) did not assess substance use post-treatment; 2) Najavits, Gallop, and Weiss (2006) included only adolescents; 3) Frisman, Ford, Lin, Mallon, and Chang (2008) did not include a measure of PTSD symptoms, and 4) when we reached out to Dr. Mueser et al. (2008) to inquire about the possibility of acquiring summary information on the subset of individuals in their sample with current SUD, he informed us that they did not have this information as they queried only lifetime SUD and he also noted that the participants did not necessarily have PTSD.
2.5. Data Items

Data necessary for computing effect sizes from continuous measures (e.g. number of drinking days) included sample size, means, and standard deviations. For dichotomous outcomes (e.g. number of participants reporting drug use), we extracted sample sizes in the relevant cells. Information on all relevant outcomes was recorded. For example, if a study reported both average drinks per drinking day and percent days heavy drinking, both measures were included. Symptom outcome assessment data were recorded for baseline, immediate post-treatment, and the longest follow-up. We restricted the meta-analytic data to these two post-treatment assessments so that the level of precision across studies was similar.

In addition, we extracted demographic and clinical features of the samples and characteristics of the treatment and control conditions. These included mean age, percentage female, percentage racial/ethnic minority, percentage meeting full PTSD diagnostic criteria, percentage meeting SUD diagnostic criteria, percentage with drug use, treatment and control condition name and type, intention-to-treat (ITT) sample size, treatment length (number of sessions or weeks), number of weeks and/or sessions required for treatment completion, percentage of participants completing treatment, treatment modality (e.g., group, individual), and treatment setting (e.g., SUD treatment clinic, residential SUD treatment, university laboratory).

Conditions were categorized into the following five groups: (1) trauma-focused, (2) non-trauma-focused, (3) CBT manualized SUD (4) SUD TAU, or (5) no/minimal treatment. All of the identified studies were included in preliminary within-subject models evaluating changes in outcomes over time associated with these five categories. Between-group comparisons that involved either trauma-focused or non-trauma-focused treatments compared with any of the other three categories (i.e., manualized SUD, SUD TAU, no/minimal treatment) were included in the between-group models. A separate set of between-group models compared either trauma-focused or non-trauma-focused treatments with manualized SUD treatments only.3

We followed Fu et al. (2011) guidance that four or more studies are needed for meta-analysis and thus did not conduct between-group tests on the two studies that included comparisons between trauma-focused and non-trauma-focused treatments (Najavits et al., 2018; Norman et al., 2019) in separate models. These studies were excluded from the primary between-group analyses but were included in sensitivity analyses in the trauma-focused vs. all comparators models. To isolate the effects of trauma-focused treatments involving empirically supported PTSD treatment components (CPT: Simpson et al., 2020; Vujanovic personal communication; PE4: Back et al., 2019; Foa et al., 2014; Ruglass et

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3To be considered in the between-group comparisons, studies needed to assign participants to at least two conditions that were evaluating distinctly different conditions rather than testing a core intervention with and without an add-on such as peer support (i.e., Possemato et al., 2019) or contingency management (i.e., Schacht, Brooner, King, Kidoff, & Peirce, 2017), or different sequencing of the same interventions (i.e., Kehle-Forbes et al., 2019).

4Foa et al. (2013) tested PE while both Back et al. (2018) and Ruglass et al. (2017) tested COPE, which integrates PE and CBT for SUD.
al., 2017) relative to the most rigorous comparators (manualized SUD), a set of sensitivity analyses involving only those studies were conducted.

2.6. Risk of bias in individual studies

Individual studies were rated with the Cochrane risk-of-bias tool (Higgins & Green, 2008). Bias was assessed across six domains including: selection bias (random sequence generation, allocation concealment), detection bias (masking of outcome assessors), attrition bias (use of intent-to-treat models that account for missing data), reporting bias (selective reporting), and other sources of bias (baseline imbalance, incomplete reporting of methods). Risk of bias was assessed as low, high, or unclear on each domain for each study.

2.7. Summary measures

Standardized effect sizes were calculated using standard meta-analytic methods (Borenstein, Hedges, Higgins, & Rothstein, 2009). For continuous outcomes, this involved first computing a within-group pre-post (or pre-follow-up) Cohen (1988). We assumed a correlation of $r_{xx} = 0.50$ between time points (which is lower than a typical test-retest correlation to account for potential changes due to intervention; Hoyt & Del Re, 2018). Between-group effects were calculated as the difference between the within-group effects (i.e., Becker, 1988). This method has the advantage of incorporating baseline data, as opposed to using post-test only. For categorical outcomes, we computed odds ratios (OR) reflecting the likelihood of a given outcome (e.g. drug use) based on group status (i.e., treatment or comparator). ORs were converted into Cohen’s $d$-units using standard methods (Borenstein et al., 2009) and incorporated into the between-group effect estimates. Effect sizes were converted into Hedges’ $g$ to account for small sample bias (Cooper, Hedges, & Valentine, 2009). The sign for each effect was adjusted so that a positive effect size always indicated improvement and/or larger improvement in the treatment group relative to the control condition (i.e., decreased symptoms). We calculated treatment retention for studies that reported these data for both the treatment and control conditions. We computed an OR reflecting the likelihood of completing treatment for those assigned to the treatment conditions relative to those assigned to the control conditions.

2.8. Synthesis of Results

Using standard meta-analytic methods (Cooper et al., 2009), effects were next aggregated within measure (e.g. across subscales of the Addiction Severity Index) and then within study using the ‘agg’ function from the ‘MAd’ package (Del Re & Hoyt, 2014) in R (R Core Team, 2018). Separate omnibus analyses were conducted to characterize within-group and between-group change at post-treatment and follow-up on PTSD or SUD symptoms and for between-group differences on treatment retention. Effects on symptoms were examined across the five within-group categories and four between-group comparisons. Thus, 36 aggregate effect sizes are reported (i.e., $2 \times 2 \times 9$). An additional four effect sizes assessed differential treatment attrition in the four between-group categories.

Some studies included multiple treatment or control groups (e.g. Foa et al., 2013). For the within-group models, each treatment and control arm contributed a unique effect size. For the between-group models we balanced using all available data without duplicating...
data because duplicating data creates a unit-of-analysis error and violates assumptions of non-independence (Higgins & Green, 2008). For the study that included four arms (two treatment, two control; Foa et al., 2013), we computed separate between-group effects for two separate treatment and control pairings. For the study that included two trauma-focused treatment groups of the same type with and without motivational enhancement therapy and one control group (Coffey et al., 2016), we combined the two treatment groups into a single group. For the study with two active conditions and a time/attention placebo (Stappenbeck et al., 2015), we included the CBT intervention (i.e., Cognitive Restructuring) rather than the mindfulness-oriented intervention. For the study with two active conditions (Simpson et al., 2021; CPT and Relapse Prevention) and a six-week assessment only condition prior to re-randomization to one of the active conditions, we included only the active conditions following re-randomization (and treated Relapse Prevention as a manualized SUD treatment).

Heterogeneity was characterized using $I^2$ (i.e., proportion of variance that occurs between studies). Random effects models were conducted with weighting based on the inverse variance of each study’s effect size using the ‘metafor’ package (Viechtbauer, 2010).

### 2.9. Risk of bias across studies

Trim-and-fill analyses using the ‘metafor’ package assessed publication bias. When funnel plot asymmetry was detected, a trim-and-fill-adjusted effect size was calculated with studies imputed to account for asymmetry. We also calculated the fail-safe N (FSN; Rosenthal, 1979). This value is intended to represent the number of unpublished non-significant results that would need to exist to nullify an observed effect (i.e., the “file drawer problem”). Based on Rosenberg (2005) guidelines, effects were considered robust to publication bias based on FSNs that were greater than five times the number of available studies plus 10.

### 2.10. Additional analyses

We tested five potential moderators of treatment effects: assessment attrition, treatment delivery platform (group vs. individual), percentage of the sample that reported drug use (as defined by each study), study recruitment site (SUD treatment clinical setting vs. community-based recruiting), and whether a trauma-focused treatment was integrated with SUD content (for trauma-focused models only).

We conducted four sensitivity analyses. First, we re-ran all within-and between-group models omitting the one study that did not formally diagnose SUD (i.e., Brief et al., personal communication). Second, we evaluated whether adding Najavits et al. (2018) and Norman et al. (2019) to the trauma-focused vs. all comparators models changed the pattern of results. Third, we examined whether restricting the trauma-focused vs. manualized SUD treatment models to those that used empirically supported PTSD treatments (Back et al., 2019; Foa et al., 2013; Ruglass et al., 2018; Simpson et al., 2021; Vujanovic, personal communication) influenced the pattern of results. Finally, we also evaluated the impact of potential outliers. While there are several methods for identifying outliers in meta-analysis (Viechtbauer & Cheung, 2010), we implemented the ‘find.outliers’ function provided by Harrer, Cuijpers, Furukawa, and Ebert (2019). This function defines outliers as studies with
confidence intervals that do not overlap the omnibus effect. Models were re-estimated with outliers excluded.

3. Results

3.1. Study selection

Our search yielded 6441 citations. After 3061 duplicates were removed, 3380 titles/abstracts were reviewed. We applied our inclusion/exclusion criteria, producing a final set of 28 studies (combined n = 3247; see Fig. 1). The earliest year of publication was 2004. Included studies are denoted with an asterisk in the reference section.

3.2. Study characteristics

Study-level characteristics are displayed in Table 1 and Table A.3 with summary statistics based on those with available data. There were 62 treatment and comparator arms across the studies that contributed to within-group effects with 19 trauma-focused, 16 non-trauma-focused, 12 manualized SUD treatment, 9 SUD TAU, and 6 no/minimal treatment. The names of all treatment and comparator conditions and their respective categories are listed in Table A.4. Overall, 24 comparisons contributed to between-group effects, 13 to trauma-focused vs. all comparators, and 11 to non-trauma-focused vs. all comparators. Among comparisons that controlled for time, attention, and treatment delivery rigor, 8 involved trauma-focused vs. manualized SUD treatments and 5 involved non-trauma-focused vs. manualized SUD treatments.

Sample sizes aggregated across all treatment and comparator conditions ranged from 12 to 386 (mean = 115.96, SD = 98.97). Treatment and comparator conditions lasted, on average, 11.69 weeks (SD = 4.34) and 15.64 sessions (SD = 7.44). On average, studies required attendance at 70.56% (SD = 22.73%) of sessions or weeks of treatment for participants to be considered completers. Collapsing across treatment completion indicators, overall, 55.01% (SD = 17.17) completed their assigned interventions, with an average treatment completion rate of 52.11% (SD = 20.86) for the trauma-focused treatments, 50.73% (SD = 10.27) for the non-trauma-focused treatments, and 55.95% (SD = 16.14) for the manualized SUD treatments (treatment completion was not relevant for SUD TAU and no/minimal treatment). The primary treatment modality was individual (81.82% of all treatments; 93.75% for trauma-focused, 73.33% for non-trauma-focused, and 100% for manualized SUD).

Participants’ average age was 40.21 (SD = 5.47), 38.88% were racial/ethnic minorities (SD = 22.92), and 46.90% were female (SD = 35.21). Most participants met full diagnostic criteria for PTSD (92.97%, SD = 11.93) and SUD (99.75%, SD = 1.01). Over half of participants reported current drug use (59.36%, SD = 24.97), although only 18 studies included this information.

5These figures pertain only to studies that provided information on diagnostic status.
3.3. Risk of bias within studies

Risk of bias varied across the studies, with 13 (53.57%) evidencing relatively low risk of bias as indicated by Cochrane bias scores of 5 or 6 out of 6 possible points (see Figure A.1 and Table A.5). Eleven (39.29%) studies scored 3 or less on the indicator. The domain at highest risk for bias was allocation concealment. Risk for bias was generally low for attrition bias (i.e., use of intent-to-treat analyses) and selective reporting. Whether randomization was carried out via random sequence generation was most frequently rated “unclear.”

3.4. Results of individual studies

Study-level effect size data are reported in Table A.6, separated by comparison, time point, and outcome domain. The specific outcome measures that were used to assess PTSD and SUD symptoms are listed by study in Table A.7.

3.5. Synthesis of results

Within-group effects across the five treatment and control conditions are displayed in Table 2 and Fig. 2. All five types of conditions were associated with statistically significant small to large magnitude reductions in PTSD and SUD symptoms, both at post-treatment and follow-up. Heterogeneity was high across almost all within-group models ($I^2 > 75%$).

Between-group effects on PTSD and SUD outcomes as well as treatment completion are displayed in Tables 3 and 4 and Fig. 3. In general, these models indicated small magnitude differences that were not statistically significant between both trauma-focused and non-trauma-focused treatments when each was compared with all comparators and with manualized SUD treatments, with some exceptions described below.

Trauma-focused treatments showed significantly larger effects on PTSD at post-treatment ($g = 0.29, [0.07, 0.52]$) than all comparators, but this difference did not carry through to follow-up. Trauma-focused treatments did not differ from all comparison types on measures of SUD at post-treatment or follow-up. When trauma-focused treatments were compared with manualized SUD treatments there were no significant differences on PTSD at post-treatment or follow-up. Trauma-focused treatments showed significantly smaller effects on SUD symptoms than manualized SUD treatments at post-treatment ($g = −0.27, [−0.48, −0.06]$), but this difference did not persist to follow-up ($g = −0.21, [−0.47, 0.04]$). Trauma-focused treatments did not differ significantly from all comparators (OR = 0.85, [0.60, 1.21]) or manualized SUD treatments (OR = 0.92, [0.63, 1.36]; Table 4) on treatment completion. Sensitivity analyses revealed that none of the patterns in the between-group models changed when the two studies comparing trauma-focused and non-trauma-focused treatments (Najavits et al., 2018; Norman et al., 2019) were included. Similarly, the between-group patterns pertaining to trauma-focused vs. manualized SUD treatments were unchanged when only the five studies involving empirically supported PTSD treatments were considered (Back et al., 2019; Foa et al., 2013; Ruglass et al., 2017; Simpson et al., 2021; Vujanovic, personal communication).

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6The effect sizes and confidence intervals for these four tests were as follows: PTSD post: 0.24 [−0.15, 0.63]; SUD post: −0.28 [−0.55, −0.01]; PTSD FU: 0.07 [−0.31, 0.44], and SUD FU: −0.01 [−0.47, 0.45].
Heterogeneity varied somewhat across the between-group models for trauma-focused treatments and confidence intervals for \( I^2 \) were generally large (Table 3). Heterogeneity was highest for comparisons with all treatments on PTSD outcomes at post-test (\( I^2 = 32.95\% \)). Heterogeneity was low (<25%; Higgins, Thompson, Deeks, & Altman, 2003) for several comparisons (e.g., with all comparators on PTSD at follow-up and SUD at post, with manualized SUD on PTSD and SUD at post and follow-up). Heterogeneity was low for treatment completion models (\( I^2 = 0.00 \)).

Non-trauma-focused treatments did not differ from all comparators on PTSD at post-treatment (\( g = 0.11, [-0.03, 0.26] \)) or follow-up (\( g = -0.10, [-0.30, 0.09] \)). Non-trauma-focused treatments also did not differ from all comparators on SUD outcomes at post (\( g = 0.12, [-0.03, 0.28] \)) or follow-up (\( g = -0.04, [-0.21, 0.13] \)). When compared to manualized SUD treatments, non-trauma-focused treatments did not differ significantly on either PTSD or SUD at post-treatment or follow-up, with one exception. Non-trauma-focused treatments were inferior to manualized SUD treatments on PTSD at follow-up (\( g = -0.28, [-0.56, -0.00], p = .048 \)). Treatment completion rates did not differ between non-trauma-focused treatments relative to all comparators (OR = 1.22, [0.93, 1.60]) or manualized SUD treatments (OR = 1.24, [0.87, 1.78]).

Heterogeneity varied somewhat across the between-group models for non-trauma-focused treatments. It was highest for non-trauma-focused treatment versus all comparators on SUD outcomes at follow-up (\( I^2 = 33.30\% \)) and was low (\( I^2 = 0.00\% \)) in several models (e.g., vs. manualized SUD on PTSD at post and follow-up and SUD at follow-up).

### 3.6. Risk of bias across studies

Funnel plot asymmetry was detected in multiple models. However, statistical significance tests did not differ for trim-and-fill adjusted models, with four exceptions. Trauma-focused treatments no longer differed from all comparators on PTSD at post-treatment (adjusted \( g = 0.22, [-0.05, 0.49] \)) and non-trauma-focused treatments were inferior to manualized SUD on SUD symptoms at follow-up (adjusted \( g = -0.27, [-0.48, -0.05]; \) Table 3). Treatment completion was higher for non-trauma-focused treatments relative to all comparators (OR = 1.30, [1.00, 1.68], \( p = .046 \)) and manualized SUD treatments (OR = 1.41, [1.01, 1.95]; Table 4, see Figs. A.2 and A.3 for corresponding funnel plots). FSN estimates indicate that all statistically significant within-group models and none of the between-group models were robust to publication bias.

### 3.7. Additional analyses

Results of moderator tests examining attrition, treatment delivery modality, percentage of participants reporting drug use, and study recruitment site are reported in Table A.8. In almost all models, these factors did not moderate effects. However, three within-group models showed a positive association between attrition and effect size estimates (i.e., higher attrition was associated with larger effect sizes). Group delivery format was associated with smaller effects in one within-group model. Higher percentage of participants reporting drug use was associated with larger effect sizes. Recruitment from SUD sites was associated with larger effects in five within-group models and two between-group models.
Results comparing effects of integrated and non-integrated trauma-focused treatments are reported in Table A.9. Integrated trauma-focused treatments showed smaller effects in two within-group models and three between-group models. Upon further examination, we found that none of the studies using an integrated trauma-focused treatment recruited from SUD clinics while 6 of 7 of studies using non-integrated trauma-focused treatments did. Therefore, meta-regressions were run controlling for recruitment site (SUD clinic vs. community-based). As shown in Table A.9, all five previously significant meta-regression coefficients were no longer statistically significant.

Sensitivity analyses pertaining to model results with the sole study that included participants with subthreshold SUD are reported in Table A.10. Significance tests for both within- and between-group models were unchanged.

Sensitivity analyses pertaining to model results with outliers removed are reported in Table A.11. Although outliers were detected in several within-group models and one between-group model, statistical significance tests did not change when they were omitted.

4. Discussion

The present meta-analysis synthesized results of the extant behavioral RCT literature pertaining to the treatment of adults with co-occurring PTSD/SUD. All within-group models showed significant effects, mostly in the moderate to large range, for both PTSD and SUD outcomes at follow-up. This pattern of results indicates that across both experimental (i.e., trauma-focused and non-trauma-focused treatments) and control conditions, participants in these studies generally improved on both primary outcomes. Within-group models show that trauma-focused and manualized SUD treatments were mostly associated with large effect sizes for both PTSD and SUD outcomes (gs = 0.80–1.11), while SUD TAU and non-trauma-focused treatments showed small to large effects (gs = 0.30–0.79). No/minimal treatment conditions were associated with small to large effects (gs = 0.49–1.29), though the large effects were based on the sole study with follow-up data wherein nearly all control participants were in SUD treatment (Mills et al., 2012). Of note, within-group results appeared robust to publication bias (trim-and-fill, FSN).

Regarding between-group models, in contrast to Roberts et al. (2015), we did not find evidence that trauma-focused treatments were associated with significantly poorer treatment retention relative to either all comparators or the manualized SUD treatments. With the exception of Coffey et al. (2016), none of the studies described having specifically addressed treatment retention for those assigned to a trauma-focused intervention. Although the reason for the discrepancy is unclear, one possible explanation is that only one of the four RCTs included in the earlier trauma-focused model had an active comparison condition (Sannibale et al., 2013), whereas in the current study eight out of twelve had an active comparison condition. The current retention finding suggests that people with PTSD/SUD may have difficulty remaining in active treatment (i.e., that which is structured and

of note, the Coffey et al. (2016) study found that adding motivational enhancement regarding session attendance to Prolonged Exposure did not lead to statistically different treatment retention relative to those assigned to receive only Prolonged Exposure in the residential rehabilitation setting in which the study took place.
encourages at home practice) regardless of whether the intervention has trauma-focused elements.

In line with Roberts and colleagues, we found that when compared with all types of comparators, trauma-focused treatments showed a small advantage for reductions in PTSD severity at post-treatment assessment ($g = 0.29$), though the advantage did not persist to the longest follow-up and was not robust to publication bias corrections. We also found that trauma-focused treatments did not out-perform all other comparators on SUD outcomes at either immediate or longest follow-up. Although Roberts and colleagues (2015) found an advantage for trauma-focused interventions on PTSD outcomes at both post-treatment and later follow-ups and SUD outcomes at later follow-ups, their group of studies only included comparisons involving no/minimal attention conditions. Although such comparisons are important (e.g. for establishing absolute efficacy; Smith & Glass, 1977), they provide a less rigorous assessment of efficacy and generally should not be used to determine when a particular treatment approach should be recommended relative to other potential therapies (i.e., relative efficacy; Wampold & Imel, 2015).

When we restricted the models to studies involving a manualized SUD treatment, not only did the post-treatment advantage for trauma-focused interventions for PTSD outcomes disappear, but the immediate post-treatment model regarding SUD outcomes indicated a small advantage for manualized SUD treatments ($g = −0.27$). Thus, when compared with trauma-focused interventions, manualized SUD treatments did not differ significantly regarding PTSD outcomes and performed somewhat better on early SUD outcomes, a pattern of findings that held up in our sensitivity analyses including only studies using trauma-focused treatments based on empirically supported PTSD interventions. It is currently not clear how manualized SUD treatments might facilitate such marked improvement in PTSD. Although it remains to be empirically tested in future research, it is possible that the behavioral skills gained in most manualized SUD treatments (e.g., communication and assertiveness, distress tolerance, anger management, contingency planning, reaching out for healthy social support) are helpful in addressing underlying dimensions of psychopathology common to both SUD and PTSD. Specifically, gaining such skills and more consistently availing oneself of adequate social support may mitigate current stress and temper the stress reactivity so common among those with PTSD and SUD (Breese, Sinha, & Heilig, 2011; Lovallo, 2006; Morris, Hellman, Abelson, & Rao, 2016; Steudte-Schmiedgen et al., 2015). Additionally, non-specific factors (e.g., therapeutic alliance, expectancy; Wampold & Imel, 2015) may play a role by increasing hope as well as facilitating stress reduction through contact with a caring treatment provider.

Turning to non-trauma-focused treatments, we found no differences between these treatments and all comparators on SUD or PTSD outcomes at post-treatment or follow-up. Three of the four comparisons with manualized SUD treatments were also non-significant. However, manualized SUD treatments significantly out-performed non-trauma-focused treatments at the longest follow-up on PTSD ($g = −0.28$). The present finding of no differences on PTSD or SUD outcomes for non-trauma-focused interventions relative to all comparators is consistent with the results obtained by Roberts et al. (2015). Importantly, the current study confirms the lack of differences based on a much larger sample of
studies. Although neither of the primary models regarding treatment retention for non-trauma-focused interventions were significant, models accounting for possible publication bias suggest that non-trauma-focused interventions may show higher treatment retention relative to all comparators and manualized SUD treatment.

While the between-group models provided some indication of potential treatment differences, none of these effects were robust to publication bias as assessed by FSN. This, coupled with potentially high risk of bias for some studies in some domains (e.g., lack of masked outcome assessors) highlights the tentative nature of these results. Importantly, however, the FSN is designed to guard against acceptance of false positives and not false null results (Rosenthal, 1979). Thus, even if numerous relevant unpublished null trials were added, the overall pattern of no or minimal between-group differences found in the present study likely would not change.

Overall, we found scant evidence that any of the tested moderators significantly influenced outcomes, potentially in part because these tests were underpowered (Valentine et al., 2010). Alongside a majority of null associations, attrition rate was associated with larger effects in three models, group delivery was linked with smaller effects in one model, and percentage of participants reporting drug use was linked with larger effects in one model. The most consistent moderator was study recruitment site. Studies conducted in SUD clinical sites showed substantially larger effects in five within-group models ($g_s = 0.48–1.01$) and three between-group models ($g_s = 0.55–1.11$), with six of the eight significant outcomes pertaining to SUD. It is possible that patients enrolled through SUD treatment clinics participated in additional SUD programming that was helpful to them and/or they had more severe substance use profiles (see Simpson et al., 2020) and thus had more room for improvement. Additionally, clinicians at SUD treatment clinics likely have more experience treating individuals with SUD (with or without PTSD) than those in university or laboratory settings where community-based recruiting was the norm. Study recruitment site also appears to account for the smaller effects obtained for integrated trauma-focused treatments relative to non-integrated trauma-focused treatments.

The central finding of this meta-analysis of behavioral RCTs for people with PTSD/SUD is that while there were medium to large within-group effects for all who received some form of treatment, between-group effects were generally small and non-significant. Although these findings may be surprising to some and are generally contrary to received wisdom (see Brady, Dansky, Back, Foa, & Carroll, 2001; Brown & Wolfe, 1994), we believe the findings are potentially positive from a public health standpoint.

Consistent with the larger psychotherapy literature (Benish, Imel, & Wampold, 2008; Frost, Laska, & Wampold, 2014; Imel, Wampold, Miller, & Fleming, 2008; Wampold & Imel, 2015; Wampold et al., 1997), the present findings suggest that when people with PTSD and SUD have access to bona fide treatments (i.e., with a cogent rationale and intended to be therapeutic; Wampold et al., 1997), they generally improve on both aspects of their comorbidity and further that the specific type of care may not be especially consequential. Indeed, the finding that manualized SUD treatments were not inferior to trauma-focused nor non-trauma-focused treatments on either PTSD or SUD outcomes and
showed modest advantages over both in two between-group models suggests that individuals with this comorbidity may address their mental health challenges with treatments that may be more accessible. Although certain patient characteristics not tested in the current analysis may moderate treatment outcomes (e.g. “treatment matching”), our results encouragingly suggest that adults with PTSD/SUD have options with regard to effective PTSD/SUD treatment.

Based on the reviewed studies, it appears that CBT treatments for SUD that include attention to and assessment of current PTSD is likely to confer benefit that is not significantly different from trauma-focused and non-trauma-focused treatments on PTSD outcomes and possibly greater benefit on SUD outcomes. It is, however, important to consider the context for these findings—a set of RCTs wherein both investigators and participants acknowledged the presence and clinical relevance of participants’ comorbid conditions, both conditions were thoroughly assessed over time, and treatment was delivered individually with the support of specific training and supervision. Thus, we do not interpret the current findings to mean that patients with comorbid PTSD/SUD can simply be given standard SUD care with no individualized attention to their PTSD. Nevertheless, patients with PTSD/SUD in addiction treatment settings may be reassured that existing manualized SUD treatments, such as Relapse Prevention (Marlatt & Gordon, 1980), may help them successfully address both their SUD and PTSD in the context of high-fidelity care and ongoing assessment of both PTSD and substance use. Such framing may be more palatable than the old admonitions that patients need to get (and stay) sober before they may be considered stable enough to undertake PTSD treatment (see Brown & Wolfe, 1994, for an overview).

These meta-analytic findings notwithstanding, the epidemiologic patterns cited earlier regarding the high rates of both PTSD and SUD chronicity (Simpson et al., 2020) suggest that much work remains to be done to close the gap between the best practices generally used in RCTs and the quality of care available through community SUD and mental health clinics (see Kilbourne et al., 2018) before the field is in a position to fully deliver on the idea that comorbid patients’ needs will be met no matter where they present for care. Additionally, because there is not yet a sufficient number of trials examining any one of the more promising trauma-focused treatments (see Table A.6 for individual study effect sizes) to test more granular meta-analytic models, we do not yet know whether one (or more) of these specific treatments will eventually prove especially efficacious. The field also has yet to systematically assess treatment acceptability beyond treatment retention and gleaning such information from both treatment completers and non-completers could help clinicians and researchers address the nearly universal low treatment completion rates in the extant relevant literature. Additionally, it would be useful to experimentally evaluate the degree to which patient preference might play a role in outcomes (see Zoellner, Roy-Byrne, Mavissakalian, & Feeny, 2019) and there is almost certainly a great deal to learn about optimizing patient/treatment matching (see Bailey et al., 2019; Hien et al., 2019). Thus, there are a number of interesting and important future research directions to be pursued and we hope that this meta-analysis will provide some useful guideposts.

The current meta-analysis has noteworthy strengths and weaknesses. Strengths include incorporating both relevant unpublished trial results and pertinent subsets of participants.
from larger published trials. This meta-analysis is better powered than previous ones, which allowed comparisons between trauma-focused or non-trauma-focused treatments and commonly provided CBT treatments for SUD matched on time and attention. Although the number of available studies was likely not sufficient to adequately power moderator tests (Valentine et al., 2010), these exploratory analyses may aid in hypothesis generation as the field collectively works to identify factors that may influence outcomes (e.g., treatment setting, patient factors reflecting need for trauma-focused treatment vs. manualized SUD).

As is commonly the case in meta-analysis, primary weaknesses relate to the meta-analytic sample itself. Although the largest review to date, as noted above, it is likely that some tests (e.g., moderators, between-group models) were underpowered. This is a particularly salient concern for the between-group models in which small effects are to be expected (Baardseth et al., 2013; Goldberg et al., 2018; Wampold & Imel, 2015). The high degree of heterogeneity in many within- and between-group models further reduced statistical power and highlights the tenuous nature of some effect size estimates. We found some evidence of publication bias for the non-trauma-focused treatment retention models, but on the whole, results did not change when accounting for this source of bias in trim-and-fill models. Additionally, many investigators did not use methods that conceal allocation during the randomization process or report whether assessments were masked or random sequence generators were used.

Both treatment completion and assessment completion across most studies was low, which can introduce a host of potential biases even when intention-to-treat analyses are conducted (i.e., biases due to data not missing at random; Graham, 2009). Low treatment and assessment completion suggests that the field has yet to develop treatment options and/or study retention methods that are either appealing or compelling enough to offset the substantial emotional dysregulation (Westphal, Aldao, & Jackson, 2017), social instability (Simpson et al., 2019), and avoidance (Naifeh, Tull, & Gratz, 2012; Simpson, Jakupcak, & Luterek, 2006) common for people with co-occurring PTSD and SUD. Strategies for supporting treatment session attendance have been tested, but trial outcomes suggest that much work remains to be done (see Coffey et al. (2016) described above and Schacht et al., (2017) for an evaluation of contingency management to improve PE session attendance). Clinical researchers could borrow from successful efforts to increase involvement of racial/ethnic minorities in clinical trials using participatory research methods (see McFarlane, Occa, Peng, Awonuga & Morgan, 2021 for a systematic review) such that individuals with lived experience pertaining to PTSD/SUD help develop and refine treatment and trial design to address the persistent problem of sub-optimal treatment and study retention.

Finally, while we opted to conduct traditional meta-analyses in an attempt to replicate and extend the extant literature, future research in this area would benefit from network meta-analyses. Such an approach would enable an evaluation of the relative efficacy of trauma-focused interventions compared to non-trauma-focused interventions given that currently only two studies have made such comparisons (Najavits et al., 2018; Norman et al., 2019).
4.1. Conclusions

The current meta-analysis largely affirms the idea that there is “no wrong door” when it comes to treatment options for individuals with PTSD/SUD (see Simpson et al., 2017). Specifically, we found evidence that trauma-focused, non-trauma-focused, manualized SUD treatments, and SUD TAU are all associated with significant improvements on both PTSD and SUD outcomes.\(^8\) Between-group differences were less consistent and much less robust. Trauma-focused treatments showed slight indications of advantage relative to all comparators regarding PTSD outcomes although manualized SUD treatments also showed slight indications of advantage relative to trauma-focused and non-trauma-focused treatments regarding SUD outcomes. These findings have important public health implications in so far as they suggest that individuals with PTSD/SUD may benefit from relatively readily available (Hendershot, Witkiewitz, George, & Marlatt, 2011; VA/DoD Management of Substance Use Disorders Workgroup, 2015) manualized CBT treatments for SUD rather than requiring specialized options that address both SUD and PTSD with the caveat that measurement based, high quality individual delivery of such care may be necessary to see the degree of improvement evidenced in the present collection of RCTs. The existence of viable treatment options for people with PTSD/SUD lays a solid foundation for future inquiries into optimizing patient-treatment matching and the role of patient preference in recovery, both uncharted but potentially quite fertile territory to explore.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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\(^8\)Note: The sole study examining outcomes at extended follow-up for those assigned to no/minimal treatment (Mills et al., 2012) also found that those randomized to find their own treatment in the community had strong within person improvements on PTSD and SUD. However because nearly all of those participants reported engaging in SUD care, this condition is more like a SUD treatment as usual comparator than a no/minimal treatment comparator.
Abbreviations:

AUD: alcohol use disorder
CBT: cognitive behavioral treatment
CPT: cognitive processing therapy
COPE: concurrent treatment of PTSD and substance use disorders using prolonged exposure
DUD: drug use disorder
FSN: fail safe N
ICBT: intent-to-treat
ITT: integrated cognitive behavioral therapy
NIAAA: national institute on alcohol abuse and alcoholism
PTSD: posttraumatic stress disorder
PE: prolonged exposure
RCT: randomized clinical trial
SUD: substance use disorder
VA/DoD: Veterans’ Affairs/Department of Defense.

References

VA/DoD Clinical Guidelines. <https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPGRevised22216.pdf> 2015 (accessed 8/28/20).
American Psychiatric Association. (2013). Diagnostic and Statistical Manual of Mental Disorders (5th ed...). Arlington, VA: Author.
Baardseth TP, Goldberg SB, Pace BT, Wislocki AP, Frost ND, Siddiqui JR, … Wampold BE (2013). Cognitive-behavioral therapy versus other therapies: redux. Clinical Psychology Review, 33(3), 395–405. 10.1016/j.cpr.2013.01.004 [PubMed: 23416876]
Babor TF, de la Fuente JR, Saunders J, & Grant M (1992). The Alcohol Use Disorders Identification Test, Guidelines For Use In Primary Health Care. Geneva, Switzerland: World Health Organization.
Back SE, Killeen T, Badour CL, Flanagan JC, Allan NP, Ana ES,… Brady K (2019). Concurrent treatment of substance use disorders and PTSD using prolonged exposure: A randomized clinical trial in military veterans. Addictive Behaviors, 90, 369–377. 10.1016/j.addbeh.2018.11.032 (*Denotes articles included in meta-analytic models). [PubMed: 30529244]
Back SE, Killeen TK, Teer AP, Hartwell EE, Federline A, Beylotte F, & Cox E (2014). Substance use disorders and PTSD: an exploratory study of treatment preferences among military veterans. Addictive Behaviors, 39(2), 369–373. 10.1016/j.addbeh.2013.09.017 [PubMed: 24199930]
Bailey K, Trevillion K, & Gilchrist G (2019). What works for whom and why: A narrative systematic review of interventions for reducing post-traumatic stress disorder and problematic substance use among women with experiences of interpersonal violence. Journal of Substance Abuse Treatment, 99, 88–103. 10.1016/j.jsat.2018.12.007 [PubMed: 30797400]
Becker BJ (1988). Synthesizing standardized mean-change measures. British Journal of Mathematical and Statistical Psychology, 41(2), 257–278.
Benish SG, Imel ZE, & Wampold BE (2008). The relative efficacy of bona fide psychotherapies for treating post-traumatic stress disorder: A meta-analysis of direct comparisons. Clinical Psychology Review, 28(5), 746–758. 10.1016/j.cpr.2007.10.005 [PubMed: 18055080]

Berenz EC, & Coffey SF (2012). Treatment of co-occurring Posttraumatic Stress Disorder and Substance Use Disorders. Current Psychiatry Reports, 14(5), 469–477. 10.1007/s11920-012-0300-0 [PubMed: 22825992]

Blanco C, Xu Y, Brady K, Pérez-Fuentes G, Okuda M, & Wang S (2013). Comorbidity of posttraumatic stress disorder with alcohol dependence among US adults: Results from National Epidemiologic Survey on Alcohol and Related Conditions. Drug and Alcohol Dependence, 132(3), 630–638. 10.1016/j.drugalcdep.2013.04.016 [PubMed: 23702490]

Boden MT, Kimerling R, Jacobs-Lentz J, Bowman D, Weaver C, Carney D… Trafton JA (2011). Seeking Safety treatment for male veterans with substance abuse disorder and post-traumatic stress disorder symptomatology. Addiction, 107, 578–586. 10.1111/j.1360-0443.2011.03658.x (*Denotes articles included in meta-analytic models).

Borenstein M, Hedges LV, Higgins JPT, & Rothstein H (2009). Introduction to Meta-analysis. Chichester, U.K: John Wiley & Sons.,

Brady KT, Dansky BS, Back SE, Foa EB, & Carroll KM (2001). Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: preliminary findings. Journal of Substance Abuse Treatment, 21(1), 47–54. 10.1016/s0740-5472(01)00182-9 [PubMed: 11516926]

Breese GR, Sinha R, & Heilig M (2011). Chronic alcohol neuroadaptation and stress contribute to susceptibility for alcohol craving and relapse. Pharmacology & Therapeutics, 129, 149–171. 10.1016/j.pharmthera.2010.09.007 [PubMed: 20951730]

Brief DJ, Rubin A, Keane TM, Enggasser JL, Roy M, Helmuth E… Rosenbloom D (2013). Web intervention for OEF/OIF veterans with problem drinking and PTSD symptoms: a randomized clinical trial. Journal of Consulting and Clinical Psychology, 81(5), 890–900. 10.1037/a0033697 (+Denotes studies describing study procedures pertaining to datasets provided by the investigators for the meta-analysis)*Denotes articles included in meta-analytic models). [PubMed: 23875821]

Brown PJ, & Wolfe J (1994). Substance abuse and post-traumatic stress disorder comorbidity. Drug & Alcohol Dependence, 35(1), 51–59. 10.1016/0376-8716(94)90110-4 [PubMed: 8082556]

Capone C, Eaton E, McGrath AC, & McGovern MP (2014). Integrated Cognitive Behavioral Therapy (ICBT) for PTSD and substance use in Iraq and Afghanistan veterans: A feasibility study. Journal Oregon Traumatic Stress Disorder Treatment, 3(4). 10.4172/2324-8947.1000134 (*Denotes articles included in meta-analytic models).

Center for Substance Abuse Treatment. (1999). Brief Interventions and Brief Therapies for Substance Abuse. Treatment Improvement Protocol (TIP) Series, No. 34.HHS Publication No. (SMA) 12–3952. Rockville, MD: Substance Abuse and Mental Health Services Administration.

Coffey SF, Schumacher JA, Nosen E, Littlefield AK, Henslee AM, Lappen A, & Stasiewicz PR (2016). Trauma-focused exposure therapy for chronic posttraumatic stress disorder in alcohol and drug dependent patients: A randomized controlled trial. Psychology of Addictive Behaviors, 30(7), 778–790. 10.1037/adb0000201 (*Denotes articles included in meta-analytic models). [PubMed: 27786516]

Coffey SF, Stasiewicz PR, Hughes P, & Brimo ML (2006). Trauma-focused imaginal exposure with Comorbid PTSD- alcohol dependent individuals: Revealing mechanisms of alcohol craving in a cue reactivity paradigm. Psychology of Addictive Behaviors, 20, 425–435. [PubMed: 17176177]

Cohen J (1988). Statistical Power Analysis for the Behavioral Sciences (2nd ed...). Hillsdale, NJ: Erlbaum.,

Cooper HM, Hedges LV, & Valentine JC (2009). The Handbook Of Research Synthesis and Meta-Analysis (2nd ed...). New York: Russell Sage Foundation.,

van Dam D, Vedel E, Ehring T, & Emmelkamp PM (2012). Psychological treatments for concurrent posttraumatic stress disorder and substance use disorder: A systematic review. Clinical Psychology Review, 32, 202–214. 10.1016/j.cpr.2012.01.004 [PubMed: 22406920]

van Dam D, Ehring T, Vedel E, & Emmelkamp PM (2013). Trauma-focused treatment for posttraumatic stress disorder combined with CBT for severe substance use disorder: A randomized
Flanagan JC, Korte KJ, Killeen TK, & Back SE (2016). Concurrent treatment of substance use and PTSD. Current Psychiatry Reports, 18(8), 70. 10.1007/s11920-016-0709-y [PubMed: 27278509]

Foa EB, Yusko DA, McLean CP, Suvak MK, Bux DA Jr., Oslin D..., Volpicelli J (2013). Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: A randomized clinical trial. JAMA, 310(5), 488–495 (*Denotes articles included in meta-analytic models). [PubMed: 23925619]

Frisman L, Ford J, Lin H, Mallon S, & Chang R (2008). Outcomes of trauma treatment using the TARGET model. Journal of Groups in Addiction & Recovery, 3, 285–303. 10.1080/15560350802424910

Frost ND, Laska KM, & Wampold BE (2014). The evidence for present-centered therapy as a treatment for posttraumatic stress disorder. Journal of Traumatic Stress, 27, 1–8. 10.1002/jts.21881 [PubMed: 24515534]

Frisman L, Ford J, Lin H, Mallon S, & Chang R (2008). Outcomes of trauma treatment using the TARGET model. Journal of Groups in Addiction & Recovery, 3, 285–303. 10.1080/15560350802424910

Frost ND, Laska KM, & Wampold BE (2014). The evidence for present-centered therapy as a treatment for posttraumatic stress disorder. Journal of Traumatic Stress, 27, 1–8. 10.1002/jts.21881 [PubMed: 24515534]

Fu R, Gartelehner G, Grant M, Shamiyan T, Sedrakyan A, Wilt TJ, & Santaguida P (2011). Conducting quantitative synthesis when comparing medical interventions: AHRQ and the Effective Health Care Program. Journal of Clinical Epidemiology, 64(11), 1187–1197. 10.1016/j.jclinepi.2010.08.010 [PubMed: 21477993]

Gielen N, Havermans RC, Tekelenburg M, & Jansen A (2012). Prevalence of posttraumatic stress disorder among patients with substance use disorder: It is higher than clinicians think it is, 10.3402/ejpt.v3i0.17734 European Journal of Psychotraumatology, 3, 10.3402/ejpt.v3i0.17734.

Goldberg SB, Tucker RP, Greene PA, Davidson RJ, Wampold BE, Kearney DJ, & Simpson TL (2018). Mindfulness-based interventions for psychiatric disorders: A systematic review and meta-analysis. Clinical Psychology Review, 59, 52–60. 10.1016/j.cpr.2017.10.011 [PubMed: 29126747]

Goldstein RB, Smith SM, Chou SP, Saha TD, Jung J, Zhang H, ... Grant BF (2016). The epidemic of DSM-5 posttraumatic stress disorder in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. Social Psychiatry and Psychiatric Epidemiology, 51(8), 1137–1148. 10.1007/s00127-016-1208-5 [PubMed: 27106853]

Graham JW (2009). Missing data analysis: Making it work in the real world. Annual Review of Psychology, 60, 549–576.

Haagen JF, Smid GE, Knipscheer JW, & Kleber RJ (2015). The efficacy of recommended treatments for veterans with PTSD: A metaregression analysis. Clinical Psychology Review, 40, 184–194. 10.1016/j.cpr.2015.06.008 [PubMed: 26164548]

Haller M, Norman SB, Cummins K, Trim RS, Xu X, Cui R, ... Tate SR (2016). Integrated cognitive behavioral therapy versus cognitive processing therapy for adults with depression, substance use disorder, and trauma. Journal of Substance Abuse Treatment, 62, 38–48. 10.1016/j.jsat.2015.11.005 (+Denotes studies describing study procedures pertaining to datasets provided by the investigators for the meta-analysis *Denotes articles included in meta-analytic models). [PubMed: 26718130]

Hamblen J (2020). Cognitive Behavioral Therapy (CBT) for PTSD in Veterans With Co-Occurring SUDs (CBT). VA Office of Research Development. Clinicaltrials.gov Identifier: NCT01357577 *Denotes articles included in meta-analytic models.

Harrer M, Cuijpers P, Furukawa TA, & Ebert DD (2019). Doing Meta-Analysis in R: A Hands-on Guide. doi:10.5281/zenodo.2551803. Chapter 6.2.

Harrington T, & Newman E (2007). The psychometric utility of two self-report measures of PTSD among women substance users. Addictive Behaviors, 32(12), 2788–2798. 10.1016/j.addbeh.2007.04.016 [PubMed: 17507172]

Hassan AN, Le Foll B, Imtiaz S, & Rehm J (2017). The effect of post-traumatic stress disorder on the risk of developing prescription opioid use disorder: Results from the National Epidemiologic Survey on Alcohol and Related Conditions III. Drug and Alcohol Dependence, 179, 260–266. doi.org/10.1016. [PubMed: 28818717]

Hawn SE, Cusack SE, & Amstadter AB (2020). A systematic review of the self-medication hypothesis in the context of posttraumatic stress disorder and comorbid problematic alcohol use. Journal of Traumatic Stress, 33, 699–708. 10.1002/jts.22521 [PubMed: 32516487]
Hendershot CS, Witkiewitz K, George WH, & Marlatt GA (2011). Relapse prevention for addictive behaviors. Substance Abuse Treatment, Prevention, and Policy, 6, 17. 10.1186/1747-597X-6-17

Hien D, Morgan-Lopez AA, Ruglass LM, Saavedra LM, Fitzpatrick S, Back S, … Norman S (2019). Project Harmony: A systematic review and meta-analysis of individual patient data of behavioral and pharmacologic trials for comorbid posttraumatic stress, alcohol and other drug use disorders. PROSPERO 2019 CRD42019146678. <https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019146678> (*Denotes articles included in meta-analytic models).

Hien DA, Cohen LR, Miele GM, Litt LC, & Capstick C (2004). Promising treatments for women with comorbid PTSD and Substance Use Disorders. American Journal of Psychiatry, 161, 1426–1432 (*Denotes articles included in meta-analytic models).

Hien DA, Wells EA, Jiang H, Suarez-Morales L, Campbell AN, Cohen LR, … Nunes EV (2009). Multisite randomized trial of behavioral interventions for women with co-occurring PTSD and Substance Use Disorders. Journal of Consulting and Clinical Psychology, 77(4), 607–619. 10.1037/a0016227 (*Denotes articles included in meta-analytic models). [PubMed: 19634955]

Higgins JP, & Green S (2008). Cochrane Handbook for Systematic Reviews of Interventions. London: Wiley & Sons.

Higgins JP, Thompson SG, Deeks JJ, & Altman DG (2003). Measuring inconsistency in meta-analyses. BMJ, 327(7414), 557–560. [PubMed: 12958120]

Hoyt WT, & Del Re AC (2018). Effect size calculation in meta-analyses of psychotherapy outcome research. Psychotherapy Research, 28(3), 379–388. [PubMed: 29179665]

Imel ZE, Wampold BE, Miller SD, & Fleming RR (2008). Distinctions without a difference: Direct comparisons of psychotherapies for alcohol use disorders. Psychology of Addictive Behaviors, 22(4), 533–543. 10.1037/a0013171 [PubMed: 19071978]

Jason LA, Mileviciute I, Aase DM, Stevens E, Digangi J, Contreras R, & Ferrari JR (2011). How type of treatment and presence of PTSD affect employment, self-regulation, and abstinence. North American Journal of Psychology, 13(2), 175–186. [PubMed: 23357959]

McFarlane SJ, Oca a, Peng W, Awonuga O, & Morgan SE (2021). Community-based participatory research (CBPR) to enhance participation of racial/ethnic minorities in clinical trials: A 10-year systematic review (Advance online publication) Health Communication, 1–18. 10.1080/10410236.2021.1943978.

Kehle-Forbes SM, Chen S, Polusny MA, Lynch KG, Koffel E, Ingram E,… Oslin DW (2019). A randomized controlled trial evaluating integrated versus phased application of evidence-based psychotherapies for military veterans with comorbid PTSD and substance use disorders. Drug and Alcohol Dependence, 205, Article 107647. 10.1016/j.drugalcdep.2019.107647 (*Denotes articles included in meta-analytic models).

Kilbourne AM, Beck K, Spaeth-Rublee B, Ramanuj P, O’Brien RW, Tomoyasu N, & Pincus HA (2018). Measuring and improving the quality of mental health care: A global perspective. World Psychiatry: Official Journal of the World Psychiatric Association (WPA), 17(1), 30–38. 10.1002/wps.20482 [PubMed: 29352529]

Killeen TK, Back SE, & Brady KT (2015). Implementation of integrated therapies for comorbid post-traumatic stress disorder and substance use disorders in community substance abuse treatment programs. Drug and Alcohol Review, 34(3), 234–241. 10.1111/dar.12229 [PubMed: 25737377]

Leeman RF, Hefner K, Frohe T, Murray A, Rosenheck RA, Watts BV, & Sofuoglu M (2017). Exclusion of participants based on substance use status: Findings from randomized controlled trials of treatments for PTSD. Behavior Research and Therapy, 89, 33–40. 10.1016/j.brat.2016.10.006

Lovallo WR (2006). Cortisol secretion patterns in addiction and addiction risk. International Journal of Psychophysiology, 59, 195–202. 10.1016/j.ijspsycho.2005.10.007 [PubMed: 16434116]

Marlatt GA, & Gordon JR (1980). Determinants of relapse: Implications for the maintenance of behavior change. In Davidson PO, & Davidson SM (Eds.), Behavioral Medicine: Changing Health Lifestyles. New York: Brunner/Mazel.

McCaughey JL, Killeen T, Gros DF, Brady KT, & Back SE (2012). Posttraumatic stress disorder and co-occurring substance use disorders: Advances in assessment and treatment. Clinical Psychological Science and Practice, 19, 283–304. 10.1111/cpsp.12006
McGovern MP, Lambert-Harris C, Alterman AI, Xie H, & Meier A (2011). A randomized controlled trial comparing Integrated Cognitive Behavioral Therapy versus individual addiction counseling for co-occurring substance use and posttraumatic stress disorders. Journal of Dual Diagnosis, 7, 207–227. 10.1080/15504263.2011.620425 (*Denotes articles included in meta-analytic models). [PubMed: 22383864]

McGovern MP, Lambert-Harris C, Xie H, Meier A, McLeman B, & Saunders E (2015). A randomized controlled trial of treatments for co-occurring substance use disorders and post-traumatic stress disorder. Addiction, 110(7), 1194–1204. 10.1111/add.12943 (*Denotes articles included in meta-analytic models). [PubMed: 25846251]

Mills KL, Teeson M, Back SE, Brady KT, Baker AL, Hopwood S, & Ewer PL (2012). Integrated exposure based therapy for co-occurring posttraumatic stress disorder and substance dependence. Journal of the American Medical Association, 308, 690–699. 10.1001/jama.2012.9071 (*Denotes articles included in meta-analytic models). [PubMed: 22893166]

Moher D, Liberati A, Tetzlaff J, Altman DG, & PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Medicine, 6(7), Article e1000097. 10.1371/journal.pmed.1000097

Morris MC, Hellman N, Abelson JL, & Rao U (2016). Cortisol, heart rate, and blood pressure as early markers of PTSD risk: A systematic review and meta-analysis. Clinical Psychology Review, 49, 79–91. 10.1016/j.cpr.2016.09.001 [PubMed: 27623149]

Moss HB, Goldstein RB, Chen CM, & Yi HY (2015). Patterns of use of other drugs among those with alcohol dependence: Associations with drinking behavior and psychopathology. Addictive Behaviors, 50, 192–198. 10.1016/j.addbeh.2015.06.041 [PubMed: 26151585]

Mueser KT, Rosenberg SD, Xie H, Jankowski MK, Bolton EE, Lu W, ... Wolfe R (2008). A randomized controlled trial of cognitive–behavioral treatment for posttraumatic stress disorder in severe mental illness. Journal of Consulting and Clinical Psychology, 76(2), 259–271. 10.1037/0022-006X.76.2.259 [PubMed: 18377122]

Myers US, Browne KC, & Norman SB (2015). Treatment engagement: Female survivors of intimate partner violence in treatment for PTSD and alcohol use disorder. Journal of Dual Diagnosis, 11, 238–247. 10.1080/15504263.1113762 (*Denotes articles included in meta-analytic models). [PubMed: 26515712]

Naifeh JA, Tull MT, & Gratz KL (2012). Anxiety sensitivity, emotional avoidance, and PTSD symptom severity among crack/cocaine dependent patients in residential treatment. Cognitive Therapy and Research, 36(3), 247–257. 10.1007/s10608-010-9337-8 [PubMed: 22791927]

Najavits LM, Gallop RJ, & Weiss RD (2006). Seeking safety therapy for adolescent girls with PTSD and substance use disorder: A randomized controlled trial. The Journal of Behavioral Health Services & Research, 33(4), 453–463. 10.1007/s11414-006-9034-2 [PubMed: 16858633]

Najavits LM, & Hien D (2013). Helping vulnerable populations: A comprehensive review of the treatment outcome literature on substance use disorder and PTSD. Journal of Clinical Psychology, 69, 433–479. 10.1002/jclp.21980 [PubMed: 23592045]

Najavits LM, Krinsley K, Waring ME, Gallagher MW, & Skidmore C (2018). A randomized controlled trial for veterans with PTSD and substance use disorder: Creating change versus seeking safety. Substance Use & Misuse, 53(11), 1788–1800. 10.1080/10826084.2018.1432653 (*Denotes articles included in meta-analytic models). [PubMed: 29461920]

Norman SB, Trim R, Haller M, Davis BC, Myers US, Colvonen PJ, ... Mayes T (2019). Efficacy of integrated exposure therapy vs integrated coping skills therapy for comorbid posttraumatic stress disorder and alcohol use disorder: A randomized clinical trial. JAMA Psychiatry, 76(8), 791–799. 10.1001/jamapsychiatry.2019.0638 (*Denotes articles included in meta-analytic models). [PubMed: 31017639]

Park TW, Cheng DM, Samet J, Winter M, & Saitz R (2015). Chronic care management for substance dependence in primary care among patients with co-occurring mental disorders. Psychiatric Services, 66, 72–79. 10.1176/appi.ps.201300414 [PubMed: 25219686]

Perez-Dandieu B, & Tapia G (2014). Treating trauma in addiction with EMDR: A pilot study. Journal of Psychoactive Drugs, 46, 303–309. 10.1080/02791072.2014.921744 (*Denotes articles included in meta-analytic models). [PubMed: 25188700]
Pietrzak RH, Goldstein RB, Southwick SM, & Grant BF (2011). Prevalence and axis I comorbidity of full and partial posttraumatic stress disorder in the USA: Results from wave 2 of the national epidemiologic survey on alcohol and related conditions. Journal of Anxiety Disorders, 25(3), 456–465. [PubMed: 21168991]

Possemato K, Johnson EM, Emery JB, Wade M, Acosta MC, Marsch LA, … Maisto SA (2019). A pilot study comparing peer supported web-based CBT to self-managed web CBT for primary care veterans with PTSD and hazardous alcohol use. Psychiatric Rehabilitation Journal, 42(3), 305–313. 10.1037/prj0000334 (*Denotes articles included in meta-analytic models). [PubMed: 30489140]

R Core Team. (2018). R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing..

Ralevski E, Olivera-Figueroa LA, & Petrakis I (2014). PTSD and comorbid AUD: A review of pharmacological and alternative treatment options. Substance Abuse and Rehabilitation, 5, 25–36. 10.2147/SAR.537399 [PubMed: 24648794]

Del Re AC & Hoyt WT (2014). MAaD: Meta-analysis with mean differences [Internet] Available from: <http://CRAN.R-project.org/package=MAaD>.

Resick PA, Monson CM, & Chard KM (2016). Cognitive Processing Therapy for PTSD: A Comprehensive Manual. New York: Guilford Press..

Resick PA, Wachen JS, Dondanville KA, Pruiksma KE, Jarvis JS, Peterson AL, … Young-McCaughan S (2017). Effect of group vs individual cognitive processing therapy in active-duty military seeking treatment for posttraumatic stress disorder: A randomized clinical trial. JAMA Psychiatry, 74(1), 28–36. 10.1001/jamapsychiatry.2016.2729 [PubMed: 27893032]

Reynolds M, Mezey G, Chapman M, Wheeler M, Drummond C, & Baldacchino A (2005). Co-morbid post-traumatic stress disorder in a substance misusing clinical population. Drug & Alcohol Dependence, 77(3), 251–258. 10.1016/j.drugalcdep.2004.08.017 [PubMed: 15734225]

Roberts NP, Roberts PA, Jones N, & Bisson JI (2015). Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: A systematic review and meta-analysis. Clinical Psychology Review, 38, 25–38. 10.1016/j.cpr.2015.02.007 [PubMed: 25792193]

Rosenberg MS (2005). The file-drawer problem revisited: A general weighted method for calculating fail-safe numbers in meta-analysis. Evolution, 59(2), 464–468. [PubMed: 15807430]

Rosenthal R (1979). The file drawer problem and tolerance for null results. Psychological Bulletin, 86(3), 638–641.

Ruglass LM, Lopez-Castro T, Papini S, Killeen T, Back SE, & Hien DA (2017). Concurrent treatment with prolonged exposure for co-occurring full or subthreshold Posttraumatic stress disorder and substance use disorders: A randomized clinical trial. Psychotherapy & Psychosomatics, 86, 150–161. 10.1159/000462977 (Denotes articles included in meta-analytic models). [PubMed: 28490022]

Sannibale C, Teesson M, Creamer M, Sitharthan T, Bryant RA, Sutherland K, & Peak-O’Leary M (2013). Randomized controlled trial of cognitive behavior therapy for comorbid posttraumatic stress disorder and alcohol use disorders. Addiction, 108 (8), 1397–1410 (*Denotes articles included in meta-analytic models). [PubMed: 25328957]

Schacht RL, Brooner RK, King VL, Kidorf MS, & Peirce JM (2017). Incentivizing attendance to prolonged exposure for PTSD with opioid use disorder patients: A randomized controlled trial. Journal of Consulting and Clinical Psychology, 85(7), 689–701. 10.1037/ccp0000208 (*Denotes articles included in meta-analytic models). [PubMed: 28414485]

Schorr I, Lotzin A, Hiller P, Sehner S, Driessen M, Hillemacher T, … Grundmann J (2019). A multisite randomized controlled trial of Seeking Safety vs. Relapse Prevention Training for women with co-occurring posttraumatic stress disorder and substance use disorders. European Journal of Psychotraumatology, 10(1), Article Article 1577092. 10.1080/20081982.2019.1577092 (*Denotes articles included in meta-analytic models).

Sells JR, Waters AJ, Schwandt ML, Kwako LE, Heilig M, George DT, & Ramchandani VA (2016). Characterization of comorbid PTSD in treatment-seeking alcohol dependent inpatients: Severity and personality trait differences. Drug and Alcohol Dependence, 163, 242–246. 10.1016/j.drugalcdep.2016.03.016 [PubMed: 27114205]

J Anxiety Disord. Author manuscript; available in PMC 2022 February 07.
Simpson TL, Hawrilenko M, Goldberg S, Browne K, Lehavot K, & Borowitz M (2020). Treatment receipt patterns among individuals with co-occurring PTSD and substance use disorders. Journal of Consulting and Clinical Psychology, 88, 1039–1051. 10.1037/ccp0000600 [PubMed: 32790452]

Simpson TL, Jakupcak M, & Luterek J (2006). Fear and avoidance of internal experiences among patients with substance use disorders and PTSD: The centrality of anxiety sensitivity. Journal of Traumatic Stress, 19, 481–491. [PubMed: 16929503]

Simpson TL, Kaysen DL, Fleming CB, Rhew IC, Jaffe AE, Desai S,… Resick PA (2021). Cognitive processing therapy and relapse prevention for comorbid posttraumatic stress disorder and alcohol use disorder: A randomized clinical trial. Manuscript under Review.

Simpson TL, Lehavot K, & Petrakis I (2017). No wrong doors: Findings from a critical review of behavioral randomized clinical trials for individuals with co-occurring alcohol/drug problems and PTSD. Alcoholism: Clinical and Experimental Research, 41(4), 681–702. 10.1111/acer.13325

Simpson TL, Rise P, Browne K, Lehavot K, & Kaysen D (2019). Clinical presentations, social functioning, and treatment receipt among individuals with comorbid lifetime PTSD and alcohol use disorders versus drug use disorders: Findings from the NESARC-III. Addiction, 114(6), 983–993. 10.1111/add.14565 [PubMed: 30694592]

Smith M, & Glass G (1977). Meta-analysis of psychotherapy outcome studies. American Psychologist, 32, 752–760.

Stappenbeck CA, Luterek JA, Kaysen D, Rosenthal CF, Gurrad B, & Simpson TL (2015). A controlled examination of two coping skills for daily alcohol use and PTSD symptom severity among dually diagnosed individuals. Behaviour Research and Therapy, 66, 8–17. 10.1016/j.brat.2014.12.013 (*Denotes articles included in meta-analytic models). [PubMed: 25617814]

Steudte-Schmiedgen S, Stalder T, Schonfeld S, Wittchen HU, Trautmann S, Alexander N, & Kirschbaum C (2015). Hair cortisol concentrations and cortisol stress reactivity predict PTSD symptom increase after trauma exposure during military deployment. Psychoneuroendocrinology, 59, 123–133. 10.1016/j.psyneuen.2015.05.007 [PubMed: 26072152]

Torchalla I, Nosen L, Rostam H, & Allen P (2012). Integrated treatment programs for individuals with concurrent substance use disorders and trauma experiences: A systematic review and meta-analysis. Journal of Substance Abuse Treatment, 42, 65–77. 10.1016/j.jsat.2011.09.001 [PubMed: 22035700]

Valentine JC, Pigott TD, & Rothstein HR (2010). How many studies do you need? A primer on statistical power for meta-analysis. Journal of Educational and Behavioral Statistics, 35(2), 215–247. 10.3102/1076998609346961

Viechtbauer W (2010). Conducting meta-analyses in R with the metafor package. Journal of Statistical Software, 36(3), 1–48.

Viechtbauer W, & Cheung MW-L (2010). Outlier and influence diagnostics for meta-analysis. Research Synthesis Methods, 1(2), 112–125. [PubMed: 26061377]

Vujoanic AA, Smith LJ, Tipton KP, & Schmitz JM (2018). A novel, integrated cognitive-behavioral therapy for co-occurring posttraumatic stress and substance use disorders: A case study. Cognitive and Behavioral Practice, 26(2), 307–322. [PubMed: 31631955]

Wampold B, & Imel ZE (2015). The Great Psychotherapy Debate: The Evidence for What Makes Psychotherapy Work (2nd ed.). New York: Routledge.

Wampold BE, Mondin GW, Moody M, Stich F, Benson K, & Ahn H (1997). A meta-analysis of outcome studies comparing bona fide psychotherapies. Empirically, “All must have prizes. Psychological Bulletin, 122, 203–215.

Westphal M, Aldao A, & Jackson C (2017). Emotion dysregulation in comorbid posttraumatic stress disorder and substance use disorders: A narrative review. Military Psychology, 29(3), 216–233. 10.1037/mil0000157

Zlotnick C, Franklin CL, & Zimmerman M (2002). Does “subthreshold” posttraumatic stress disorder have any clinical relevance? Comprehensive Psychiatry, 43(6), 413–419. [PubMed: 12439826]

Zlotnick C, Johnson J, & Najavits LM (2009). Randomized controlled pilot study of cognitive-behavioral therapy in a sample of incarcerated women with Substance Use Disorder and PTSD. Behavior Therapy, 40, 325–336. 10.1016/j.beth.2008.09.004 [PubMed: 19892078]

J Anxiety Disord. Author manuscript; available in PMC 2022 February 07.
Zoellner LA, Roy-Byrne PP, Mavissakalian M, & Feeny NC (2019). Doubly randomized preference trial of prolonged exposure versus sertraline for treatment of PTSD. The American Journal of Psychiatry, 176(4), 287–296. 10.1176/appi.ajp.2018.17090995 [PubMed: 30336702]
Fig. 1.
PRISMA flow diagram.
Fig. 2.
Forest plot of within-group effects separated by treatment type, domain, and time point. SUD = substance use disorder symptoms; Trauma = trauma-focused treatment; Non-trauma = non-trauma-focused treatment; Manual SUD = manualized SUD treatment; SUD TAU = SUD treatment-as-usual; No tx = no treatment control; FU = follow-up.
Fig. 3.
Forest plot of between-group effects separated by comparison, domain, and time point.
Trauma = trauma-focused treatment; v. = versus; all = all comparators with the exception of trauma-focused or integrated non-trauma-focused; Manual SUD = manualized SUD treatment; Non-trauma = non-trauma-focused treatment; FU = follow-up. SUD = substance use disorder symptoms.
Table 1

Participant-level characteristics by study.

| Study | ITT N | Treatment | Comparator | Age | % Female | % Racial/Ethnic Minority | % Met PTSD Diagnostic Criteria | % Met SUD Diagnostic Criteria | % with Current Drug Use |
|-------|-------|-----------|------------|-----|----------|--------------------------|-------------------------------|-------------------------------|------------------------|
| Back et al. (2019) | 81 | ITF | Manual SUD | 40.4 | 9.9 | 39.5 | 100 | 100 | 37.1 |
| Boden et al. (2011) | 98 | NTF | TAU | 54 | 0 | 81 | NA | 100 | 80.6 |
| Brief PC | 386 | NTF | No/minimal tx | 32.15 | 13.40 | 22.25 | NA | NA | NA |
| Capone et al. (2014) | 44 | NTF | TAU | 34.29 | 4.55 | 15.85 | 100 | 100 | 38.6 |
| Coffey et al. (2016) | 126 | TF | TAU | 34 | 46 | 20.6 | 100 | 100 | NA |
| van Dam, Ehring, Vedel, and Emmelkamp (2013) | 34 | TF | Manual SUD | 42.3 | 32.4 | 26.5 | 61.8 | 100 | 55.9 |
| Fon et al. (2013) | 165 | TF (+Nal) | Manual SUD | 42.7 | 34.5 | 69.7 | 100 | 100 | NA |
| Haller PC | 101 | ITF | TAU | 46.4 | 10.9 | 37.6 | 100 | 100 | 58.5 |
| Hamblen (2020) | 129 | TF | TAU | 44.2 | 5.4 | 32.8 | 100 | 100 | 92 |
| Hien, Cohen, Miele, Litt, and Capstick (2004) | 75 | NTF | Manual SUD | 36 | 100 | 36 | 88 | 100 | 65.3 |
| Hien et al. (2009) | 353 | NTF | TAU | 39.2 | 100 | 54.4 | 80.4 | 100 | 91.2 |
| Kehle-Forbes et al. (2018) | 183 | ITF | TF | 44.1 | 7.75 | 58.95 | 100 | 100 | 18 |
| McGovern, Lambert-Harris, Alterman, Xie, and Meier (2011) | 53 | NTF | Manual SUD | 37.3 | 56.6 | 8.7 | 100 | 100 | 47.2 |
| McGovern et al. (2015) | 221 | NTF | Manual SUD | 35.3 | 59.3 | 4.5 | 100 | 100 | 51.1 |
| Mills et al. (2012) | 103 | ITF | No/minimal tx | 33 | 62.1 | 5.8 | 100 | 100 | 79.6 |
| Myers, Browne, and Norman (2015) | 40 | NTF | Manual SUD | 42.2 | 100 | 48.4 | 80.6 | 100 | NA |
| Najavits et al. (2018) | 52 | ITF | NTF | 48.7 | 26.9 | 40 | 100 | 100 | 50 |
| Norman et al. (2019) | 119 | ITF | NTF | 41.6 | 10.1 | 34.5 | 95.8 | 100 | NA |
| Perez-Dandieu and Tapia (2014) | 12 | TF | TAU | 29.5 | 100 | NA | 100 | 100 | 83.3 |
| Possemato et al. (2019) | 30 | NTF | NTF | 38.6 | 6.7 | 20 | 76.7 | 100 | NA |
| Ruglass et al. (2017) | 110 | ITF | Manual SUD | 44.4 | 36.4 | 81.8 | 64.5 | 100 | 98.2 |
| Sannibale et al. (2013) | 62 | ITF | Manual SUD | 41.2 | 53 | NA | 100 | 95 | 15 |
| Study                                      | ITT N | Treatment | Comparator | Age | % Female | % Racial/Ethnic Minority | % Met PTSD Diagnostic Criteria | % Met SUD Diagnostic Criteria | % with Current Drug Use |
|--------------------------------------------|-------|-----------|------------|-----|----------|-------------------------|-------------------------------|-------------------------------|--------------------------|
| Schacht et al. (2017)                      | 58    | TF        | TF         | 37.4| 79       | 29                      | 100                           | 100                          | 100                      |
| Schafer et al. (2019)                      | 343   | NTF       | Manual SUD | 40.97| 100      | 9.6                     | NA                            | 100                          | NA                       |
| Simpson et al. (2021)                      | 101   | TF        | Manual SUD | 42.1| 56       | 47                      | 100                           | 100                          | 38.6                     |
| Stappenbeck et al. (2015)                  | 78    | NTF       | No/minimal tx | 44.3| 48.7     | 57.7                    | 100                           | 100                          | NA                       |
| Vujanovic, Smith, Tipton, and Schmitz (2018) | 41    | ITF       | Manual SUD | 44.9| 53.7     | 75.6                    | NA                            | 100                          | NA                       |
| Zlotnick, Johnson, and Najavits (2009)      | 49    | NTF       | TAU        | 34.6| 100      | 53.1                    | 83.5                          | 100                          | NA                       |

Note: ITT N = intention-to-treat sample size; NA = not available; PC = Personal Communication; Manual SUD = manualized SUD treatment; No tx = no/minimal treatment; TAU = SUD TAU; NA = information not collected/reported; NTF = not trauma-focused; TF = trauma-focused; ITF = integrated trauma-focused; NAL = Naloxone; PL = placebo drug.

1. Participants received SUD TAU and a general healthy lifestyle or health-oriented attention placebo control.
2. Participants received an integrated CBT intervention to address depression and SUD.
3. Studies that did not contribute to between-group analyses.
4. Unpublished studies at time analyses undertaken.
| Treatment   | Domain   | Time | k     | ES       | $I^2$          | $k_{imp}$ | ES$_{adj}$ | FSN |
|------------|----------|------|-------|----------|---------------|-----------|------------|-----|
| Trauma     | PTSD     | post | 17    | 1.11 [0.86, 1.35] | 85.37 [73.66, 93.62] | 4         | 0.93 [0.65, 1.21] | 3223 |
| Trauma     | SUD      | post | 16    | 0.82 [0.47, 1.16]  | 93.55 [88.77, 97.77]  | 0         | 0.82 [0.47, 1.16]  | 1376 |
| Trauma     | PTSD     | FU   | 15    | 1.10 [0.81, 1.39]  | 87.49 [77.34, 94.85]  | 0         | 1.10 [0.81, 1.39]  | 2305 |
| Trauma     | SUD      | FU   | 15    | 0.97 [0.62, 1.33]  | 92.98 [87.45, 97.18]  | 0         | 0.97 [0.62, 1.33]  | 2009 |
| Non-trauma | PTSD     | post | 14    | 0.65 [0.45, 0.84]  | 79.67 [62.03, 93.21]  | 0         | 0.65 [0.45, 0.84]  | 1178 |
| Non-trauma | SUD      | post | 13    | 0.44 [0.29, 0.59]  | 72.47 [44.35, 89.02]  | 5         | 0.55 [0.41, 0.70]  | 709  |
| Non-trauma | PTSD     | FU   | 12    | 0.76 [0.53, 0.99]  | 78.82 [55.06, 91.35]  | 0         | 0.76 [0.53, 0.99]  | 934  |
| Non-trauma | SUD      | FU   | 12    | 0.43 [0.20, 0.67]  | 86.36 [72.03, 95.30]  | 0         | 0.48 [0.24, 0.72]  | 479  |
| Manual SUD | PTSD     | post | 13    | 0.85 [0.58, 1.11]  | 79.26 [56.96, 91.99]  | 2         | 0.76 [0.50, 1.02]  | 800  |
| Manual SUD | SUD      | post | 13    | 0.87 [0.41, 1.33]  | 94.70 [89.48, 98.46]  | 0         | 0.87 [0.41, 1.33]  | 704  |
| Manual SUD | PTSD     | FU   | 11    | 1.01 [0.70, 1.31]  | 75.30 [45.91, 92.13]  | 0         | 1.01 [0.70, 1.31]  | 628  |
| Manual SUD | SUD      | FU   | 11    | 0.80 [0.43, 1.18]  | 87.61 [73.58, 96.32]  | 0         | 0.80 [0.43, 1.18]  | 469  |
| SUD TAU    | PTSD     | post | 10    | 0.58 [0.30, 0.86]  | 85.71 [68.45, 96.28]  | 1         | 0.65 [0.35, 0.94]  | 449  |
| SUD TAU    | SUD      | post | 8     | 0.30 [0.16, 0.45]  | 54.15 [26.95, 97.93]  | 0         | 0.30 [0.16, 0.45]  | 108  |
| SUD TAU    | PTSD     | FU   | 8     | 0.79 [0.54, 1.05]  | 77.46 [47.09, 94.21]  | 0         | 0.79 [0.54, 1.05]  | 481  |
| SUD TAU    | SUD      | FU   | 8     | 0.52 [0.16, 0.88]  | 91.73 [79.59, 98.25]  | 0         | 0.52 [0.16, 0.88]  | 164  |
| No tx      | PTSD     | post | 5     | 0.49 [0.27, 0.71]  | 41.91 [0.00, 92.12]  | 0         | 0.49 [0.27, 0.71]  | 58   |
| No tx      | SUD      | post | 5     | 0.61 [0.29, 0.92]  | 75.46 [28.67, 97.13]  | 0         | 0.61 [0.29, 0.92]  | 108  |
| No tx      | PTSD     | FU   | 1     | 1.04 [0.65, 1.43]  | NA               | NA        | NA         | 10   |
| No tx      | SUD      | FU   | 1     | 1.29 [0.92, 1.66]  | NA               | NA        | NA         | 16   |

Note: k = number of treatment or control arms contributing to effect size estimate; ES = effect size in Hedges’ $g$ units; $I^2$ = heterogeneity; $k_{imp}$ = number of studies imputed to account for funnel plot asymmetry; ES$_{adj}$ = trim-and-fill adjusted effect size; SUD = substance use disorder symptoms; No tx = no treatment control; Trauma = trauma-focused treatment; Manual SUD = manualized SUD treatment; Integ non-trauma = integrated non-trauma-focused treatment; SUD TAU = SUD treatment-as-usual; FU = follow-up; NA = not available due to insufficient studies.
| Comparison          | Domain | Time | k   | ES     | ESadj  | kimp | I²   | FSN   |
|---------------------|--------|------|-----|--------|--------|------|------|-------|
| Trauma v. all       | PTSD   | post | 12  | 0.29 0.07, 0.82 | 3.29 0.00, 9.211 | 2 | 0.22 [0.05, 0.49] | 44° | 3.95 [0.00, 9.218] |
| Trauma v. all       | SUD    | post | 11  | −0.11 [−0.34, 0.11] | 25.34 [0.00, 9.218] | 1 | −0.15 [−0.37, 0.07] | 0 | 1.05 [0.00, 36.77] |
| Trauma v. all       | SUD    | post | 10  | −0.01 [−0.24, 0.22] | 20.95 [0.00, 8.354] | 1 | −0.01 [−0.31, 0.19] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. all       | FSD    | post | 10  | 0.08 [−0.23, 0.32] | 21.72 [0.00, 8.528] | 2 | −0.11 [−0.43, 0.09] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. all       | SUD    | post | 8   | 0.15 [−0.06, 0.37] | 4.39 [0.00, 8.882] | 3 | 0.11 [−0.38, 0.12] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. all       | SUD    | post | 8   | −0.21 [−0.47, 0.04] | 6.66 [0.00, 9.271] | 0 | 0.21 [−0.47, 0.04] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. all       | SUD    | post | 10  | 0.12 [−0.05, 0.28] | 4.73 [0.00, 5.861] | 0 | 0.12 [−0.05, 0.28] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. Manual SUD| PTSD   | post | 7   | 0.01 [−0.25, 0.28] | 0.00 [0.00, 8.882] | 1 | −0.02 [−0.28, 0.08] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. Manual SUD| SUD    | post | 8   | 0.15 [−0.06, 0.37] | 4.39 [0.00, 8.882] | 3 | 0.11 [−0.38, 0.12] | 0 | 0.00 [0.00, 9.218] |
| Trauma v. Manual SUD| SUD    | post | 10  | 0.12 [−0.05, 0.28] | 4.73 [0.00, 5.861] | 0 | 0.12 [−0.05, 0.28] | 0 | 0.00 [0.00, 9.218] |
| Non-trauma v. all   | PTSD   | post | 7   | −0.10 [−0.38, 0.09] | 23.33 [0.00, 6.701] | 1 | 0.12 [−0.03, 0.28] | 5 | 0.12 [−0.03, 0.28] |
| Non-trauma v. all   | FSD    | post | 8   | 0.01 [−0.25, 0.28] | 0.00 [0.00, 8.882] | 1 | −0.02 [−0.28, 0.08] | 0 | 0.00 [0.00, 9.218] |
| Non-trauma v. all   | SUD    | post | 8   | 0.15 [−0.06, 0.37] | 4.39 [0.00, 8.882] | 3 | 0.11 [−0.38, 0.12] | 0 | 0.00 [0.00, 9.218] |
| Non-trauma v. Manual SUD| PTSD   | post | 4   | 0.01 [−0.25, 0.28] | 0.00 [0.00, 8.882] | 3 | 0.11 [−0.38, 0.12] | 0 | 0.00 [0.00, 9.218] |
| Non-trauma v. Manual SUD| FSD    | post | 4   | −0.21 [−0.44, 0.02] | 0.00 [0.00, 8.882] | 1 | −0.28 [−0.43, 0.05] | 1 | 0.00 [0.00, 9.218] |
| Non-trauma v. Manual SUD| SUD    | post | 4   | 0.21 [−0.18, 0.60] | 0.00 [0.00, 8.882] | 3 | −0.11 [−0.40, 0.19] | 0 | 0.00 [0.00, 9.218] |

Note: k = number of comparisons contributing to effect size estimate; ES = effect size in Hedges’ g units; ESadj = trim-and-fill adjusted effect size; FSN = fail-safe N with superscripted a for instances in which FSN indicated a significant effect was not robust to publication bias; SUD = substance use disorder symptoms; Non-trauma = integrated non-trauma-focused treatment; Trauma = trauma-focused treatment; v. = versus; Manual SUD = manualized SUD treatment; FU = follow-up.
| Comparison                  | k  | OR           | $I^2$ | k_{imp} | OR_{adj} | k_{out} | OR_{out} | FSN   |
|-----------------------------|----|--------------|-------|---------|----------|---------|----------|-------|
| Trauma v. all               | 8  | 0.85 [0.60, 1.21] | 0.00 [0.00, 72.80] | 2      | 0.94 [0.68, 1.31] | 0 | 0.85 [0.60, 1.21] | 0 |
| Trauma v. Manual SUD        | 6  | 0.92 [0.63, 1.36] | 0.00 [0.00, 83.67] | 0      | 0.92 [0.63, 1.36] | 0 | 0.92 [0.63, 1.36] | 0 |
| Non-trauma v. all           | 6  | 1.22 [0.93, 1.60] | 0.00 [0.00, 71.98] | 2      | 1.30 [1.00, 1.68] | 0 | 1.22 [0.93, 1.60] | 0 |
| Non-trauma v. Manual SUD    | 5  | 1.24 [0.87, 1.78] | 0.00 [0.00, 79.37] | 2      | 1.41 [1.01, 1.95] | 0 | 1.24 [0.87, 1.78] | 0 |

Note: $k =$ number of comparisons contributing to effect size estimate; OR = odds ratio, with ORs > 1 indicating higher treatment completion in the experimental group relative to the control condition; $I^2 =$ heterogeneity; $k_{imp} =$ number of studies imputed to account for funnel plot asymmetry; $OR_{adj} =$ trim-and-fill adjusted effect size; $k_{out} =$ number of outliers detected; $OR_{out} =$ odds ratio estimate with outliers removed; FSN = fail-safe N; Non-trauma = integrated non-trauma-focused treatment; Trauma = trauma-focused treatment; v. = versus; Manual SUD = manualized SUD treatments