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Review

Exposure therapy for PTSD: A meta-analysis

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ABSTRACT

Posttraumatic stress disorder (PTSD) is associated with high morbidity and functional impairment in the absence of effective treatment. Exposure therapy for PTSD is a trauma-focused treatment that typically includes in vivo and/or imaginal exposure. The goal of this meta-analysis was to examine the overall efficacy of exposure therapy for PTSD compared to various control conditions. We also assessed the efficacy of individual exposure-based treatments and the potentially moderating impact of various demographic, clinical, and treatment-related factors. PsycINFO and Medline were searched for randomized controlled trials of exposure-based therapies for adult PTSD. A total of 934 abstracts were screened for initial eligibility; of these, 65 articles met inclusion criteria and were included in the meta-analysis (total $N = 4929$ patients). Exposure therapy showed large effects relative to waitlist and treatment-as-usual, a small effect relative to non-trauma-focused comparators and a negligible effect relative to other trauma-focused treatments or medication. At follow-up most effects sizes were stable, except for a medium effect favoring exposure over medication. The individual exposure-based therapies examined were similarly effective. Moderator analyses revealed larger effect sizes in studies with fewer sessions, younger samples, fewer participants diagnosed with substance use disorder, and fewer participants on psychiatric medication. Effect sizes were also larger in studies of refugees and civilians compared to military samples, studies of PTSD related to natural disasters and transportation accidents vs. other traumatic events, and studies of individual vs. group therapy. Findings support the overall efficacy of exposure therapy and highlight that there are a number of efficacious exposure-based therapies available.

Recent estimates indicate that posttraumatic stress disorder (PTSD) affects 3.9% of the population worldwide. In the absence of effective treatment, PTSD often becomes chronic and is associated with significant psychiatric and medical comorbidity (Kessler, Chiu, Demler, & Walters, 2005; Sareen., 2005). Nearly a decade after PTSD was officially recognized and codified in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; American Psychiatric Association (APA), 2019), studies demonstrating the successful application of exposure therapy to treat PTSD began to shift perceptions of PTSD from intractable to treatable, demonstrating that significant symptom reduction was achievable. Exposure therapies emphasize confrontation with fear-evoking memories of the traumatic event (i.e., imaginal exposure) as well as situations or stimuli that are avoided or distress-inducing (i.e., in vivo exposure). These early studies of exposure therapy for PTSD focused on imaginal exposure, specifically, "implosive" (flooding) therapy (Boudewyns & Hyer, 1990; Cooper & Clum, 1989; Keane, Fairbank, Caddell, & Zimering, 1989) in which clients were guided through graduated imaginal exposure to trauma-related scenes. This work directly informed the development of prolonged exposure therapy (PE), a specific exposure therapy protocol that has been studied extensively. Although PE may be considered the exemplar exposure therapy for PTSD, several other exposure-based therapies for PTSD, including narrative exposure therapy (NET; Schauer, Neuner, Elbert, Brown, & Collins, 2005; Schauer, Schauer, Neuner, & Elbert, 2011) and written exposure therapy (WET; Sloan & Marx, 2019) have also gained empirical support.

There are now a number of evidence-based psychotherapies available for PTSD. Among the most consistently and extensively supported are trauma-focused treatments, which include exposure therapies, cognitive approaches such as cognitive processing therapy (CPT; Resick

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et al., 2017) and cognitive therapy (Ehlers et al., 2003), other types of cognitive behavioral therapy (e.g., Blanchard et al., 2003) as well as eye movement desensitization and reprocessing therapy (EMDR; Shapiro & Maxfield, 2002). Indeed, recent meta-analyses and systematic reviews investigating the efficacy of PTSD treatments in adults (Bisson, 2013; Cusack et al., 2016; Jonas et al., 2013; Kessler et al., 2005; Lewis, Roberts, Andrew, Starling, & Bisson, 2020; Watts et al., 2013) all show the largest effects for trauma-focused psychotherapies. These meta-analyses have examined a broad range of psychotherapies for PTSD (grouped in different ways) rather than focusing in depth on any specific treatment approach. There have been recent meta-analyses demonstrating the efficacy of specific exposure therapies (e.g., virtual reality exposure: Deng et al., 2019; NET: Lely et al., 2019), however, the most recent meta-analysis of PE was conducted by Powers and colleagues over a decade ago and included 13 studies (Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010). Therefore, one motivation for the current investigation was to update the Powers et al. meta-analysis, including all studies published since then. Another motivation was to examine the efficacy of exposure therapy in depth, as well as the efficacy of various exposure-based therapies, which has not been examined in previous meta-analyses.

In the current meta-analysis, we focused on exposure therapy broadly, rather than on one specific exposure protocol, such as PE. All exposure-based therapies for PTSD include the same key component(s): imaginal exposure and/or in vivo exposure, although the implementation of these components varies across specific protocols. Imaginal exposure has been implemented through verbal narration, virtual reality, and writing. Both imaginal and in vivo exposure may be implemented with or without a therapist present. Across protocols, exposure sessions vary in length and number. However, all exposure-based therapies help clients approach trauma-related memories and/or stimuli for the purpose of therapeutic learning. Thus, we defined the scope of our analysis atheoretically based on the primary technique used in treatment. This is similar to other meta-analyses and reviews that have grouped together therapies that are "trauma-focused," but here we are focusing on a defined subset of trauma-focused treatments. Focusing on exposure therapy broadly also allows us to report on the efficacy of different specific exposure protocols. Of note, we included EMDR in our analysis despite it often being classified separately from exposure therapy and cognitive-behavioral therapy more broadly. Although the variant of exposure used in EMDR (brief, not-verbalized, dual attention) is different from that used in, for example, PE (prolonged, verbalized, focused attention), it is nonetheless imaginal exposure. Debate around the added utility of bilateral stimulation or whether EMDR works through different mechanisms than do other exposure therapies, (see Cuijpers, Veen, Sijbrandij, Yoder, & Cristea, 2020; Lee & Cuijpers, 2013), is irrelevant to whether the primary treatment technique is exposure.

The primary aims of this study were to examine: (1) the efficacy of exposure-based psychotherapies relative to control conditions among adults diagnosed with PTSD and (2) the effects across exposure-based psychotherapy protocols. We predicted that exposure-based psychotherapies would show large effects compared to waitlist and treatment-as-usual (TAU), small to medium effects compared to non-trauma-focused treatments, and negligible effects or small effects compared to medication and to other trauma-focused treatments that do not meet our criterion for "exposure-based." We also aimed to explore relationships between effect sizes and study sample characteristics, including civilian/military status, trauma type, gender, age, racial/ethnic identity, psychiatric medication use, and psychiatric comorbidities.

1. Methods

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Page et al., 2020) and a review protocol was made for this study (CRD42021240240) that can be accessed at https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=240240.

1.1. Inclusion criteria

Inclusion criteria for studies were: (1) reported in English, (2), randomized controlled study design, (3) adult participants (age 18+ years) with clinically diagnosed PTSD, (4) outcomes that measured PTSD severity, (5) at least one exposure-based treatment condition, and (6) at least one non-exposure control group (any intervention that did not meet our exposure-based criteria). "Exposure-based" was operationalized as a majority of the treatment sessions focusing on exposure. Thus, treatments such as brief eclectic therapy, trauma-management therapy, or the Internet-delivered treatment *Interapy* which focus on exposure in 50% of their sessions, or cognitive behavioral treatments that focus on exposure in 50% or fewer of the sessions, were excluded. The modality of exposure delivery (e.g., telehealth, virtual reality) was not an exclusion criterion.

Studies were excluded if they tested combined or integrated treatment for PTSD and a comorbid condition (e.g., concurrent exposure for PTSD and treatment for substance use disorder), tested a self-directed or self-help treatment, or included less than 10 participants in each treatment condition.

1.2. Data sources and search strategy

Journal articles were identified using the PsycINFO and Medline electronic databases through October 2020 (no specified start date; search performed on November 3rd, 2020), with the following search terms: "Posttraumatic Stress Disorder" AND "Random*" AND "Therapy or Treatment" AND "Exposure or Flooding or Implosive". After agreeing to expand our study inclusion criteria, on January 24th, 2021, a second search was conducted to identify EMDR trials using the following search terms: "Posttraumatic Stress Disorder" AND "Random*" AND "Therapy or Treatment" AND "EMDR" OR "Eye Movement Desensitization and Reprocessing" OR "Eye-Movement Desensitization and Reprocessing". Both searches were limited to English-language articles and adult (age 18 years or older) populations. We also checked the reference lists of prior meta-analyses and review papers that examined treatments for PTSD.

1.3. Study selection

Two authors (among C.P.M., H.C.L., and M.L.M.) reviewed each abstract for initial eligibility; discrepancies were discussed until a resolution was reached. Raters then reviewed full texts of eligible studies based on abstract review. Reasons for exclusion were coded for all studies that were not eligible upon full-text review. Any additional studies identified by searching reference lists of other reviews and meta-analyses were screened and coded following the same process. On April 5th, 2021 and again on October 7th, 2021, our search was re-run prior to the final analysis to identify any studies that were published after the initial search date. We also sought unpublished studies by inquiring with colleagues via listservs and social media.

1.4. Data coding

Coded study variables fell into three categories: study-related, treatment-related, and sample-related. *Study-related variables* included article author; primary PTSD outcome; assessment type (self-report or interview); exposure group sample size; control group sample size; outcome means and standard deviations at pre-, post, and follow-up (if available; otherwise, *d*, *t* or *F* values were entered); duration of follow-up; and study year. *Sample-related variables* included percentage of participants on psychiatric medication; mean age of participants; percentage of participants who identified as women; percentage of

participants with a diagnosis of major depression; percentage of participants with a substance use disorder; sample type (civilian, active duty, veteran, or refugee); trauma type (combat, sexual assault, natural disaster, transportation accident, medical trauma, and mixed). For studies conducted in countries where the majority of the population identifies racially as White, we also coded the percentage of participants who identified as racial minorities. *Treatment-related variables* included mean number of sessions in the exposure intervention; mean number of sessions in the control intervention; exposure therapy type (imaginal, in vivo, or combination); exposure therapy modality (individual, group, or combination); exposure treatment package (PE, NET, EMDR, WET, or "other" exposure therapy); and control treatment package (waitlist, treatment-as-usual [TAU], medication, non-trauma-focused therapy, or trauma-focused therapy).

If studies did not report data for the coded variables, attempts were made to contact study investigators via email to obtain the missing data. If the exposure dose included a range, the middle value of the range was coded.

1.5. Reliability

Fourteen articles (21.5%) were randomly selected from the pool of included studies for inter-rater reliability analyses. The original coder and one additional coder (among C.P.M., H.C.L., and M.L.M.) independently coded the selected articles. We then calculated intraclass correlation coefficients (continuous variables) and kappa coefficients (categorical variables) to assess inter-rater reliability. Values for the primary variables of interest (means and SDs for exposure and control groups at each time point for the study outcome variables) and moderators of interest were all 0.86 or higher, indicating excellent inter-rater reliability across variables.

1.6. Treatment classification

Two authors (C.P.M. and H.C.L.) classified the exposure treatments and control conditions for all studies. Exposure therapies were coded as PE, NET, EMDR, WET, or "other" "exposure therapy. Note that treatments similar to existing exposure protocols, but which did not follow those protocols explicitly, were coded as "other" exposure therapy. For example, treatments that included both in vivo and imaginal exposure (e.g., Bryant et al., 2008) but did not follow the PE protocol, and treatments that used written exposure (e.g., written account condition in Resick et al., 2008) but did not follow the WET protocol, were included in the "other" category to protect the integrity of the treatment protocols, which differs from how prior meta-analyses have approached this issue (e.g., Powers et al., 2010).

Control conditions were classified as waitlist (including minimal attention conditions), TAU (including routine clinical care, standard psychiatric support and placebo medication), psychiatric medication (paroxetine, fluoxetine, sertraline), non-trauma-focused therapy (supportive therapies, psychodynamic therapy, interpersonal therapy, body-focused therapies, present-centered therapy, stress inoculation therapy, and meta-cognitive therapy), and trauma-focused treatments (variants of cognitive processing therapy, cognitive therapy, and brief eclectic therapy). Treatments were coded as trauma-focused if they directly addressed thoughts, feelings, and/or memories of the traumatic event using a primary component of exposure and/or cognitive restructuring but did not meet our criterion for "exposure-based."

1.7. Risk of bias

Selected studies were independently assessed for risk of bias (RoB) using the Cochrane Risk of Bias tool 2.0 for randomized trials (Sterne et al., 2019). This tool involves coding for risk of bias arising from five domains: 1) the randomization process, 2) deviations from the intended intervention (i.e., treatment non-adherence), 3) missing outcome data, 4) measurement of outcome, and 5) selection of reported result. We focused on our primary outcome (PTSD severity) for evaluation of risk of bias. All studies were coded by two independent raters (among C.P.M., H.C.L., and M.L.M.) and discrepancies were discussed until a consensus was reached.

Overall study ratings can be derived from the domain ratings, such that the overall study is coded as 'low risk' only if all domains are 'low risk' and a study is coded as 'high risk' if any domains are coded as 'high risk'. We analyzed the impact of RoB by quantifying domain codes (low risk = 0, some concerns = 1, high risk = 2) yielding a total risk score ranging from 0 to 10 for each study.

1.8. Data synthesis

Outcomes for exposure and control samples were compared. We considered a network, rather than pairwise, meta-analysis (Rouse, Chaimani, & Li, 2017), as such an analysis might yield a clearer understanding of the differences in efficacy among the exposure variants. However, this approach assumes that there are no imbalances in effect modifiers between different types of direct comparisons (e.g., different exposure types and controls) (Jansen & Naci, 2013), and we do not believe this assumption is met.

The primary variable of interest was the mean score on a standardized measure of PTSD. Intent-to-treat (ITT) data were used to provide a more conservative estimate of treatment effects that more closely represents clinical practice (Abraha et al., 2015; McCoy, 2015). In rare cases when ITT data were unavailable, completer data were used. Data were analyzed using Comprehensive Meta-Analysis Version 2.2 (Borenstein, Hedges, Higgins, & Rothstein, 2007) using strategies from Borenstein, Hedges, Higgins, and Rothstein (2009). Effect sizes (Hedges's g) were calculated using a random effects model and weighted for inverse variance. Hedges's g is a small-sample correction for Cohen's d, for which effect sizes of 0.2, 0.5 and 0.8 are traditionally interpreted as small, medium and large, respectively (Cohen, 1988). The 95% confidence interval (CI) was calculated for each effect size estimate. Calculation of g for pre-post designs requires an estimate of the correlation (r) between the pre- and posttreatment scores; because this was not available in published reports, r was conservatively estimated at 0.7 according to the recommendation of Rosenthal (1991). Between-group effects, which assess the difference between exposure and control groups at posttreatment were calculated as $d = \frac{\overline{X}_1 - \overline{X}_2}{S_{within}}$, where $S_{within} = \sqrt{\frac{(n_1-1)\ S_1^2 + (n_2-1)\ S_2^2}{n_1+n_2-2}}$, n_1 and n_2 are the sample sizes of the two groups, and S_1 and S_2 are the standard deviations of the two groups. All d scores were converted to g using the standard correction procedure that adjusts for degrees of freedom (Hedges, 1981).

Publication bias was assessed using funnel plots, examining asymmetry of effect size against standard error. Duval and Tweedie's (2000) Trim and Fill was used; this method trims asymmetric studies from the right-hand side to locate the unbiased effect (in an iterative procedure), and then fills the plot by re-inserting the trimmed studies on the right as well as their imputed counterparts to the left of the mean effect. The I^2 statistic was used to assess heterogeneity. The I^2 statistic is expressed as the percentage of variation due to true heterogeneity rather than chance and is interpreted as follows: 25% = little heterogeneity, 50% = moderate heterogeneity, and 75% = high heterogeneity (Higgins, Thompson, Deeks, & Altman, 2003). To test the file drawer effect (the probability that unpublished null results would eliminate the obtained results), for each result the fail-safe N (FSN), or the number of null results that would be needed to overturn a significant result, was calculated. Generally, if the FSN is greater than or equal to 5 times the number of studies in the analysis plus 10, the obtained results are considered robust against the file drawer effect (Rosenthal, 1991).

Meta-regression was used to explore the relationship between continuous moderator variables (study year, mean number of sessions, percentage of participants who dropped out of the exposure therapy

group and the control group, and percentage of participants who: identified as women, identified as ethnic or racial minorities, were diagnosed with depression, were diagnosed with a substance use disorder, or were taking psychiatric medication) and effect size in the exposure therapy groups. Categorical moderator variables (sample type, trauma type, exposure type, and treatment modality) were explored by separating the samples by moderator variable and examining between-group heterogeneity using the *Q* statistic.

Additional statistics (risk of bias comparisons) were conducted using SPSS v. 26.

2. Results

2.1. Literature search

Our searches yielded 934 manuscripts. Abstracts were screened for potential eligibility. Full texts of 136 manuscripts were reviewed and 65 studies meeting our eligibility criteria were identified and included in the analyses, representing a total of 4929 patients (2557 received exposure-based therapy and 2372 received a control intervention). See Fig. 1 for the PRISMA flow diagram of selected studies and reasons for study exclusion. See Appendix A for a list of the included studies. Coded characteristics of all included studies are available in Appendix B.

2.2. Primary outcomes

Overall, when comparing conditions at posttreatment on PTSD measures, exposure therapy was superior to control conditions, with a large effect size (k [number of comparisons]) = 77, $g = 0.860$, 95% CI = 0.685–1.035 (see Fig. 2). Heterogeneity across studies was high ($I^2 = 87.16$). The Trim and Fill procedure (random effects) identified no missing studies. FSN was 9421, suggesting that this finding is robust against the file drawer effect.

At follow-up, exposure was associated with a small to medium effect size on PTSD measures ($k = 35$, $g = 0.528$, 95% CI = 0.316–0.739, $p < 0.001$). Heterogeneity was high ($I^2 = 85.984$). The Trim and Fill procedure (random effects) identified no missing studies. FSN was 990, suggesting that this finding is robust against the file drawer effect.

Table 1 shows the effects of exposure therapy vs. various control conditions at posttreatment on PTSD measures. Note that because some studies included more than one control group, the total k for subgroup comparisons is more than 77 (for this, we used all comparisons, assuming independence). As can be seen in the Table, exposure was superior to both wait list and TAU, with large effect size estimates. The effect of exposure was small compared to non-trauma-focused therapy, and negligible compared to medications and trauma-focused therapy. Heterogeneity across control conditions was significant, $Q(4) = 75.170$,

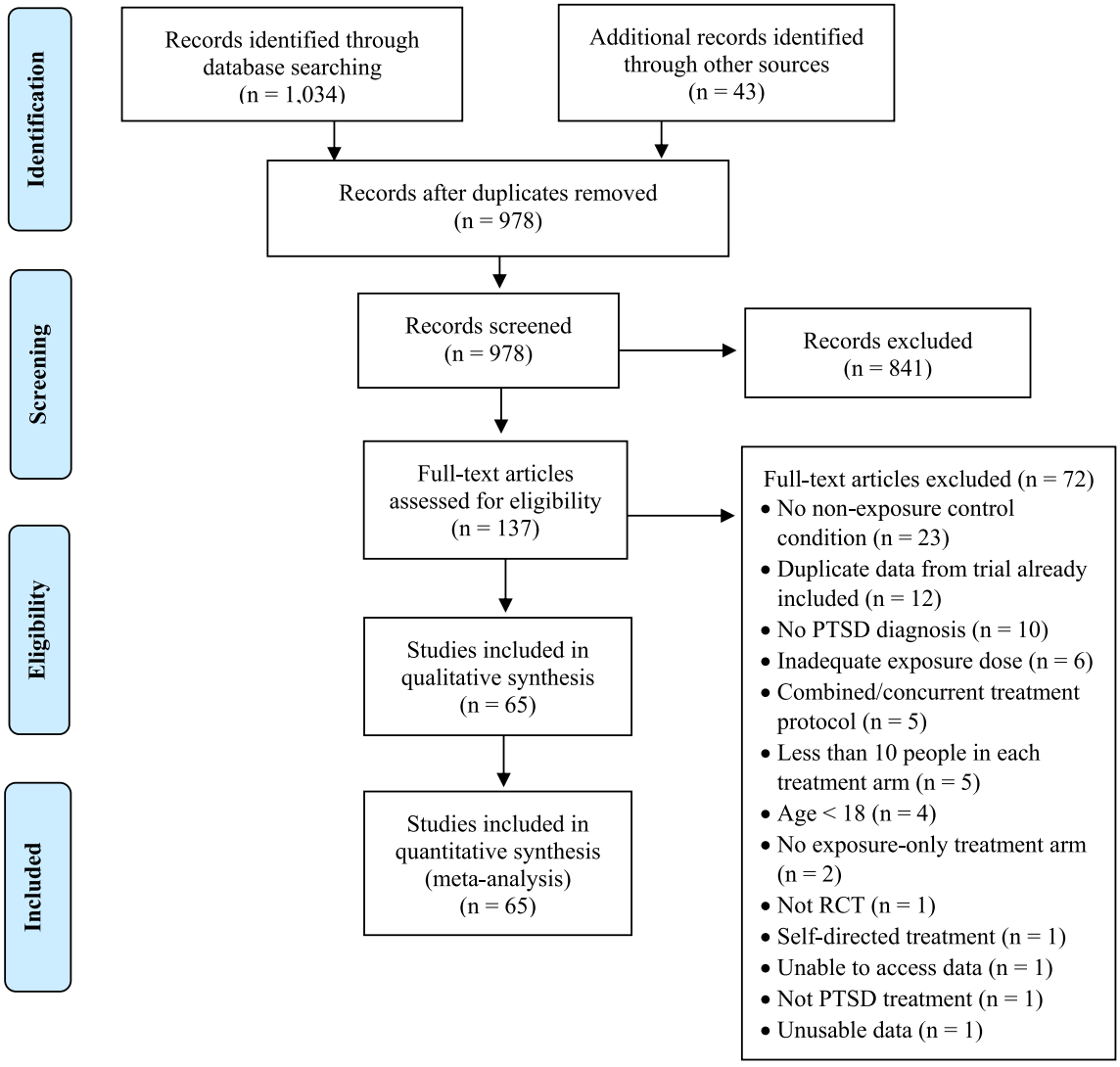

Fig. 1. PRISMA Flow Diagram of Articles Selected for Meta-Analysis.

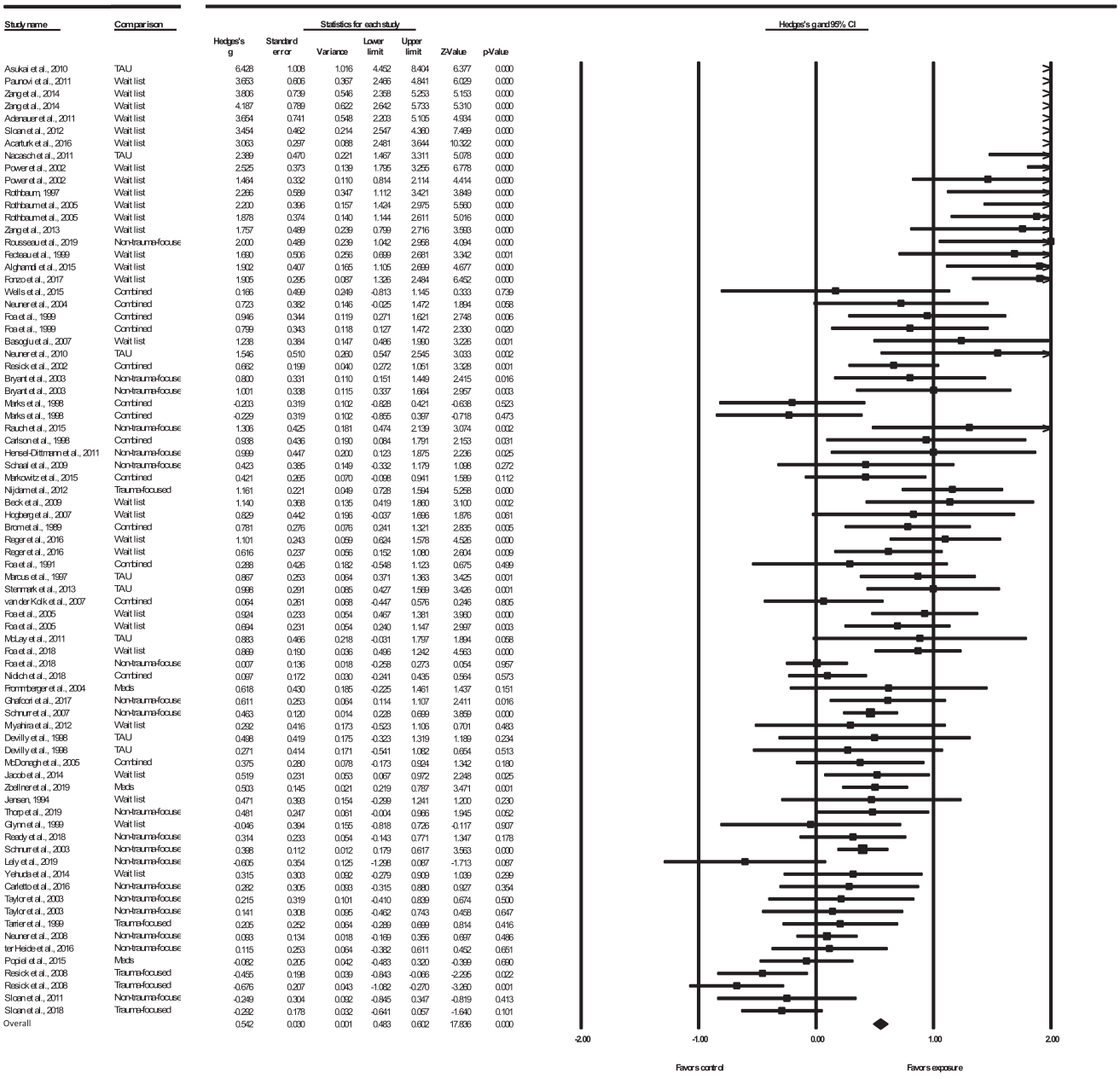

Fig. 2. Forest plot of mean effect sizes for exposure therapy at post-treatment.

Table 1
Efficacy of exposure therapy vs. various control conditions on PTSD measures at posttreatment.

Comparison	*k*	*g*	95% CI	FSN
Wait list	35	1.524	1.235–1.814	5172
TAU	10	1.248	0.684–1.813	211
Non-trauma-focused	35	0.301	0.16–0.436	307
Medications	4	0.145	−0.312-0.602	–
Trauma-focused	8	−0.154	−0.56-0.257	–

Note. CI = confidence interval, FSN = fail-safe N, TAU = Treatment as Usual.

$p < 0.001$.

We then examined the effects of various exposure therapy packages. Note that because some studies included more than one exposure group, the total *k* for subgroup comparisons is more than 77 (again, we used all comparisons, assuming independence). Heterogeneity across treatment packages was significant, $Q(4) = 10.048$, $p = 0.040$. Pairwise comparisons indicated that both NET ($k = 13$, $g = 1.297$, CI = 0.729–1.865) and EMDR ($k = 17$, $g = 1.060$, CI = 0.589–1.531) had larger effects than the "other" exposure therapies ($k = 29$, $g = 0.469$, CI = 0.221–0.717), $Q(1) = 6.857$, $p = 0.009$ and $Q(1) = 4.696$, $p = 0.030$, respectively. There were no other significant differences between exposure treatments (*ps* = 0.577–0.900). WET had the highest effect size ($k = 2$, $g = 1.557$, CI = −2.114-5.227), but this was based on only two studies and the confidence interval included 0. Effects were medium for PE ($k = 31$, $g = 0.714$, CI = 0.476–0.951) and other exposure therapies ($k = 29$, $g = 0.469$, CI = 0.221–0.717).

Table 2 shows the effects of exposure therapy vs. various control conditions at follow-up on PTSD measures. Exposure was superior to both wait list and TAU, with large effect size estimates. The effect of exposure was medium compared to medications and non-trauma-focused therapy, and nonexistent compared to trauma-focused therapy. Heterogeneity across control conditions was significant, $Q(4) =$

Table 2
Efficacy of exposure therapy vs. various control conditions on PTSD measures at follow-up.

Comparison	*k*	*g*	95% CI	FSN
TAU	2	1.803	0.851–0.725	–
Wait list	5	1.623	0.786–2.461	205
Medications	2	0.554	0.131–0.978	–
Non-trauma-focused	23	0.409	0.234–0.583	288
Trauma-focused	8	−0.211	−0.406- -0.015	6

Note. CI = confidence interval, FSN = fail-safe N, TAU = Treatment as Usual.

36.688, $p < 0.001$.

We then examined the effects of various exposure therapy packages at follow-up. Heterogeneity across treatment packages was not significant, $Q(4) = 3.561$, $p = 0.469$, indicating no significant differences across exposure treatments at follow-up. At follow-up, there were large effects for EMDR ($k = 5$, $g = 0.954$, CI = −0.099-2.008) and WET ($k = 2$, $g = 0.855$, CI = −1.831-3.540), although the confidence intervals both included 0. NET ($k = 6$, $g = 0.648$, CI = 0.231–1.065) and PE ($k = 13$, $g = 0.521$, CI = 0.209–0.833) were associated with medium effects at follow-up, and other exposure therapies ($k = 14$, $g = 0.277$, CI = −0.004-0.551) was associated with a small effect.

2.3. Moderator outcomes

Continuous moderators are shown in Table 3. Study year, percentage of women, and the percentage of participants diagnosed with major depression were not significant predictors of outcome. The number of sessions in the protocol was significantly associated with effect size; longer treatments were associated with smaller effects. In the subset of studies conducted in countries where the majority of the population identifies racially as White (k = 54), the percentage of participants identifying as a racial minority was also not significant, but there was a trend towards more racially diverse samples showing better outcomes. The percent of participants identifying as Hispanic/Latinx was not significantly associated with outcomes. The percent of participants on psychiatric medications was significant, with greater medication use associated with attenuated outcomes. Mean age was significant, with worse outcomes for older participants. The percentage of participants diagnosed with a substance use disorder was significant, with a greater proportion of participants with a substance use disorder associated with worse outcomes.

Categorical moderators are shown in Table 4. Sample type was associated with significant heterogeneity, $Q(3) = 15.688$, $p = 0.001$. As shown in the Table, civilian and refugee samples were associated with large effects, whereas active duty and Veteran samples were associated with medium effects. Type of trauma was significant, $Q(5) = 17.827$, $p = 0.003$; natural disasters and transportation-related trauma were associated with higher effect sizes than were the other trauma types.

Table 3
Meta-regression of continuous moderator variables predicting PTSD outcomes from exposure therapy at posttreatment.

Moderator	*Z*	*p*
Study year	−0.871	0.384
Number of sessions in protocol	−2.793	0.005
Mean age	−2.282	0.022
% Women	1.178	0.235
% Racial minority[a]	1.885	0.059
% Hispanic/Latinx[a]	0.764	0.445
% Diagnosed with major depression	−1.056	0.291
% Diagnosed with a substance use disorder	−2.434	0.015
% On medications		
	−4.459	< 0.001

[a] Examined only among subset of studies conducted in countries where the majority of the population identifies racially as White (k = 68).

Table 4
Categorical moderators of PTSD outcomes from exposure therapy at posttreatment.

Moderator	*k*	*g*	95% CI	FSN
Sample type				
Refugee	8	1.288	0.458–2.119	173
Civilian	50	0.944	0.695–1.193	4005
Active duty	4	0.630	0.098–1.161	32
Veteran	15	0.498	0.294–0.702	192
Trauma type				
Natural disaster	4	2.615	1.259–3.972	74
Transportation	5	1.374	0.167–2.580	57
Combat	17	0.758	0.426–1.091	499
Mixed	38	0.767	0.531–1.002	1917
Sexual assault	12	0.764	0.275–1.253	168
Medical	1	0.282	−0.315-0.880	–
Exposure type				
In vivo	1	1.238	0.486–1.990	–
Imaginal	49	0.929	0.672–1.186	2773
Combination	42	0.629	0.424–0.835	1476
Treatment Modality				
Individual	74	0.880	0.694–1.066	8058
Group	3	0.501	0.150–0.851	14

Note. CI = confidence interval, FSN = fail-safe N.

Type of exposure was significant, $Q(2) = 10.181$, $p = 0.006$. As shown in Table 4, in vivo and imaginal exposure were associated with large effects, whereas combined exposure was associated with a medium effect. Finally, treatment modality was not significant, $Q(2) = 3.566$, $p = 0.059$; there was a trend for individual therapy to be associated with a stronger effect than group therapy, which was not robust against the file drawer effect.

2.4. Risk of bias

Risk of bias assessments for the included studies is summarized in Appendix C. Ten studies were coded as 'low risk' of bias; 31 were coded as 'some risk' of bias; 24 were coded as 'high risk' of bias. The median risk of bias score was 2 (range = 0–8) and 13 studies had a total risk of bias score of 5 or greater. High risk of bias was most frequently due to nonadherence to the intervention (i.e., lack of fidelity assessment or a high proportion of participants not completing the full treatment protocol plus failure to use an intention to treat (ITT) analytic approach) or a significant proportion of missing data (i.e., high dropout plus differential dropout across condition and/or reasons suggesting for drop suggesting that attrition may be due to mental health status).

A one-way ANOVA revealed a significant difference in risk of bias scores according to treatment package, $F_{4,66} = 5.391$, $p = 0.001$. LSD follow-up tests indicated that "other" exposure therapies had a higher risk score than did WET, PE and NET ($ps < 0.05$; see Table 5). EMDR had a higher risk score than did NET. Meta-regression indicated that there was a significant relationship between risk of bias score and effect size, $Z = 3.245$, $p + 0.001$, with studies with a higher risk of bias score reporting larger effects.

We re-ran the analyses, selecting only samples with a RoB score of 4 or lower. As shown in Table 6, wait list and TAU comparisons were

Table 5
Risk of Bias Scores by Treatment Package.

Exposure-Based Therapy	k	Mean	Std. Deviation
Other	24	3.92	2.302
EMDR	15	2.80	2.513
PE	20	1.90	1.586
NET	10	1.00	0.816
WET	2	0.50	0.707

Note. CI = confidence interval, FSN = fail-safe N, EMDR = Eye Movement Desensitization and Reprocessing, NET = Narrative Exposure Therapy, PE = Prolonged Exposure, WET = Written Exposure Therapy.

Table 6
Efficacy of exposure therapy vs. various control conditions on PTSD measures at posttreatment, selecting samples with a risk of bias score of 4 or lower.

Comparison	*k*	*g*	95% CI	FSN
TAU	6	1.841	0.862–2.819	120
Wait list	21	1.746	1.342–2.150	2236
Non-trauma-focused	21	0.253	0.099–0.407	117
Medications	3	0.050	−0.478-0.578	0
Trauma-focused	5	−0.092	−0.664-0.481	0

Note. CI = confidence interval, FSN = fail-safe N, TAU = Treatment as Usual.

associated with large effects, whereas the effect compared to non-trauma-focused therapy was small. The effects compared to medications and trauma-focused therapy were negligible. Heterogeneity was significant, $Q(4) = 97.258$, $p < 0.001$.

We then examined effects for the various exposure treatment packages, again selecting those samples with a RoB score of 4 or lower. Heterogeneity was not significant, $Q(4) = 8.562$, $p = 0.073$.

3. Discussion

The results of this meta-analysis demonstrate the efficacy of exposure therapy for reducing PTSD symptoms among adults diagnosed with PTSD. As hypothesized, effect sizes varied as a function of the comparison condition. Exposure therapy was superior to waitlist and TAU conditions with large effects, showed a small effect compared to non-trauma-focused therapy, and was not different from trauma-focused therapy or medication (SSRIs) at posttreatment. These findings are consistent with the pattern observed in prior meta-analyses, which have also found strong effects for exposure compared to waitlist and TAU, and few differences among various trauma-focused therapies (Bisson, 2013; Watts et al., 2013).

The pattern of effect sizes at follow-up was very similar to post-treatment with one exception. In contrast to posttreatment, where there was a negligible effect for exposure therapy relative to medication, by follow-up, there was a medium effect favoring exposure. This suggests that the therapeutic gains achieved during exposure therapy are better maintained over time than for medication. This is consistent with a meta-analysis showing that trauma-focused therapies resulted in greater sustained benefit over time than medications for PTSD (Lee et al., 2016). Otherwise, follow-up findings were consistent with those of Ehring et al. (2014) which showed stable effects at follow-up and suggests some symptom worsening at follow-up.

Effect sizes for individual exposure-based therapy types were medium to large, which is generally consistent with prior meta-analyses (e.g., EMDR: Chen et al., 2014; PE: Powers et al., 2010; NET: Wei & Chen, 2021). This highlights that there are many available exposure-based therapies that are effective in reducing PTSD symptom severity. NET and EMDR had higher effect sizes than other exposure therapies, suggesting that they may be relatively more efficacious. However, it is important to note that effect sizes across the individual therapies cannot be directly compared because effect sizes are impacted by many factors (e.g., sample characteristics, assessment type, control condition) that vary across each set of studies. Only direct comparisons can yield information about the relative effectiveness of exposure-based therapies. To date, direct comparisons have not found EMDR superior to other exposure therapies (Lee, Gavriel, Drummond, Richards, & Greenwald, 2002; Nijdam, Gersons, Reitsma, de Jongh, & Olff, 2012; Rothbaum, Astin, & Marsteller, 2005; Taylor et al., 2003; van den Berg et al., 2015). No studies to our knowledge have compared NET with another exposure therapy. Effect sizes for exposure therapies at follow-up were the same as at post-treatment, except for NET, which had a large effect at post-treatment and a medium effect at follow-up.

Most of the included studies had methodological limitations that introduced some risk of bias ($k = 31$) and a significant minority of studies were rated as high risk of bias ($k = 24$), consistent with previous meta-analyses (e.g., Cusack et al., 2016). Risk of bias was highest for other exposure therapies and EMDR, then PE, NET, and WET. When we excluded 13 studies with a risk of bias rating of 5 or higher, we found the same pattern of effect sizes across comparators, namely large effects compared to TAU and waitlist, a small effect compared to non-trauma-focused treatments, and a negligible effect compared to medication and trauma-focused treatment. In this subset of studies, the pattern of effect sizes for individual exposure-based therapies was also similar to that of the full sample, except that PE was associated with a large, rather than a medium effect.

We identified several variables that moderated the impact of exposure therapy on PTSD. Studies of refugee and civilian samples showed larger effects that those focusing on veterans or active duty military personnel. This is consistent with findings of prior meta-analyses (Bradley, Greene, Russ, Dutra, & Westen, 2005; Straud, Siev, Messer, & Zalta, 2019; Watts et al., 2013) showing smaller effects for veteran studies compared to civilian studies. The medium-large effect size for combat trauma suggests that trauma type alone is unlikely to account for the smaller effect size of exposure-based therapy in military vs. civilian samples. It has been hypothesized that this pattern is due to the nature of trauma exposure across military populations, with deployment-related trauma being more often extended, repeated, and intense as well as including morally injurious experiences more often relative to civilian trauma (Steenkamp, Litz, Hoge, & Marmar, 2015). In addition, military samples are also more likely than civilians to report traumatic events during childhood (Blosnich, Dichter, Cerulli, Batten, & Bossarte, 2014) which could complicate their clinical presentation and limit recovery. One meta-analysis found that the complexity of the trauma moderated the effect size of trauma-focused therapy, with smaller effects for trauma-focused treatment in both veteran and refugee samples (Gerger, Munder, & Barth, 2014). In contrast, we found the largest effects for exposure therapy in refugee samples.

Effect sizes also differed across trauma types, with large effects for natural disasters and transportation-related trauma, medium effects for combat, mixed-trauma, and sexual assault, and a small effect for medical-related trauma. Other research has found that certain traumatic events are differentially linked to PTSD severity, chronicity, and comorbidities (Smith, Summers, Dillon, & Cougle, 2016), which may in turn impact therapy outcomes. Our finding is broadly consistent with data suggesting that specific PTSD treatments have less benefit relative to non-specific treatments for PTSD related to more "complex" trauma (i.e., childhood, multiple, or intentional trauma) as compared to PTSD related to noncomplex trauma (Gerger et al., 2014). Whether the trauma is interpersonal in nature (Oehlman Forbes, Lee, & Lakeman, 2020) or morally injurious (Griffin et al., 2019) has also been theorized to impact treatment outcomes.

The proportion of the sample diagnosed with substance use disorder was associated with an attenuated effect size. This suggests that exposure therapy may be less effective as a stand-alone treatment for those with PTSD and substance use disorders. Indeed, studies have shown that integrating exposure therapy with substance use disorder treatment is effective in reducing PTSD and substance use (e.g., Back et al., 2019; Norman et al., 2019). However, we excluded studies testing treatments designed specifically to target comorbid conditions. We also found a smaller effect size among studies with a greater proportion of participants taking psychiatric medication. Certain medications, namely benzodiazepines, have been found to interfere with the effects (Guina, Rossetter, DeRhodes, Nahhas, & Welton, 2015) or maintenance (Rosen et al., 2013) of exposure therapy. Use of psychiatric medication may also be an indicator of clinical complexity and/or treatment resistance.

In terms of demographic factors, we found that studies with a greater proportion of older participants were associated with a smaller effect size. It has been hypothesized that chronicity of PTSD and associated functional impairments may account for diminished effects in older populations (Dinnen, Simiola, & Cook, 2015), a pattern that has been

observed across anxiety disorders more broadly (e.g., Gould, Coulson, & Howard, 2012; Wetherell et al., 2013). Among studies conducted in countries where the majority of the population identifies racially as White, we found a negligible effect for the proportion of the sample identifying as ethnic or racially minoritized groups, although there was a trend for studies with greater racial diversity to have larger effects. The null result is consistent with a recent study that found comparable outcomes following PE, sertraline, or their combination among African American and White participants (Kline, Feeny, & Zoellner, 2020). Finally, we found that the proportion of women in the sample did not moderate the effect size for exposure-based therapies, which contrasts with findings from two previous meta-analyses showing larger effects for studies with more women participants (Sloan, Feinstein, Gallagher, Beck, & Keane, 2013; Watts et al., 2013).

Studies testing exposure therapy protocols with a greater number of sessions had a smaller effect size. We coded the total number of sessions (range = 1–30), rather than the number of sessions that focuses on exposure, which was not always reported. Thus, the finding does not necessarily suggest that there are smaller effects when the dose of exposure is greater. Longer protocols often include a similar number of exposure sessions and a greater number of non-exposure sessions as compared to shorter protocols. Longer PTSD protocols may have greater treatment dropout than shorter protocols (Imel, Laska, Jakupcak, & Simpson, 2013) and those who dropout tend to have worse outcomes (Berke et al., 2019). Thus, it may be longer protocols have smaller effects because of higher dropout, however, which we did not examine because treatment dropout is often not reported separately from study (i.e., assessment) dropout. Alternately, it may be that longer protocols are more often used with more complex patient populations and that complexity of presentation accounts for attenuated effects. We also found a larger effect for studies testing in vivo exposure or imaginal exposure alone versus protocols that combined in vivo and imaginal exposure. Combined protocols tended to be longer and tended to include more non-exposure components than protocols using a single exposure type. It may also be that combined treatment protocols tend to be used with more complex patient populations.

3.1. Strengths and limitations

The current meta-analysis has a number of strengths. First, our meta-analysis was conducted in accordance with the PRISMA guidelines (Page et al., 2020) and was pre-registered in PROSPERO. Second, our analysis represents an update and expansion to previous meta-analyses of individual exposure therapies. Notably, the most recent prior meta-analysis of PE (Powers et al., 2010) was published more than 10 years ago and the number of RCTs evaluating PE has increased considerably over the past decade. We expanded on the Powers et al. (2010) meta-analysis by including additional exposure-based therapies (i.e., EMDR, NET, WET) and investigating numerous treatment moderators. We classified therapies as exposure-based if the majority of sessions focused on exposure and as non-exposure control conditions if they did not meet this criterion. Almost all therapies included in this study fell very clearly into one grouping or the other, with the possible exception of brief eclectic therapy ($k = 1$), which was classified as a non-exposure-based control but included exposure in one third of the sessions. Third, we included a follow-up assessment in our meta-analysis in order to assess durability of exposure effects. Fourth, we used a validated tool for evaluating risk of bias of the included studies (Sterne et al., 2019), which covered a wide range of potential sources of bias and examined our primary outcomes of interest both in the full sample of studies and the subset of studies with lower risk of bias scores.

There are a number of potentially important limitations of this work. First, several of the comparison conditions (e.g., TAU, $k = 10$; pharmacotherapy, $k = 4$) had low sample sizes, therefore the findings from these comparisons should be interpreted with caution. Second, as noted above, the methodological quality of the studies included in our meta-analysis was mixed, with few studies being rated as "low" risk of bias. This may in part be due to evolving standards in the field for analyzing and reporting results of clinical trials. For example, older studies typically did not employ ITT analyses or used methods for handling missing data (e.g., last-observation-carried-forward) that are problematic, whereas ITT analyses and multilevel modeling approaches to missing data have become more widely used in recent studies. Nevertheless, including vs. excluding studies with higher risk of bias did affect the effect size estimates somewhat, suggesting that the methodological rigor of the included studies is an important consideration for treatment outcome meta-analyses. It may be helpful for future clinical trial researchers to consult the Cochrane Risk of Bias tool when planning and conceptualizing the study and reporting their findings in order to improve methodological quality and reporting clarity. Third, by focusing on exposure therapy, we excluded other effective trauma-focused therapies such as cognitive processing therapy (e.g., Resick, Nishith, Weaver, Astin, & Feuer, 2002) and cognitive therapy (e.g., Ehlers, Clark, Hackmann, McManus, & Fennell, 2005), which have been shown to be equally effective to exposure in prior meta-analyses (Lewis et al., 2020; Powers et al., 2010). Fourth, by requiring a diagnosis of PTSD as part of our inclusion criteria, we excluded studies that enrolled participants with subclinical PTSD, so the findings may not generalize to this population. Fifth, moderators were examined at the study level, not the participant level. While this is standard for meta-analyses, it is important to note that findings about study-level moderators cannot be used to draw conclusions about individual participant-level moderators. Last, our examination of demographic moderators was limited by what was reported in the studies. For example, not all studies reported the race and ethnicity of participants, which may have impacted the results of our moderator analyses. In addition, we had intended to examine the proportion of the sample with gender identities other than (presumably cisgender) men and women, but this was not reported in any of the included studies. Establishing and adhering to guidelines in the field for reporting important diversity characteristics, including gender, ethnicity, race, and disability status (American Psychiatric Association (APA), 2021) in research will facilitate moderator analyses and may inform the development of culturally adapted treatments for PTSD.

4. Conclusion

Despite these limitations, the current findings provide evidence that exposure therapy is effective for treating adult PTSD. Our findings are consistent with major clinical practice guidelines that recommend trauma-focused treatments as first-line interventions for PTSD (American Psychological Association (APA), 2017; International Society for Traumatic Stress Studies (ISTSS), 2018; National Institute for Health and Care Excellence (NICE), 2018; US Department of Veterans Affairs (VA/DoD), 2017). All exposure-based therapies examined were effective in reducing PTSD symptoms and these effects were relatively well maintained over ~6 months follow-up. Further increases in treatment effects may require a better understanding of the mechanisms underlying exposure that are responsible for therapeutic change, which may differ across various exposure-based therapies. Effect sizes for each of the individual exposure-based therapies examined were all large, highlighting that exposure is efficacious across several treatment protocols. We recommend that treatment selection between exposure-based therapies be guided by accessibility and patient preference (Watts et al., 2013) when possible, rather than differences in the reported (large) effect sizes. Exposure therapy was not equally effective across patient demographic and clinical characteristics or delivery modalities. Further research on moderators of exposure-based therapy is needed in order to develop treatment selection models that can increase the clinical impact of treatments by matching them with patients who are most likely to benefit.

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Declaration of Competing Interest

There are no competing interests from any co-authors related to the preparation of this manuscript.

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