

# Trauma-focused psychotherapies for post-traumatic stress disorder: A systematic review and network meta-analysis

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## Funding information

Preparation of this paper was supported by a National Health and Medical Research Council (NHMRC) Early Career Fellowship (GNT1122203) awarded to David Berle. The NHMRC had no role in the design of the study, data collection, data analysis, interpretation of data, or in the writing or revision of the manuscript.

## Abstract

**Introduction:** Meta-analytic reviews suggest similar outcomes across trauma-focused psychotherapies for adults with post-traumatic stress disorder (PTSD). However, this conclusion may be premature due to suboptimal statistical-review methodologies. Network meta-analysis (NMA) allows a detailed rank-ordering of the efficacy of established psychotherapy interventions derived from indirect evidence as well as results from direct head-to-head comparisons.

**Objective:** We sought to determine the efficacy and attrition rates of psychotherapy interventions for PTSD by applying NMA.

**Methods:** We searched EMBASE, PsychINFO, PTSDpubs and PubMed for randomised controlled trials that compared psychotherapies either head-to-head or against controls for adults with PTSD. A frequentist NMA was used to compare direct and indirect effects to determine the efficacy and attrition rates of psychotherapy interventions.

**Results:** Of the 5649 papers identified, 82 trials comprising of 5838 patients were included. The network comprised 17 psychotherapies and four control conditions. Network estimates indicated superior efficacy of meta-cognitive therapy and cognitive processing therapy over other psychotherapies (ESs between = 0.26 and 2.32). Written exposure therapy and narrative exposure therapy were associated with lower risk of drop out when considered alongside other psychotherapies. Confidence in the network meta-analytic estimates was considered moderate for both outcomes.

**Conclusions:** In broad terms, therapeutic commensurability was evident. Nevertheless, with additional studies and larger sample sizes, meta-cognitive and written exposure therapies could indeed differentiate themselves from other approaches as having favourable efficacy and acceptability respectively. These findings may inform clinical decision-making, as well as guide future research for PTSD.

## KEYWORDS

acceptability, efficacy, network meta-analysis, psychotherapy, PTSD, review

## 1 | INTRODUCTION

Post-traumatic stress disorder (PTSD) is characterised by exposure to trauma and symptom clusters including re-experiencing of the traumatic event, avoidance of stimuli associated with the trauma, negative alterations in cognition and mood, and hyperarousal.<sup>1</sup> It is common (8.3% lifetime prevalence<sup>2</sup>) and associated with multiple negative outcomes, including functional impairment,<sup>3</sup> suicidality,<sup>4</sup> co-occurring psychological disorders<sup>5,6</sup> and physical morbidity.<sup>7,8</sup>

There is an apparent consensus within the PTSD field that trauma-focused psychotherapies are, for the most part, comparable so far as efficacy and adherence are concerned.<sup>9-11</sup> In some respects, this is surprising. Even though all trauma-focused psychotherapies are thought to involve a meaningful processing of the trauma memory in some respect, the proposed underlying mechanisms of trauma-focussed approaches, and indeed, the specific approaches of each respective intervention nonetheless vary. Comparable efficacy and adherence of trauma-focused psychotherapies have been supported by meta-analytic reviews that consistently suggest that cognitive behaviour therapy (CBT), exposure therapies and eye movement desensitisation and reprocessing (EMDR) are similarly effective in treating PTSD.<sup>9,11-14</sup> A meta-analysis by Ourgin<sup>14</sup> found no difference between cognitive therapy (CT) and exposure therapy; however, findings were analysed from only five studies. A Cochrane review<sup>15</sup> reported no statistically significant differences between trauma focussed-cognitive behaviour therapy (TF-CBT), EMDR and Stress Management post-treatment. Further, the authors reported that TF-CBT, EMDR and CBT were more effective than other therapies (ie non-directive, supportive, person-centred counselling, hypnotherapy and psychodynamic therapy). A comprehensive meta-analysis by Watts et al.<sup>11</sup> reported effect sizes indicating superior efficacy for cognitive processing therapy (CPT;  $g = 1.69$ ), exposure and CT ( $g = 1.52$ ) and prolonged exposure (PE;  $g = 1.38$ ).

The above reviews have informed the development of treatment guidelines and most guidelines recommend TF-CBTs. These are considered to include CT, CPT and PE therapy, as well as EMDR.<sup>16-19</sup>

However, the evidence base has been built upon studies which have rarely included more than two treatment arms and meta-analytic methodologies have not, until recently, been able to incorporate indirect evidence across studies which compare different combinations of approaches. For instance, the above-mentioned reviews of Bisson et al.<sup>15</sup> and Watts et al.<sup>11</sup> relied on evidence derived only from a series of separate head-to-head comparisons, limiting their findings. Therefore, the assumption of equality of outcomes across trauma-focused psychotherapies may have

### Summations

- Our network meta-analysis did not identify highly divergent levels of efficacy and acceptability among psychotherapies.
- Meta-cognitive therapy and cognitive processing therapy were nonetheless the most efficacious of the included psychotherapies.
- Narrative exposure therapy and written exposure therapy had relatively high rates of treatment completion when considered alongside other psychotherapies.

### Limitations

- We included psychotherapy approaches which have been subject to few trials and which await replication efforts from independent investigators.
- Our review was limited to individual face-to-face psychotherapies.

been prematurely conferred. In contrast, a full account of the evidence base would additionally consider indirect evidence, whereby the superiority of a given intervention can be ascertained even in instances where direct head-to-head comparison studies have not been conducted.

Network meta-analysis (NMA) holds particular promise when considering the relative efficacy of a broad range of psychotherapies. The approach provides a statistical methodology for evidence synthesis that can integrate both direct and indirect evidence from multiple treatment comparisons to estimate the inter-relationships across treatments.<sup>20</sup> The NMA approach may be particularly useful when synthesising a clinical literature characterised by a broad array of different therapeutic modalities and 'brands' which have not always been directly compared—such as PTSD.

To date, there have been three NMAs exploring psychotherapeutic efficacies for adults diagnosed with PTSD. However, a significant limitation of each of these has been the lumping of multiple separate psychotherapies into TF-CBT or 'psychotherapy' clusters, thus calling for a NMA whereby the relative efficacy and adherence of individual psychotherapies can be ascertained. For instance, Gerger et al.<sup>10</sup> synthesised data from 66 randomised controlled trials (RCTs) and reported no superior interventions, with similar efficacy reported for CBT, CT, EMDR and exposure therapy. However, this NMA did not define a distinction between CBT, exposure therapies, or CT and included these all within a TF-CBT framework for the final NMA model, reducing the granularity and clinical utility of

these results. Finally, publications were restricted to 1980 until 2010, such that recent RCTs were not included.

The second NMA by Merz, Schwarzer and Gerger<sup>21</sup> examined the efficacy and acceptability of psychotherapies, pharmacotherapies or combined treatment approaches, at post-treatment and long-term follow-up. In this context, acceptability referred to the proportion of participants completing treatment rather than dropping out due to adverse effects of the intervention. Their results indicated a superiority of psychotherapies over pharmacotherapy at long-term follow-up, and no differences in acceptability across comparisons. This study utilised data from only 12 RCTs, with long-term follow-up not reported for the full sample (six studies only). Most importantly, however, the findings do not allow a comparison of the relative efficacy of each individual psychotherapy, as each approach was analysed under the broad umbrella of 'psychotherapy'. Thus, CBT, PE, EMDR and Seeking Safety (a CBT- and psychodynamic-derived group therapy for PTSD and co-morbid substance use that proscribes exploration of trauma memories<sup>22</sup>) were analysed as a unitary intervention category, precluding an assessment of psychotherapeutic (non)similarity.

A third NMA was recently reported by Mavranouzouli and colleagues.<sup>23</sup> These authors delineated EMDR from TF-CBT, but did not distinguish between individual TF-CBTs, such as CPT and exposure-based interventions. Also, Mavranouzouli et al.<sup>23</sup> did not consider acceptability in their analyses. Acceptability would appear to be a vital outcome to understand with regard to the non-distinctiveness of TF-CBTs, given that the common concern that exposure-based approaches may be associated with high rates of treatment dropout and discontinuation.

The large number of meta-analytic reviews has missed an opportunity to truly integrate the sizable body of PTSD psychotherapeutic literature and to examine whether some therapies are indeed more efficacious and acceptable than others. The NMA approach holds great promise for identifying the most efficacious and acceptable interventions for PTSD; however, the application of NMA has likewise, until now, overlooked the opportunity to identify whether some TF-CBTs are more efficacious and acceptable than others. Therefore, in this study, the aim was to conduct a comprehensive systematic review and NMA to inform clinical practice by comparing psychotherapies to evaluate their efficacy on PTSD symptom reduction, as well as their acceptability defined as all-cause discontinuation.<sup>24</sup>

## 2 | METHOD

The review was registered with the International prospective register of systematic reviews (PROSPERO

CRD42019119814), and we report the results consistent with the PRISMA extensions statement for NMA.<sup>25</sup>

### 2.1 | Search strategy and selection criteria

A comprehensive and systematic literature search was conducted to determine studies for inclusion for the NMA. The databases of EMBASE, PsychINFO, PTSDPubs and PubMed were searched from their inception to 21 January 2020. Search terms included MeSH terms as well as search terms such as "post-traumatic stress disorder" AND "psychotherapy" AND "randomised controlled trial". See Supplementary Material S1 for specific search term strategies. The principal investigator (BJ) and second author (AL) independently screened all titles and abstracts of studies identified by the electronic search. The full texts of any study deemed potentially eligible ( $n = 220$ ) were then also independently screened by investigators BJ and AL, and disagreement was resolved by discussion. See Supplementary Material S2 for the excluded trials.

We included RCTs comparing bona-fide psychotherapies to control (ie waitlist), or another psychotherapy, for the treatment of adults ( $\geq 18$  years old and of both sexes), with a primary diagnosis of PTSD according to the standard operationalised diagnostic criteria in the Diagnostic and Statistical Manual of Mental Disorders (DSM-III-R<sup>26</sup>; DSM-IV-TR<sup>27</sup>; DSM-IV<sup>28</sup>; and DSM-5<sup>29</sup>) and the International Classification of Diseases and related health problems (ICD-9<sup>30</sup>; ICD-10<sup>31</sup>). Studies derived from DSM-III<sup>1</sup> criteria were not included due to significant changes to the PTSD diagnostic criteria from DSM-III<sup>1</sup> to DSM-III-R,<sup>26</sup> as well as publication date, which may have violated the transitivity assumption. Two studies were excluded for this, and other reasons (see Supplementary Material S2 for further details). Papers were required to be in English and published in a peer-reviewed journal. In contrast to the stated PROSPERO registration (CRD42019119814), we did not require adherence of primary studies to the CONSORT statement as we were not always able to reliably determine whether this was the case. So far as the description of therapies is concerned, at least two of the following had to be fulfilled for study inclusion: (a) a citation to an established school or approach to psychotherapy, (b) a description of the therapy that contained a reference to a psychological process (eg operant conditioning), (c) a reference to a treatment manual that was used to guide the delivery of the treatment and/or (d) the identification of active ingredients. See Supplementary Material S1 for definition and description of bona-fide

psychotherapies. We considered only individual, face-to-face psychotherapies (eg excluding group or conjoint interventions) to improve methodological rigour and to help inform practitioners working with individuals in routine treatment settings, where trauma-focused therapies involving the processing of idiosyncratic trauma memories are typically administered in an individual therapy context. Additionally, we only included studies which reported a direct comparison between at least two individual psychotherapy modalities, or between a psychotherapy and control condition, and we thus excluded studies of sequential treatments if direct comparison data between individual interventions could not be extracted. A variety of active and waitlist conditions have been utilised in the literature. The control conditions were combined into four separate nodes (waitlist, active supportive therapy, treatment-as-usual and psychoeducation). Supplementary Material S1 highlights the key features of each unique control condition which informed the categorisation process.

## 2.2 | Outcomes

The primary outcome was efficacy, represented by PTSD symptomatic change from baseline to post-treatment on a validated scale for PTSD. Long-term follow-up was outside the scope of the project. When PTSD symptoms were measured with more than one validated rating scale, a pre-defined hierarchy based on psychometric properties and consistency of use across included trials was utilised (see Supplementary Material S1). More frequently used scales and self-rated PTSD symptoms were preferred. Self-rated scales were favoured over interview-based measures given that proportionately few studies administered interview-based measures at post-treatment and because self-report measures do not have the addition of interviewer-based variance beyond respondent-based variance alone. Results from intention-to-treat (ITT) analyses were preferred over results from completer analyses. Between-group post-treatment standardised mean differences (SMD) with 95% confidence intervals (95% CIs) were calculated, with an effect of 0.24 to imply clinical importance.<sup>32</sup>

A secondary outcome was acceptability. Consistent with previous network meta-analytic reviews,<sup>21,24,33</sup> acceptability refers to treatment discontinuation calculated by the proportion of patients who withdrew for any reason. Favourable acceptability reflects the completion of therapy or absence of discontinuation, and encompasses the notions of treatment adherence and non-attrition. Odds ratios (OR) with 95% CIs were used as a measure of the association between the psychotherapeutic approach and acceptability.

## 2.3 | Data extraction

Data were extracted from the included studies by BJ using a structured form. Sample sizes, baseline and end of treatment means, and standard deviations (*SDs*) were extracted for effect size calculation for each treatment group. Where CIs were reported, conversions to *SDs* were calculated according to formulas provided by Higgins and Green.<sup>34</sup> Authors of 22 studies were contacted due to insufficient data reported in the primary paper, with authors of four studies providing the relevant information.<sup>35-38</sup> In addition to the data required for effect size calculation, other characteristics of trials were also extracted to identify potential effect modifiers, these being index trauma type (eg interpersonal violence), year of publication and diagnostic criteria.

## 2.4 | Risk of Bias

The Cochrane Risk of Bias assessment tool was used to assess the quality of included studies.<sup>39</sup> The assessment of the risk of bias included a brief training period whereby BJ and a co-rater reached consensus with a random sample of selected studies ( $n = 10$ ), with the remainder being assessed by BJ. In addition, the Confidence in Network Meta-Analysis (CINeMA) platform was used to evaluate the quality of studies across the network.<sup>40,41</sup>

## 2.5 | Review of the network geometry

Published RCTs including patients with PTSD were analysed. In the network, each psychotherapy is indicated by a node, and comparisons between psychotherapies are shown by the links between the nodes.

## 2.6 | Data analysis

For the primary analyses, SMD were estimated for continuous efficacy outcomes and ORs for dichotomous attrition outcomes using pairwise comparisons and NMA. The study effect sizes were then synthesised using a random-effects NMA model. Frequentist network meta-analyses were conducted using CINeMA, which integrates the R *netmeta* package.<sup>40</sup> In the NMA, the heterogeneity variance parameter was assumed to be the same for all treatment comparisons. Heterogeneity was considered low with a value of  $\tau^2 = 0.04$ , moderate as  $\tau^2 = 0.09$  and high heterogeneity as  $\tau^2 = 0.16$ .<sup>42</sup>

Consistency, that is, the agreement between direct and indirect evidence was statistically evaluated using a global

design-by-treatment interaction model,<sup>43</sup> and locally, by separating direct evidence from indirect evidence.<sup>44</sup> The transitivity assumption was further evaluated by comparing the distribution of methodological variables that could act as effect modifiers across treatment comparisons in a pairwise meta-regression. A Knapp-Hartung method of meta-regression was conducted with separate estimates of  $\tau^2$  for each subgroup.<sup>42</sup> Estimates of  $\tau^2$  were calculated using the maximum likelihood method.<sup>42</sup> Waitlist was utilised as the standard comparator due to the condition being the most commonly compared control ( $n$  treatment arms = 57). To rank the treatment, each therapy was plotted for each NMA estimate variable compared to waitlist.<sup>44</sup> To determine whether the network was susceptible to small-study bias, a funnel plot comparing studies with waitlist was produced, with asymmetry assessed with the Egger's regression test.<sup>45</sup>

### 3 | RESULTS

#### 3.1 | Results of the search

Results of the systematic search identified 5649 citations. Independent screening of titles and abstracts yielded high agreement between raters (Cohen's Kappa = .94; 99.32% agreement), resulting in 220 eligible articles retrieved in full-text (see Figure 1 for PRISMA diagram). Screening full-text articles yielded high inter-rater reliability (Cohen's Kappa = .95; 97.73% agreement). Overall, 82 RCTs were included in the analysis, comprising 5775 participants (see Supplementary Material S1 for full reference list). The included studies were conducted between 1991 and 2020, comparing 17 psychotherapies and four control conditions.

#### 3.2 | Description of studies

The ITT outcomes were reported in 66% of the studies. The mean treatment arm size was 34.40 participants (median = 28,  $SD = 28.22$ ). In total, 3543 participants were randomly assigned to an active psychotherapy, with 2295 randomly assigned to a control (eg waitlist, active supportive therapy, TAU or psychoeducation). See Table 1 for characteristics of included studies.

A number of included studies were based upon small sample sizes, and some network nodes were comprised of relatively few studies. We nonetheless included these studies in our review on the basis that they may be informative so far as the potential value of new and emerging therapy modalities are concerned. A more refined 'sensitivity analysis' excluding network nodes comprised of less

than three studies and studies with fewer than 18 participants in either arm is provided in Supplementary Material S2 for the interested reader.

#### 3.3 | Description of network geometry

Figure 2 shows the network of eligible comparisons for PTSD psychotherapies. All therapies, except psychodynamic therapy (PDT) and dialogical exposure therapy (DET), had at least one non-active control comparison. Waitlist was the most compared control condition, being compared to 15 psychotherapies and control conditions. Three psychotherapies (DET, PDT and Skills training in affective and interpersonal regulation followed by exposure [STAIR-PE]) were connected via a single condition comparison. The network was relatively well-connected, with the evidence set comprising 52 of the possible 210 comparisons

Only STAIR-PE was not directly compared with at least one other active therapy in the network. The gold-standard treatments were adequately connected with CBT, CPT, EMDR and PE being directly compared to six, six, seven and 14 conditions, respectively.

#### 3.4 | Treatment efficacy

Network and direct estimates are displayed in Table 2. The  $\tau^2$  estimate of 0.31 suggested high between-study heterogeneity for the NMA.<sup>42</sup> For network estimates, meta-CT (MCT) performed significantly better than CBT, EMDR, NET, PDT, VRET and all control conditions. CPT also performed significantly better than all control comparisons, as well as CBT and VRET. PE performed significantly more favourably than CBT and control conditions, with the exception of Psychoeducation. PDT and STAIR-PE were therapies with no significant comparisons to any other therapy or control condition.

Head-to-head studies were also synthesised separately to identify treatment differences, displayed above the diagonal in Table 2. Direct comparisons indicate significant treatment efficacy compared to waitlist for CBT, CPT, CT, EMDR, MCT, NET, PE, SIT and WET. Further, PE effects were significantly greater than active supportive therapy (ACTST). Finally, PE was also significantly greater than TAU, as was CPT significantly greater than ACTST; however, significant inconsistency between NMA estimate and direct effects were detected between this comparison. The global test of inconsistency based on the random-effects design-by-treatment interaction model was not significant,  $\chi^2(43) = 20.72$ ,  $p = 1.00$ .

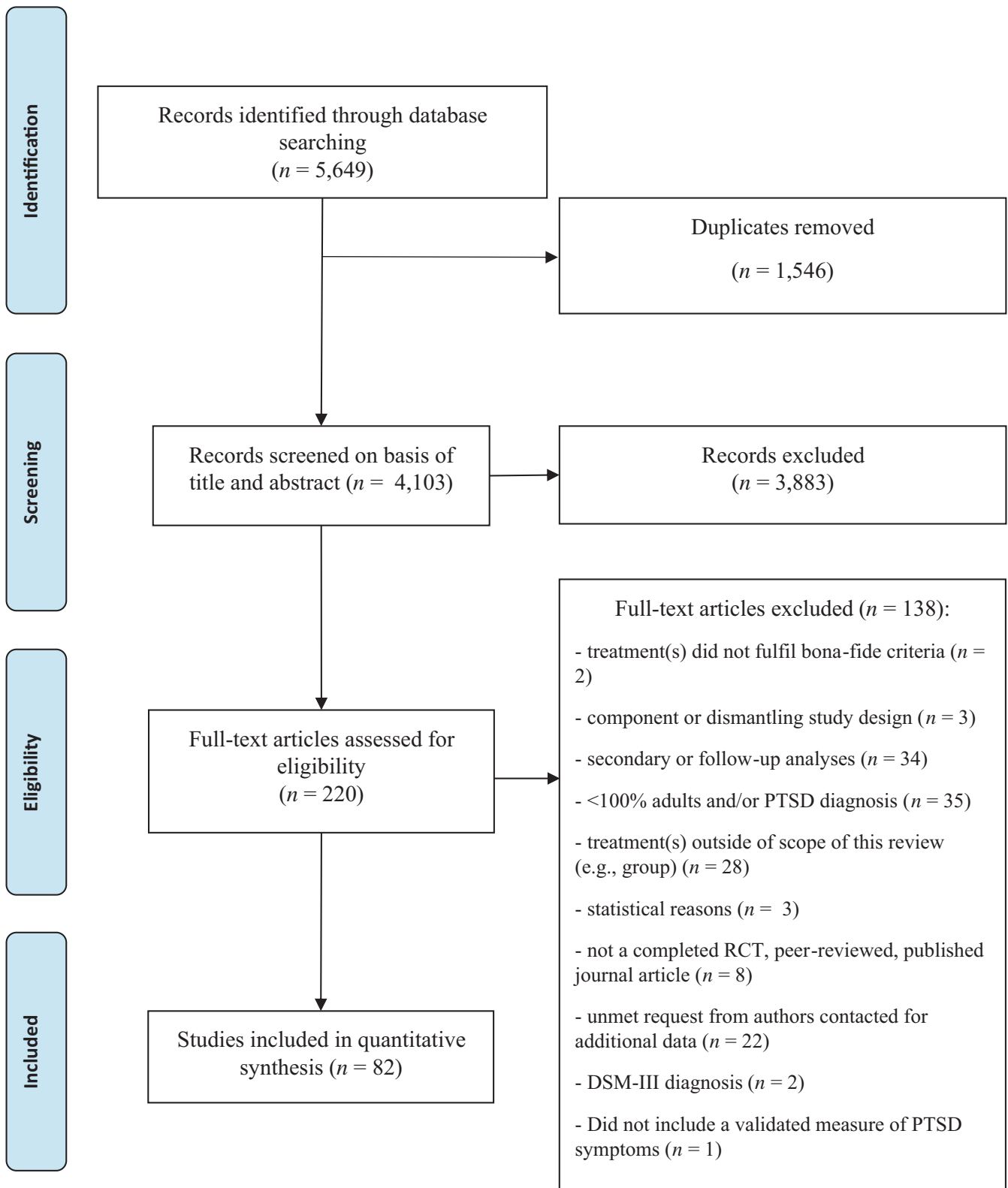


FIGURE 1 PRISMA diagram of study selection flow

A forest plot displaying all network meta-analytic estimates compared to waitlist can be seen in Figure 3. For forest plots comparing active treatments compared to CBT, CPT, EMDR and PE, see Supplementary Material S2.

### 3.5 | Treatment acceptability

Network and direct estimates for treatment acceptability are displayed in Table 3. The  $\tau^2$  estimate of 0.06 suggested

TABLE 1 Characteristics of included studies

| Study reference <sup>a</sup> | Intervention   | No. randomised | Trauma Index  | Diagnostic Criteria | Mean age (SD)                                    | % Female       | Scale   |
|------------------------------|----------------|----------------|---|---------------------|--|----------------|---|
| Acarturk et al. (2016)       | EMDR<br>WL     | 49<br>49       | Refugee   | DSM-IV              | 33.32 (11.09)<br>34.03 (10.00)                   | 79.20<br>68.70 | Impact of Event Scale-Revised (IES-R) <sup>51</sup>                           |
| Aldahadha et al. (2012)      | EMDR<br>WL     | 25<br>26       | MVA   | DSM-IV-TR           | <b>26.41 (range 19–37)</b>                       | 54             | Post-traumatic Stress Scale <sup>52</sup>                                     |
| Asukai et al. (2010)         | PE<br>TAU      | 12<br>12       | Mixed (physical, sexual, accident)  | DSM-IV              | 27.1 (5.4)<br>31.4 (8.8)                         | 91.66<br>83.33 | IES-R <sup>51</sup>   |
| Basoglu et al. (2005)        | CBT<br>WL      | 31<br>28       | Natural disaster  | DSM-IV              | <b>36.3 (11.5)</b>                               | <b>84.70</b>   | Clinician-Administered PTSD Scale (CAPS) <sup>53</sup>                        |
| Bryant et al. (2019)         | CBT<br>WL      | 33<br>34       | Emergency services  | DSV-IV              | 44.7 (10.7)<br>43.4 (7.8)                        | 12<br>29       | CAPS <sup>53</sup>  |
| Buhmann et al. (2016)        | CBT<br>WL      | 70<br>68       | Refugee   | DSM-5               | 46 (8)<br>47 (8)                                 | 42<br>29       | HTQ <sup>54</sup>   |
| Butollo et al. (2016)        | CPT<br>DET     | 74<br>67       | Mixed (interpersonal, accident, other)  | DSM-IV              | 37.99 (12.1)<br>33.67 (10.3)                     | 64.90<br>67.20 | IES-R <sup>51</sup>   |
| Capezzani et al. (2013)      | EMDR<br>CBT    | 11<br>10       | Cancer  | DSM-IV              | 50.82 (7.74)<br>52.70 (8.68)                     | 100<br>80      | IES-R <sup>51</sup>   |
| Carletto et al. (2016)       | EMDR<br>ACTST  | 25<br>25       | Health-related  | DSM-IV              | 39.52 (11.68)<br>40.66 (10.03)                   | 75<br>86.36    | IES-R <sup>51</sup>   |
| Carlson et al. (1998)        | EMDR<br>WL     | 12<br>10       | Military  | DSM-IV              | 45.4 (3.5)<br>52.7 (8.6)                         | 0<br>0         | Impact of Event Scale (IES) <sup>55</sup>                                     |
| Cloitre et al. (2002)        | STAIR-PE<br>WL | 31<br>27       | Physical or sexual  | DSM-IV              | <b>34 (7.22)</b>                                 | 100<br>100     | Modified Post-traumatic Stress Disorder Symptom Scale (MPSS-SR) <sup>56</sup> |
| Coffey et al. (2006)         | PE<br>ACTST    | 8<br>7         | Sexual and Physical   | DSM-IV              | <b>37.6 (8.0)</b>                                | <b>67</b>      | IES-R <sup>51</sup>   |
| Coffey et al. (2016)         | PE<br>PSYED    | 45<br>41       | Mixed   | DSM-IV-TR           | 34.7 (range 31.6–37.8)<br>32.9 (range 29.5–36.2) | 42<br>51       | IES-R <sup>51</sup>   |
| Cottraux et al. (2008)       | CBT<br>ACTST   | 31<br>29       | Mixed (Car accident, physical assault, rape, witness to extreme violence, incest, family violence, witness death, surgery, miscellaneous) | DSM-IV              | 43.18 (10.6)<br>37.20 (9.2)                      | 74.19<br>31.03 | PCL <sup>57</sup>   |
| Devilly & Spence (1998)      | EMDR<br>TAU    | 19<br>16       | Military  | DSM-III-R           | <b>50.1 (6.48)</b>                               | 0<br>0         | Mississippi PTSD Scale <sup>58</sup>  |

(Continues)

TABLE 1 (Continued)

| Study reference <sup>a</sup> | Intervention | No. randomised | Trauma Index  | Diagnostic Criteria | Mean age (SD)             | % Female  | Scale   |
|------------------------------|--------------|----------------|---|---------------------|---------------------------|-----------|---|
| Devilly et al. (1999)        | CBT          | 15             | Mixed (accident, disaster, physical, sexual, war)                             | DSM-IV              | 35.92 (14.53)             | 58.33     | IES <sup>55</sup>                                     |
|                              | EMDR         | 17             |   |                     | 40.18 (10.90)             | 72.73     |   |
| Duffy et al. (2007)          | CT           | 29             | civil conflict in Northern Ireland  | DSM-IV              | 44.1 (11.3)               | 34        | Post-traumatic Diagnostic Scale (PDS) <sup>59</sup>   |
|                              | WL           | 29             |   |                     | 43.7 (12.3)               | 45        |   |
| Dunne et al. (2012)          | CBT          | 13             | MVA   | DSM-IV              | <b>32.54 (7.09)</b>       | <b>50</b> | IES-R <sup>51</sup>                                   |
|                              | WL           | 13             |   |                     |                           |           |   |
| Ehlers et al. (2005)         | CT           | 14             | Mixed (accident, physical, witness death)                                     | DSM-IV              | 35.4 (10.9)               | 57        | PDS <sup>59</sup>                                     |
|                              | WL           | 14             |   |                     | 37.8 (11.2)               | 43        |   |
| Ehlers et al. (2003)         | CT           | 28             | MVA   | DSM-IV              | –                         | –         | PDS <sup>59</sup>                                     |
|                              | PSYED        | 28             |   |                     | –                         | –         |   |
|                              | WL           | 29             |   |                     | –                         | –         |   |
| Ehlers et al. (2014)         | CT           | 31             | Mixed (interpersonal violence, accident/disaster, Death/harm to others/other) | DSM-IV              | 41.5 (11.7)               | 58.10     | PDS <sup>59</sup>                                     |
|                              | ACTST        | 30             |   |                     | 37.8 (9.9)                | 56.70     |   |
|                              | WL           | 30             |   |                     | 36.8 (10.5)               | 60        |   |
| Fecteau & Nicki (1999)       | CBT          | 13             | MVA   | DSM-IV              | <b>41.3 (range 25–63)</b> | <b>70</b> | IES <sup>55</sup>                                     |
|                              | WL           | 11             |   |                     |                           |           |   |
| Feske (2008)                 | PE           | 9              | Sexual and Physical   | DSM-IV              | <b>43.1 (range 29–55)</b> | 100       | PTSD Diagnostic Scale–Interview (PDS-I) <sup>60</sup> |
|                              | TAU          | 12             |   |                     |                           | 100       |   |
| Foa et al. (1999)            | PE           | 25             | Sexual and Physical   | DSM-III-R           | <b>34.9 (10.6)</b>        | 100       | PSS-I <sup>61</sup>                                   |
|                              | SIT          | 26             |   |                     |                           | 100       |   |
|                              | PE-SIT       | 30             |   |                     |                           | 100       |   |
|                              | WL           | 15             |   |                     |                           | 100       |   |
| Foa et al. (2005)            | PE           | 79             | Sexual  | DSM-IV              | <b>31.3 (9.8)</b>         | 100       | PSS-I <sup>61</sup>                                   |
|                              | WL           | 26             |   |                     |                           | 100       |   |
| Foa et al. (2018)            | PE           | 110            | Military  | DSM-IV-TR           | 32.89 (7.05)              | 9.20      | PCL <sup>57</sup>                                     |
|                              | ACTST        | 110            |   |                     | 32.54 (7.45)              | 15        |   |
|                              | WL           | 40             |   |                     | 32.70 (7.68)              | 5         |   |
| Fonzo et al. (2017)          | PE           | 36             | Mixed   | DSM-IV              | 34.42 (10.23)             | 64        | PCL <sup>57</sup>                                     |
|                              | WL           | 30             |   |                     | 39.03 (10.35)             | 66        |   |
| Forbes et al. (2012)         | CBT          | 30             | Military  | DSM-IV              | 53.13 (13.97)             | 7         | PCL <sup>57</sup>                                     |
|                              | TAU          | 29             |   |                     | 53.62 (13.33)             | 0         |   |

(Continues)



TABLE 1 (Continued)

| Study reference <sup>a</sup>  | Intervention | No. randomised | Trauma Index   | Diagnostic Criteria | Mean age (SD) | % Female | Scale   |
|-------------------------------|--------------|----------------|--|---------------------|---------------|----------|---|
| Ford et al. (2011)            | TARGET       | 48             | Mixed  | DSM-IV SCID         | 30.7 (6.9)    | 100      | CAPS <sup>53</sup>                                    |
|                               | ACTST        | 53             |  |                     |               | 100      |   |
|                               | WL           | 45             |  |                     |               | 100      |   |
| Ford et al. (2018)            | TARGET       | 17             | Military   | DSM-IV              | 51.82         | 0        | CAPS <sup>53</sup>                                    |
|                               | PE           | 14             |  |                     | 52.60         | 0        |   |
| Ghafoori et al. (2017)        | PE           | 47             | Mixed - exposure to violence, complex trauma           | DSM-5               | 35.1 (12.8)   | 83       | PCL <sup>57</sup>                                     |
|                               | PSYED        | 24             |  |                     | 35.3 (10.4)   | 83       |   |
|                               | NET          | 15             | Refugee  | DSM-IV              | -             | -        | CAPS <sup>53</sup>                                    |
| Hensel-Dittmann et al. (2011) | SIT          | 13             |  |                     | -             | -        |   |
|                               | CBT          | 12             | Refugee  | DSM-IV              | 49.92 (9.23)  | 60       | CAPS <sup>53</sup>                                    |
| Hinton et al. (2009)          | WL           | 12             |  |                     | 49.08 (7.56)  | 60       |   |
|                               | EMDR         | 13             | Occupational (train)                                   | DSM-IV              | 43 (8)        | 30       | IES <sup>55</sup>                                     |
| Hogberg et al. (2007)         | WL           | 11             |  |                     | 43 (11)       | 18.18    |   |
|                               | NET          | 38             | War  | DSM-IV-TR           | 46.86 (11.73) | 100      | CAPS <sup>53</sup>                                    |
| Jacob et al. (2014)           | WL           | 38             |  |                     |               |          |   |
|                               | EMDR         | 15             | Military   | DSM-III-R           | 43.1 (2.84)   | 0        | Structured Interview for PTSD (SI-PTSD) <sup>62</sup> |
| Kohler et al. (2017)          | EMDR         | 78             | Military   | DSM-IV              | 32.00 (7.95)  | 8        | PDS <sup>59</sup>                                     |
|                               | WL           | 18             |  |                     |               | 11       |   |
| Kubany et al. (2004)          | CBT          | 59             | Domestic Violence                                      | DSM-IV              | 42.2 (10.1)   | 100      | CAPS <sup>53</sup>                                    |
|                               | WL           | 62             |  |                     |               | 100      |   |
| Lee et al. (2002)             | PE-SIT       | 13             | Mixed (sexual, physical, MVA, military, witness death) | DSM-IV              | 34 (17.16)    | 46       | IES <sup>55</sup>                                     |
|                               | EMDR         | 13             |  |                     | 36.58 (13.58) |          |   |
| Lely et al. (2019)            | NET          | 18             | Mixed  | DSM-IV-TR           | 62.65 (5.89)  | 28       | CAPS <sup>53</sup>                                    |
|                               | ACTST        | 15             |  |                     | 62.47 (6.24)  | 27       |   |
| Levi et al. (2016)            | CBT          | 95             | Military   | DSM-IV              | 30.8 (11.44)  | 0        | PTSD Questionnaire <sup>63</sup>                      |
|                               | PDT          | 148            |  |                     | 33.4 (11.45)  | 0        |   |
| Lindauer et al. (2008)        | BET          | 10             | Mixed  | DSM-IV              | 39.7 (8.5)    | 50       | SI-PTSD <sup>62</sup>                                 |
|                               | WL           | 10             |  |                     | 37.2 (9.9)    | 40       |   |
| Maguen et al. (2017)          | CBT          | 17             | Military   | DSM-IV              | 61.2 (12.3)   | 0        | PCL <sup>57</sup>                                     |
|                               | WL           | 16             |  |                     | 61.1 (14)     | 0        |   |

(Continues)

TABLE 1 (Continued)

| Study reference <sup>a</sup> | Intervention | No. randomised | Trauma Index                            | Diagnostic Criteria | Mean age (SD)    | % Female | Scale                |
|------------------------------|--------------|----------------|---|---------------------|------------------|----------|----------------------|
| Markowitz et al. (2015)      | PE           | 38             | Mixed (sexual, physical, interpersonal) | DSM-IV              | 41.76 (11.99)    | 55       | PSS-SR <sup>61</sup> |
|                              | ACTST        | 40             |   |                     | 38.12 (11.21)    | 70       |                      |
|                              | IPT          | 32             |   |                     | 40.62 (11.48)    | 88       |                      |
| McLay et al. (2011)          | VRET         | 10             | Military                                | DSM-IV              | 28 (range 22–43) | 10       | CAPS <sup>53</sup>   |
|                              | TAU          | 10             |   |                     | 29 (range 21–45) | 0        |                      |
| McLay et al. (2017)          | VRET         | 43             | Military                                | DSM-IV              | 33 (8.33)        | 7        | CAPS <sup>53</sup>   |
|                              | PE           | 38             |   |                     | 32 (7.71)        | 0        |                      |
| McDonagh et al. (2005)       | CBT          | 29             | Sexual                                  | DSM-IV              | 39.8(9.9)        | 100      | CAPS <sup>53</sup>   |
|                              | ACTST        | 22             |   |                     | 39.6(9.6)        | 100      |                      |
|                              | WL           | 23             |   |                     | 42(9.8)          | 100      |                      |
| Miyahira et al. (2012)       | VRET         | 29             | Military                                | DSM-IV              | –                | 5        | CAPS <sup>54</sup>   |
|                              | WL           | 13             |   |                     | –                |          |                      |
| Monson et al. (2006)         | CPT          | 30             | Military                                | DSM-IV              | 54.9 (6.5)       | 6.70     | PCL <sup>57</sup>    |
|                              | WL           | 30             |   |                     | 53.1(6.1)        | 3.30     |                      |
| Morath et al. (2014)         | NET          | 19             | Mixed                                   | DSM-IV-TR           | 28.7 (9.54)      | 32       | CAPS <sup>53</sup>   |
|                              | WL           | 19             |   |                     | 30.1 (8.21)      | 32       |                      |
| Mueser et al. (2008)         | CBT          | 54             | Mixed                                   | DSM-IV              | 45.13 (9.83)     | 75.90    | CAPS <sup>53</sup>   |
|                              | TAU          | 54             |   |                     | 43.30 (11.41)    | 81.50    |                      |
| Nacasch et al. (2011)        | PE           | 15             | Military                                | DSM-IV              | 34.8 (11.4)      | –        | PSS-I <sup>61</sup>  |
|                              | TAU          | 15             |   |                     | 33.7 (11.9)      | –        |                      |
| Neuner et al. (2004)         | NET          | 17             | Refugee                                 | DSM-IV              | 31.9 (6.7)       | 53.50    | PDS <sup>60</sup>    |
|                              | ACTST        | 14             |   |                     | 33.8 (7.9)       | 57.10    |                      |
|                              | PSYED        | 12             |   |                     | 34.2 (6.9)       | 75       |                      |
| Neuner et al. (2008)         | NET          | 111            | Refugee                                 | DSM-IV              | 34.4 (12.2)      | 49.50    | PDS <sup>60</sup>    |
|                              | ACTST        | 111            |   |                     | 35.2 (12.8)      | 46.80    |                      |
|                              | WL           | 55             |   |                     | 35.6 (14.0)      | 50.90    |                      |
| Neuner et al. (2010)         | NET          | 16             | Refugee                                 | DSM-IV              | 31.1 (7.80)      | 32.3     | PDS <sup>60</sup>    |
|                              | TAU          | 16             |   |                     | 31.6 (7.7)       | 32.3     |                      |
| Nijdam et al. (2012)         | BET          | 70             | Civilian trauma                         | DSM-IV              | 38.3 (12.2)      | 51.40    | IES-R <sup>51</sup>  |
|                              | EMDR         | 70             |   |                     | 37.3 (10.6)      | 61.40    |                      |
| Pacella et al. (2012)        | PE           | 34             | Trauma related to HIV status            | DSM-IV              | 46 (5.8)         | 37       | PSS-I <sup>61</sup>  |
|                              | WL           | 24             |   |                     | 48 (7.0)         |          |                      |

(Continues)

TABLE 1 (Continued)

| Study reference <sup>a</sup> | Intervention | No. randomised | Trauma Index   | Diagnostic Criteria | Mean age (SD)      | % Female  | Scale                |
|------------------------------|--------------|----------------|--|---------------------|--------------------|-----------|----------------------|
| Paunovic & Ost (2001)        | CBT          | 8              | Refugee  | DSM-IV              | 37.9 (7.6)         | 15        | PSS-SR <sup>61</sup> |
|                              | PE           | 8              |  |                     |                    |           |                      |
| Perez-Dandieu et al. (2015)  | EMDR         | 6              | Mixed  | DSM-IV              | 29.67 (3.14)       | 100       | PCL <sup>57</sup>    |
|                              | TAU          | 6              |  |                     | 29.33 (2.94)       | 100       |                      |
| Power et al. (2002)          | EMDR         | 51             | Mixed  | DSM-IV              | 38.6 (11.8)        | 31        | IES <sup>55</sup>    |
|                              | WL           | 34             |  |                     | 36.5 (11.6)        | 34        |                      |
| Rauch et al. (2015)          | PE           | 18             | Military   | DSM-IV              | <b>31.9 (7.6)</b>  | <b>9</b>  | CAPS <sup>53</sup>   |
|                              | ACTST        | 18             |  |                     |                    |           |                      |
| Ready et al. (2010)          | VRET         | 5              | Military   | DSM-IV SCID         | 57 (3.02)          | 0         | CAPS <sup>53</sup>   |
|                              | ACTST        | 6              |  |                     | 58 (3.02)          | 0         |                      |
| Reger et al. (2016)          | VRET         | 54             | Military   | DSM-IV-TR           | 29.52 (6.47)       | 4         | CAPS <sup>53</sup>   |
|                              | PE           | 54             |  |                     | 30.89 (7.09)       | 6         |                      |
|                              | WL           | 54             |  |                     | 30.39 (6.45)       | 2         |                      |
| Resick et al. (2002)         | CPT          | 62             | Sexual   | DSM-IV              | <b>32 (9.9)</b>    | 100       | PSS-SR <sup>63</sup> |
|                              | PE           | 62             |  |                     |                    | 100       |                      |
|                              | WL           | 47             |  |                     |                    | 100       |                      |
| Rogers et al. (1999)         | PE           | 6              | Military   | DSM-III-R           | -                  | -         | IES <sup>55</sup>    |
|                              | EMDR         | 6              |  |                     | -                  | -         |                      |
| Rothbaum (1997)              | EMDR         | 10             | Sexual   | DSM-III-R           | 31.6 (9.8)         | 100       | IES <sup>55</sup>    |
|                              | WL           | 8              |  |                     | 37.5 (11.1)        | 100       |                      |
| Schnurr et al. (2007)        | PE           | 141            | Mixed  | DSM-IV              | 44.6               | 100       | PCL <sup>57</sup>    |
|                              | ACTST        | 143            |  |                     | 44.9               | 100       |                      |
|                              | WET          | 24             | Mixed (sexual, physical, MVA, military, witness death)   | DSM-IV              | <b>19.8 (0.8)</b>  | -         | PSS-I <sup>61</sup>  |
| Sloan et al. (2012)          | WL           | 23             |  |                     |                    | -         |                      |
|                              | WET          | 22             | MVA  | DSM-IV              | <b>46.5 (13.1)</b> | <b>65</b> | CAPS <sup>53</sup>   |
| Sloan et al. (2018)          | WL           | 24             |  |                     |                    |           |                      |
|                              | WET          | 63             | Mixed (sexual, physical, MVA, military, death, accident) | DSM-5               | 44.9 (14.8)        | 47.60     | CAPS <sup>53</sup>   |
| Steel et al. (2017)          | CPT          | 63             |  |                     | 42.8 (14.4)        | 47.60     |                      |
|                              | CBT          | 30             | Mixed  | DSM-IV              | 43.8 (10.1)        | 40        | CAPS <sup>53</sup>   |
| Surrís et al. (2013)         | TAU          | 31             |  |                     | 40.7 (10.2)        | 35.50     |                      |
|                              | CPT          | 72             | Sexual   | DSM-IV              | 44.6 (10.5)        | 83        | PCL <sup>57</sup>    |
|                              | ACTST        | 57             |  |                     | 48.4 (8.2)         | 88        |                      |

(Continues)

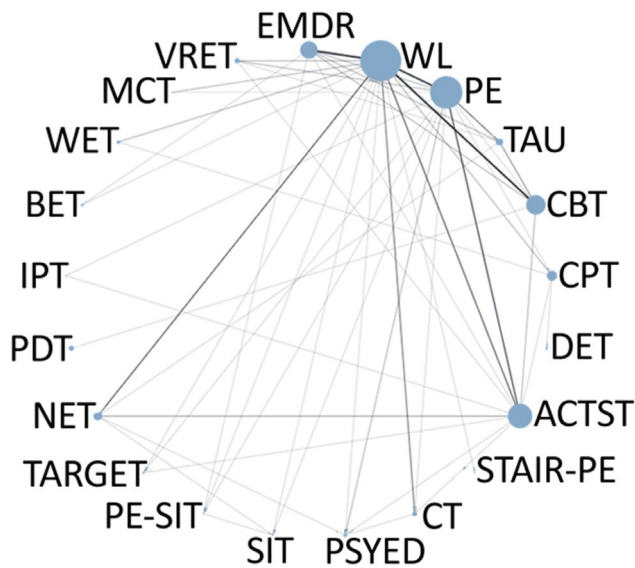
TABLE 1 (Continued)

| Study reference <sup>a</sup> | Intervention     | No. randomised | Trauma Index  | Diagnostic Criteria | Mean age (SD)                             | % Female             | Scale                |
|------------------------------|------------------|----------------|---|---------------------|---|----------------------|----------------------|
| Tarrier et al. (1999)        | CT<br>PE         | 37<br>35       | Mixed   | DSM-III-R           | <b>38.6 (11.6)</b>                        | <b>42</b>            | CAPS <sup>53</sup>   |
| ter heide et al. (2016)      | EMDR<br>WL       | 37<br>37       | Refugee   | DSM-IV              | 43.1(10.7)<br>39.8 (11.9)                 | 16.70<br>38.90       | CAPS <sup>53</sup>   |
| Thorp et al. (2019)          | PE<br>ACTST      | 41<br>46       | Military  | DSM-IV-TR           | 66.51 (6.21)<br>64.43 (4.49)              | 0<br>0               | CAPS <sup>53</sup>   |
| van Emmerik et al. (2008)    | CBT<br>WL        | 26<br>25       | mixed (MVA, nonsexual violence, sexual violence, other)                               | DSM-IV              | 38.88 (10.88)<br>39.58 (10.71)            | 57.70<br>68          | IES <sup>55</sup>    |
| van den Berg et al. (2015)   | PE<br>EMDR<br>WL | 53<br>55<br>47 | Mixed   | DSM-IV-TR           | 42.6 (10.3)<br>40.4 (11.3)<br>40.3 (9.7)  | 57<br>55<br>51       | PSS-SR <sup>61</sup> |
| Vera et al. (2011)           | PE<br>TAU        | 7<br>7         | Mixed   | DSM-IV              | <b>45.8</b>                               | 0<br>0               | CAPS <sup>53</sup>   |
| Wells et al. (2012)          | MCT<br>WL        | 10<br>10       | Mixed (physical, MVA, robbery, accident, witness death)                               | DSM-IV              | 33.4 (13.4)<br>41.3 (13.7)                | 60<br>50             | IES <sup>55</sup>    |
| Wells et al. (2015)          | MCT<br>PE<br>WL  | 11<br>11<br>10 | Mixed (sexual, physical, fire, military, robbery)                                     | DSM-IV              | 40.6 (11.9)<br>40.5 (10.9)<br>42.7 (18.5) | 27.27<br>27.27<br>40 | IES <sup>55</sup>    |
| Zang et al. (2013)           | NET<br>WL        | 11<br>11       | Mixed (Earthquake/ difficult life condition/accidental injury/family disease or loss) | DSM-IV              | 56.64 (12.22)<br>54.82 (11.59)            | 72.72<br>81.81       | IES-R <sup>51</sup>  |
| Zang et al. (2014)           | NET<br>WL        | 10<br>10       | Earthquake  | DSM-IV              | 53.50 (1.24)<br>50.90 (1.23)              | 90<br>100            | IES-R <sup>51</sup>  |

Note.: Bold typeface indicates data reported for total study sample, instead of per treatment arm.

Abbreviations: Active Supportive Therapy (control); ACTST; BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PDT, Psychodynamic Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control). All studies: mean age 39.88 years ( $SD = 8.67$ ), with 52.62% of the total participant pool being women.

aFull citations for each included study are reported in Section 6 of the Supplementary Material.



**FIGURE 2** The network structure for PTSD psychotherapies. The size of each node is proportional to the number of participants, and the width of the lines is proportional to the number of trials comparing each pair of interventions. ACTST; Active Supportive Therapy (control); BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); PDT, Psychodynamic Therapy; SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control)

low between-study heterogeneity for the NMA.<sup>42</sup> Network estimates show NET had significantly fewer dropouts compared to ACTST, CPT, DET, PE, PE-SIT, PSYED and VRET. WET had significantly fewer dropouts compared to ACTST, CPT, CT, DET, EMDR, PE, PE-SIT, PSYED, SIT, STAIR-PE and VRET. WL produced fewer dropouts only compared to CPT, PE and VRET. PE had significantly higher dropout rates than ACTST, BET, CBT, EMDR, IPT, TARGET and TAU. VRET also had significantly higher dropout rates than ACTST, BET, CBT, EMDR, IPT, PDT, TARGET and TAU. MCT was the only therapy with no significant comparisons to either active treatments or control conditions.

Head-to-head studies were also synthesised separately to assess for acceptability, displayed in the upper section of Table 3. Direct comparisons indicate significant treatment acceptability of ACTST over PE, WET over CPT, and WL over CPT, PE and VRET.

Finally, splitting indirect from direct evidence<sup>43</sup> also highlighted significant inconsistency between the following non-significant comparisons: ACTST versus NET, PE versus EMDR, WL versus EMDR and SIT versus NET. The global test of inconsistency based on the random-effects design-by-treatment interaction model was also significant,  $\chi^2(42) = 61.63, p = 0.03$ .

### 3.6 | Ranking of outcomes

Table 4 presents the ranking of treatments and control conditions on efficacy and acceptability compared to waitlist.<sup>46</sup> Three therapies (WET, IPT and EMDR) appear in the superior half of therapies for both efficacy and acceptability. VRET and STAIR-PE were therapies that did not fall in the superior half of ranks in either acceptability or efficacy. Figure 4 presents the NMA estimates for efficacy and acceptability.

### 3.7 | Assessment of transitivity

Subgroup analyses were conducted through a meta-regression to identify the impact of potential effect modifiers (index trauma type, DSM edition used for diagnosis and year of publication). Gender was not explored as it is confounded by trauma type (eg samples of sexual assault survivors often 100% female and military involvement often 100% male). The test of the model was non-significant ( $F = 0.02, df = 3, 77, p = 0.995$ ), and the goodness-of-fit test was significant ( $\tau^2 = 0.46, I^2 = 80.53\%, Q = 395.39, df = 77, p < 0.001$ ). No effect modifier was a significant individual covariate (index trauma type  $p = 0.83$ ; DSM  $p = 0.98$ ; publication year  $p = 0.92, R^2 = <0.01$ ).

### 3.8 | Risk of Bias

Risk of bias (RoB) was considered low in two studies (2.40%); some concerns in 60 (73.20%); and high in 20 (24.40%; see Figure 5). See Supplementary Material S1 for further discussion of the assessments per study. The network meta-analyses relied predominantly on evidence with moderate RoB with low-to-moderate indirectness. Confidence in the network of meta-analyses was considered mostly moderate for efficacy and low to moderate for acceptability outcomes. Mixed evidence comparisons with low confidence within the efficacy network included CBT:PDT; PE:PE-SIT; PE:SIT; PE-SIT:SIT; PE-SIT:WL and SIT:WL. Mixed evidence comparisons with low confidence within the acceptability network included ACTST:NET, ACTST:PSYED; ACTST:VRET, BET:EMDR, BET:WL, CCBT:TAU, CPT:DET, CT:PSYED,

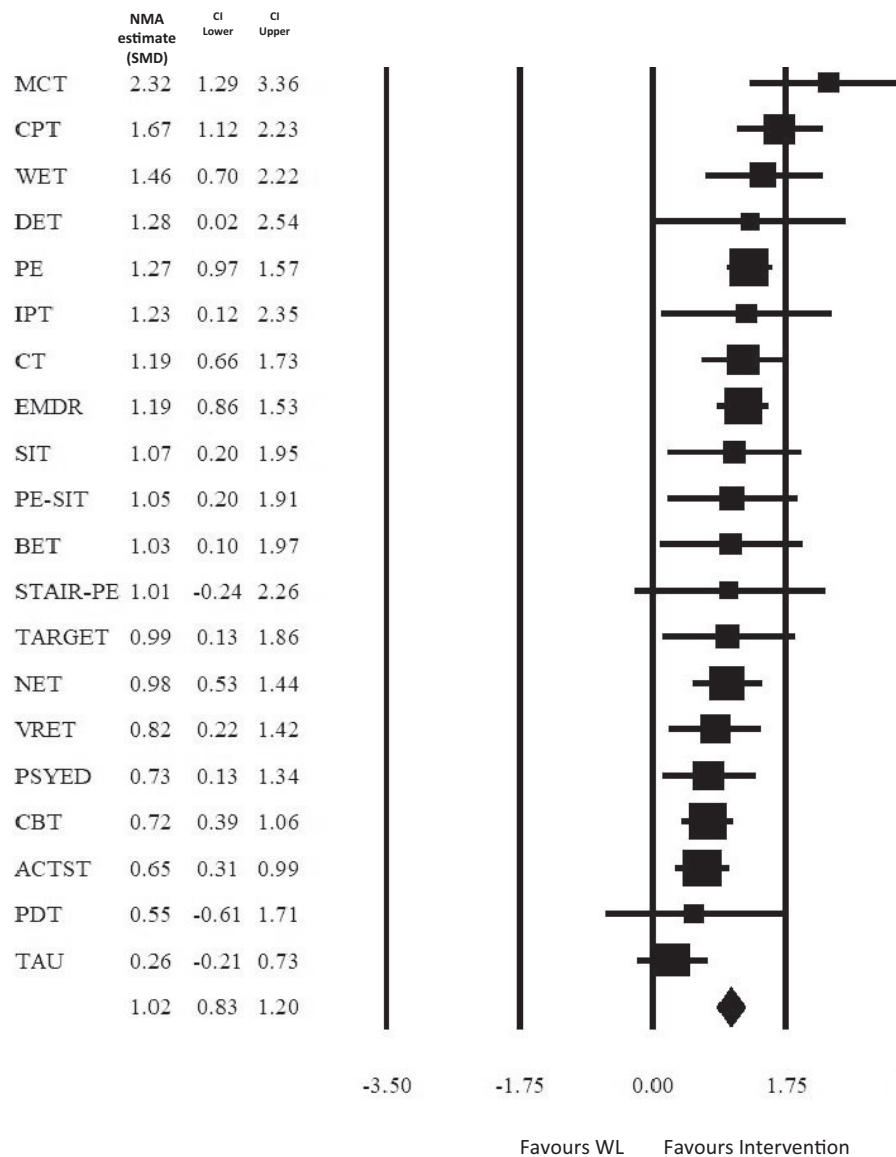
TABLE 2 Standardised mean differences (SMD; 95% CI) of Direct and overall Network Estimates of Efficacy

|                             |                          |                             |                          |                          |                          |                             |                          |                          |                          |
|-----------------------------|--------------------------|-----------------------------|--------------------------|--------------------------|--------------------------|-----------------------------|--------------------------|--------------------------|--------------------------|
| ACTST                       | -0.10 (-0.97, 0.77)      | <b>3.09 (1.83, 4.35)**</b>  | 0.91 (-0.29, 2.12)       | 0.02 (-1.22, 1.26)       | 0.85 (-0.45, 2.14)       | -0.15 (-0.86, 0.56)*        |                          |                          |                          |
| -0.39 (-1.37, 0.60)         | BET                      |                             |                          | 0.30 (-0.87, 1.46)       |                          |                             |                          |                          |                          |
| -0.08 (-0.51, 0.35)         | 0.31 (-0.67, 1.29)       | CBT                         |                          | 0.37 (-0.64, 1.37)       |                          |                             |                          |                          |                          |
| <b>-1.02 (-1.62, -0.43)</b> | -0.64 (-1.72, 0.44)      | <b>-0.95 (-1.57, -0.32)</b> | CPT                      | -0.39 (-1.53, 0.74)      |                          |                             |                          |                          |                          |
| -0.54 (-1.13, 0.05)         | -0.15 (-1.22, 0.92)      | -0.46 (-1.08, 0.16)         | 0.49 (-0.27, 1.24)       | CT                       |                          |                             |                          |                          |                          |
| -0.63 (-1.92, 0.65)         | -0.25 (-1.81, 1.32)      | -0.56 (-1.85, 0.74)         | 0.39 (-0.74, 1.53)       | -0.10 (-1.46, 1.27)      | DET                      |                             |                          |                          |                          |
| <b>-0.54 (-0.98, -0.10)</b> | -0.16 (-1.08, 0.76)      | -0.47 (-0.90, -0.04)        | 0.48 (-0.15, 1.11)       | -0.01 (-0.63, 0.62)      | 0.09 (-1.21, 1.39)       | EMDR                        |                          |                          |                          |
| -0.58 (-1.68, 0.52)         | -0.19 (-1.64, 1.25)      | -0.50 (-1.65, 0.65)         | 0.44 (-0.78, 1.67)       | -0.04 (-1.26, 1.18)      | 0.05 (-1.61, 1.72)       | -0.04 (-1.19, 1.11)         | IPT                      |                          |                          |
| <b>-1.68 (-2.75, -0.60)</b> | -1.29 (-2.68, 0.10)      | <b>-1.60 (-2.68, -0.52)</b> | -0.65 (-1.82, 0.51)      | -1.14 (-2.29, 0.02)      | -1.04 (-2.67, 0.58)      | <b>-1.13 (-2.21, -0.05)</b> | -1.10 (-2.60, 0.41)      | MCT                      |                          |
| -0.33 (-0.82, 0.16)         | 0.06 (-0.97, 1.09)       | -0.25 (-0.80, 0.29)         | <b>0.69 (0.00, 1.39)</b> | 0.21 (-0.48, 0.89)       | 0.30 (-1.02, 1.63)       | 0.21 (-0.33, 0.76)          | 0.25 (-0.93, 1.43)       | <b>1.35 (0.23, 2.47)</b> | NET                      |
| 0.10 (-1.10, 1.29)          | 0.48 (-0.10, 1.97)       | 0.17 (-0.94, 1.29)          | 1.12 (-0.16, 2.40)       | 0.64 (-0.64, 1.91)       | 0.73 (-0.97, 2.44)       | 0.64 (-0.55, 1.84)          | 0.68 (-0.92, 2.28)       | <b>1.77 (0.22, 3.33)</b> | 0.43 (-0.81, 1.67)       |
| <b>-0.62 (-0.97, -0.27)</b> | -0.24 (-1.20, 0.73)      | <b>-0.55 (-0.95, -0.14)</b> | 0.40 (-0.18, 0.98)       | -0.09 (-0.65, 0.48)      | 0.01 (-1.27, 1.29)       | -0.07 (-0.49, 0.33)         | -0.04 (-1.14, 1.05)      | <b>1.05 (0.01, 2.10)</b> | -0.29 (-0.79, 0.21)      |
| -0.41 (-1.30, 0.49)         | -0.02 (-1.26, 1.22)      | -0.33 (-1.23, 0.57)         | 0.62 (-0.39, 1.62)       | 0.13 (-0.86, 1.13)       | 0.23 (-1.29, 1.74)       | 0.14 (-0.72, 1.00)          | 0.17 (-1.21, 1.56)       | 1.27 (-0.06, 2.60)       | -0.08 (-1.01, 0.86)      |
| -0.09 (-0.72, 0.55)         | 0.30 (-0.80, 1.40)       | -0.01 (-0.68, 0.66)         | <b>0.94 (0.14, 1.73)</b> | 0.45 (-0.28, 1.18)       | 0.55 (-0.84, 1.93)       | 0.46 (-0.22, 1.13)          | 0.49 (-0.74, 1.73)       | <b>1.59 (0.41, 2.77)</b> | 0.24 (-0.45, 0.94)       |
| -0.42 (-1.33, 0.48)         | -0.04 (-1.31, 1.23)      | -0.35 (-1.27, 0.58)         | 0.60 (-0.42, 1.62)       | 0.11 (-0.88, 1.13)       | 0.21 (-1.32, 1.74)       | 0.12 (-0.80, 1.04)          | 0.16 (-1.24, 1.55)       | 1.25 (-0.09, 2.60)       | -0.09 (-0.99, 0.80)      |
| -0.37 (-1.66, 0.93)         | 0.02 (-1.54, 1.58)       | -0.29 (-1.58, 1.00)         | 0.66 (-0.71, 2.02)       | 0.17 (-1.19, 1.53)       | 0.27 (-1.51, 2.04)       | 0.18 (-1.11, 1.47)          | 0.21 (-1.46, 1.89)       | 1.31 (-0.31, 2.93)       | -0.04 (-1.36, 1.29)      |
| -0.34 (-1.21, 0.54)         | 0.05 (-1.22, 1.32)       | -0.26 (-1.18, 0.66)         | 0.69 (-0.32, 1.70)       | 0.20 (-0.80, 1.20)       | 0.30 (-1.22, 1.82)       | 0.21 (-0.71, 1.12)          | 0.24 (-1.14, 1.62)       | 1.34 (0.00, 2.68)        | -0.01 (-0.97, 0.95)      |
| 0.38 (-0.14, 0.90)          | 0.77 (-0.25, 1.79)       | 0.46 (-0.04, 0.96)          | <b>1.41 (0.76, 2.05)</b> | <b>0.92 (0.23, 1.61)</b> | 1.02 (-0.29, 2.32)       | <b>0.93 (0.41, 1.45)</b>    | 0.96 (-0.21, 2.14)       | <b>2.06 (0.94, 3.18)</b> | <b>0.71 (0.12, 1.31)</b> |
| -0.17 (-0.82, 0.47)         | 0.21 (-0.89, 1.31)       | -0.10 (-0.76, 0.57)         | <b>0.85 (0.06, 1.64)</b> | 0.36 (-0.42, 1.15)       | 0.46 (-0.92, 1.84)       | 0.37 (-0.30, 1.04)          | 0.47 (-0.83, 1.64)       | <b>1.50 (0.32, 2.68)</b> | 0.16 (-0.57, 0.88)       |
| -0.81 (-1.63, 0.00)         | -0.43 (-1.63, 0.77)      | -0.74 (-1.56, 0.08)         | 0.21 (-0.59, 1.01)       | -0.28 (-1.20, 0.65)      | -0.18 (-1.57, 1.20)      | -0.27 (-1.10, 0.55)         | -0.24 (-1.58, 1.11)      | 0.86 (-0.42, 2.14)       | -0.49 (-1.36, 0.39)      |
| <b>0.65 (0.31, 0.99)</b>    | <b>1.03 (0.10, 1.97)</b> | <b>0.72 (0.39, 1.06)</b>    | <b>1.67 (1.12, 2.23)</b> | <b>1.19 (0.65, 1.72)</b> | <b>1.28 (0.02, 2.54)</b> | <b>1.19 (0.86, 1.53)</b>    | <b>1.23 (0.11, 2.34)</b> | <b>2.32 (1.29, 3.36)</b> | <b>0.98 (0.52, 1.43)</b> |

Note: Direct estimates are displayed above the comparison line, NMA estimates sit below. Bold = significant effect ( $p < 0.05$ ) with estimates above 0 favouring intervention in the column, \* $p < 0.1$ ; \*\* $p < 0.05$  for significant inconsistency detected between direct and indirect evidence, ^ means no inconsistency comparison due to lack of indirect evidence.

Abbreviations: Active Supportive Therapy (control); ACTST; BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PDT, Psychodynamic Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control).

|                     |                          |                          |                          |                          |                        |                          |                                 |                          |                                |                                |                     |
|---------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------------------|--------------------------|---------------------------------|--------------------------|--------------------------------|--------------------------------|---------------------|
|                     | <b>0.67 (0.16, 1.18)</b> |                          | -0.13<br>(-1.46, 1.21)   |                          | 0.04<br>(-1.14, 1.22)  |                          | 0.54<br>(-1.20, 2.27)           |                          | <b>-0.80</b><br>(-1.33, -0.27) |                                | -1.25 (-2.71, 0.21) |
|                     | -0.17 (-1.29, 0.94)^     | -0.12<br>(-1.58, 1.34)   |                          |                          |                        |                          | -0.15<br>(-1.00, 0.71)          |                          | <b>-0.74</b><br>(-1.14, -0.35) |                                |                     |
|                     |                          | -0.38<br>(-1.52, 0.76)   |                          |                          |                        |                          | -0.57<br>(-1.77, 0.63)          | -0.14<br>(-1.27, 1.00)   | <b>-1.14</b><br>(-1.97, -0.30) |                                |                     |
|                     | 0.09 (-1.10, 1.29)       |                          | -0.17 (-1.38, 1.04)      |                          |                        |                          |                                 |                          | <b>-1.12</b><br>(-1.75, -0.48) |                                |                     |
|                     | -0.34<br>(-1.28, 0.60)   | -0.35<br>(-1.70, 1.00)   |                          |                          |                        |                          | -0.74<br>(-1.84, 0.37)          |                          | <b>-1.17</b><br>(-1.58, -0.76) |                                |                     |
|                     | 0.28 (-0.97, 1.53)       |                          |                          |                          |                        |                          |                                 |                          |                                |                                |                     |
|                     | -0.99<br>(-2.42, 0.45)   |                          |                          |                          |                        |                          |                                 |                          | <b>-2.50</b><br>(-3.67, -1.34) |                                |                     |
|                     |                          |                          | -0.19 (-1.50, 1.12)      | -0.25<br>(-1.63, 1.14)   |                        |                          | -1.01<br>(-2.32, 0.30)          |                          | <b>-1.12</b><br>(-1.72, -0.52) |                                |                     |
| PDT                 |                          |                          |                          |                          |                        |                          |                                 |                          |                                |                                |                     |
| -0.72 (-1.91, 0.46) | PE                       | -0.21<br>(-1.44, 1.02)   | -0.32 (-1.15, 0.51)      | -0.14<br>(-1.38, 1.11)   |                        | 0.02 (-1.49, 1.54)       | <b>-1.54</b><br>(-2.29, -0.79)* | -0.33<br>(-1.16, 0.51)   |                                | <b>-1.27</b><br>(-1.68, -0.86) |                     |
| -0.50 (-1.94, 0.93) | 0.22 (-0.65, 1.08)       | PE-SIT                   |                          | 0.08 (-1.17, 1.32)       |                        |                          |                                 |                          |                                | -1.53 (-2.85, 0.21)            |                     |
| -0.19 (-1.49, 1.12) | 0.54 (-0.05, 1.13)       | 0.32 (-0.70, 1.34)       | PSYED                    |                          |                        |                          |                                 |                          |                                | 0.12 (-1.09, 1.33)             |                     |
| -0.52 (-1.97, 0.93) | 0.20 (-0.69, 1.08)       | -0.02<br>(-1.08, 1.04)   | -0.34 (-1.37, 0.70)      | SIT                      |                        |                          |                                 |                          |                                | <b>-1.61</b><br>(-2.95, -0.27) |                     |
| -0.46 (-2.17, 1.24) | 0.26 (-1.03, 1.54)       | 0.04 (-1.47, 1.55)       | -0.28 (-1.67, 1.11)      | 0.06 (-1.47, 1.58)       | STAIR-PE               |                          |                                 |                          |                                | -1.01 (-2.26, 0.23)^           |                     |
| -0.44 (-1.88, 1.01) | 0.29 (-0.59, 1.16)       | 0.07 (-1.13, 1.27)       | -0.25 (-1.28, 0.78)      | 0.09 (-1.13, 1.30)       | 0.03 (-1.49, 1.55)     | TARGET                   |                                 |                          |                                | -1.00 (-2.20, 0.19)            |                     |
| 0.29 (-0.94, 1.51)  | <b>1.01 (0.54, 1.47)</b> | 0.79 (-0.15, 1.73)       | 0.47 (-0.25, 1.19)       | 0.81 (-0.15, 1.77)       | 0.75 (-0.58, 2.08)     | 0.72 (-0.24, 1.68)       | TAU                             | 0.65 (-0.78, 2.10)       |                                |                                |                     |
| -0.27 (-1.57, 1.02) | 0.45 (-0.15, 1.05)       | 0.23 (-0.79, 1.26)       | -0.09 (-0.91, 0.73)      | 0.25 (-0.79, 1.29)       | 0.19 (-1.19, 1.58)     | 0.16 (-0.87, 1.20)       | -0.56<br>(-1.24, 0.13)          | VRET                     |                                | -0.52 (-1.42, 0.38)            |                     |
| -0.91 (-2.30, 0.47) | -0.19<br>(-0.99, 0.61)   | -0.41<br>(-1.54, 0.73)   | -0.73 (-1.69, 0.23)      | -0.39<br>(-1.54, 0.76)   | -0.45<br>(-1.91, 1.01) | -0.48<br>(-1.62, 0.67)   | -1.20<br>(-2.06, -0.34)         | -0.64<br>(-1.60, 0.32)   | WET                            | <b>-1.41</b><br>(-2.35, -0.47) |                     |
| 0.55 (-0.61, 1.71)  | <b>1.27 (0.97, 1.57)</b> | <b>1.05 (0.20, 1.91)</b> | <b>0.73 (0.13, 1.34)</b> | <b>1.07 (0.20, 1.95)</b> | 1.01 (-0.23, 2.26)     | <b>0.99 (0.12, 1.85)</b> | 0.26 (-0.20, 0.73)              | <b>0.82 (0.22, 1.42)</b> | <b>1.46 (0.70, 2.22)</b>       | WL                             |                     |



**FIGURE 3** Forest Plot of NMA estimates compared to waitlist. ACTST; Active Supportive Therapy (control); BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); PDT, Psychodynamic Therapy; SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control)

EMDR:PE-SIT, EMDR:WL, NET:SIT, NET:TAU, PE:PE-SIT, PE:SIT, PE:VRET, PE-SIT:SIT and PE-SIT:WL. Mixed evidence comparisons with very low confidence within the acceptability network included CBT:PDT, SIT:WL and STAIR-PE:WL. See Supplementary Material S1 for further discussion of the inclusion of these outcomes in the grading of confidence in NMA.

The funnel plot in Figure 6 summarises the assessment of publication bias. Examination of the 82 studies (where the mean of comparisons was used for multi-arm studies) indicated asymmetry with missing trials in the

areas of non-significance. The Egger's test was significant ( $p < 0.001$ ) indicating the presence of small-study bias.

### 3.9 | Sensitivity analysis

The results of the sensitivity analysis are reported in Supplementary Material S2. Table S4 of the Supplementary Material indicates that the rank order and magnitude of network estimates of efficacy and acceptability remained broadly similar in the more refined sample.



## 4 | DISCUSSION

This NMA addressed the comparative efficacy and acceptability of PTSD psychotherapies in adults. In contrast to previous reviews, we analysed findings at the level of individual intervention types rather than under a collective banner of ‘TF-CBT’. In this respect, our findings have particular value for clinicians who typically apply one or another TF-CBT approach, such as exposure-based or CT, rather than a generic TF-CBT intervention. Our finding of differing levels of efficacy and acceptability across therapy modalities suggests that the tendency among researchers to assume apparent comparability, whether applied across all psychotherapies or only within trauma-focused psychotherapies, may have been conferred prematurely and that there are differences in symptom change and dropout rates between different psychotherapies, and even within ‘trauma-focused’ interventions. The effect sizes of MCT and CPT were approximately double that of EMDR and IPT, among others. Likewise, participants had approximately half the odds of discontinuing from WET and NET when compared to PE, MCT and CPT, among others.

Our results suggest that MCT was most efficacious; however, it is noted that there were high rates of inconsistency with sensitivity analyses, suggesting inflation of effect sizes. Additionally, CPT and NET were also more efficacious than other therapy conditions, with interpersonal, stress-based and exposure-adjunct therapies inferior to other active therapies. While previous reviews have supported the relative efficacy of CPT compared to inactive control conditions,<sup>47</sup> to the best of our knowledge, no previous reviews have allowed consideration of the efficacy of MCT and CPT in the context of multiple other trauma-focused psychotherapies.

Our review also examined treatment acceptability. To the best of our knowledge, no previous review has considered treatment acceptability for PTSD from such a comprehensive synthesis of the psychological therapy literature. This is an important limitation in the extant literature given that efficacy and acceptability need to be considered hand-in-hand when considering the most appropriate treatment approaches for PTSD. We found that written and narrative approaches reported the lowest rates of dropouts compared to therapeutic and control conditions. Of note, PE-SIT produced significantly higher ORs to treatment and control conditions indicating a greater risk of dropout in this treatment. The results from the network suggest an absence of violations of transitivity and the absence of statistically significant global inconsistency, although this is not evidence against inconsistency.<sup>48</sup> It is noted there was large heterogeneity across the network for both outcomes, as well as suspected small-study publication bias of trials compared to waitlist.

Previous analyses of Gerger et al.<sup>10</sup> Watts et al.<sup>11</sup> and Bisson et al.<sup>9</sup> led to speculations of therapeutic synonymy. However, our findings are the first to confirm this assertion when comparing a large number of discrete therapy approaches. In contrast to Gerger et al.<sup>10</sup> who condensed the literature to include five psychotherapeutic nodes, we included comparisons of 21 intervention arms, and examined a more rigorous, stringent and contemporary evidence base. This paper also extends the recent Merz<sup>21</sup> paper of 12 RCTs, by highlighting head-to-head psychotherapeutic comparisons, as well as demarcating the efficacy between psychotherapies, rather than collapsing all therapies into one comparison. While our results are broadly consistent with Mavranouzouli et al.<sup>23</sup> to the extent that EMDR and TF-CBTs were generally found to be better than waitlist, our findings provide additional insight into the relative efficacy of individual TF-CBT approaches, such as CPT, which was ranked more efficacious than a number of other TF-CBT interventions such as CBT, PE and CT, as well as regarding the acceptability of TF-CBT interventions.

The state of the literature and a number of design limitations in the evaluation of psychotherapies served as limitations for our analyses, and in turn, the implications which can be drawn from our findings. First, according to the GRADE framework, the majority of the individual studies included in the review were of low and moderate quality. However, it is noted that the gold-standard tool utilised is biased against psychotherapy, particularly with the inability to blind participants to their treatment condition. Second, the emerging status of three psychotherapies that have not been subjected to many RCTs necessitated in a reliance on head-to-head comparisons for those approaches. It is also acknowledged that the division between ITT and completer reporting in trials may have an impact on transitivity. Finally, we note that the efficacy values for some approaches may have been inflated by the use of waiting list control conditions, as waiting lists have been identified as a potential source of placebo effects which could serve to artificially inflate estimated effect sizes.<sup>49</sup>

We also acknowledge some methodological aspects of our review, which also serve as limitations. At the review level, group formats and non-face-to-face interventions were excluded to limit lack of transitivity; however, this resulted in the discounting of therapies such as Mindfulness Based Stress Reduction, Dialectical Behaviour Therapy, telehealth and Internet-based delivered trials whose efficacies are acknowledged.<sup>16,19</sup> We also analysed only average treatment effects, with this methodological approach being unable to investigate the potential clinical and demographic modifiers of treatment response, at the individual patient level. It is also noted that our review included many nodes,

**TABLE 3** Odds Ratios (ORs; 95% CI) of direct and overall network estimates of acceptability

|                          |                           |                          |                          |                          |                          |                          |                           |                    |                           |                          |
|--------------------------|---------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------------|--------------------|---------------------------|--------------------------|
| ACTST                    | 1.43 (0.49, 4.12)         | 0.46 (0.18, 1.15)        | 3.33 (0.31, 35.59)       | 0.22 (0.02, 2.22)        | 2.97 (0.87, 10.11)       | 4.62 (1.72, 12.45)**     |                           |                    |                           |                          |
| 0.50 (0.18, 1.41)        | BET                       |                          |                          | 0.63 (0.27, 1.48)^       |                          |                          |                           |                    |                           |                          |
| 0.73 (0.43, 1.23)        | 1.44 (0.52, 3.98)         | CBT                      |                          | 0.46 (0.09, 2.45)        |                          |                          |                           |                    | 0.92 (0.46, 1.84)^        |                          |
| 1.77 (0.99, 3.19)        | <b>3.52 (1.15, 10.78)</b> | <b>2.45 (1.22, 4.89)</b> | CPT                      | 0.89 (0.30, 2.58)^       |                          |                          |                           |                    |                           |                          |
| 1.16 (0.43, 3.14)        | 2.31 (0.59, 9.00)         | 1.61 (0.57, 4.54)        | 0.66 (0.22, 1.97)        | CT                       |                          |                          |                           |                    |                           |                          |
| 2.00 (0.59, 6.78)        | 3.97 (0.84, 18.68)        | 2.76 (0.77, 9.88)        | 1.13 (0.39, 3.29)        | 1.72 (0.37, 7.97)        | DET                      |                          |                           |                    |                           |                          |
| 0.80 (0.45, 1.43)        | 1.59 (0.68, 3.72)         | 1.10 (0.63, 1.93)        | <b>0.45 (0.22, 0.93)</b> | 0.69 (0.24, 1.98)        | 0.40 (0.11, 1.46)        | EMDR                     |                           |                    |                           |                          |
| 0.48 (0.16, 1.44)        | 0.95 (0.22, 4.18)         | 0.66 (0.20, 2.17)        | <b>0.27 (0.08, 0.92)</b> | 0.41 (0.10, 1.76)        | 0.24 (0.05, 1.21)        | 0.60 (0.18, 2.01)        | IPT                       |                    |                           |                          |
| 1.57 (0.08, 30.37)       | 3.12 (0.14, 70.00)        | 2.17 (0.11, 42.91)       | 0.89 (0.04, 17.79)       | 1.35 (0.06, 29.89)       | 0.79 (0.03, 18.98)       | 1.97 (0.10, 39.17)       | 3.28 (0.14, 75.58)        | MCT                |                           |                          |
| <b>0.42 (0.19, 0.91)</b> | 0.83 (0.24, 2.88)         | 0.58 (0.24, 1.39)        | 0.24 (0.09, 0.61)        | 0.36 (0.11, 1.23)        | <b>0.21 (0.05, 0.87)</b> | 0.53 (0.21, 1.29)        | 0.87 (0.23, 3.31)         | 0.27 (0.01, 5.62)  | NET                       |                          |
| 0.79 (0.33, 1.89)        | 1.57 (0.46, 5.38)         | 1.09 (0.54, 2.19)        | 0.45 (0.17, 1.19)        | 0.68 (0.19, 2.37)        | 0.40 (0.09, 1.69)        | 0.99 (0.41, 2.41)        | 1.65 (0.42, 6.52)         | 0.50 (0.02, 10.73) | 1.88 (0.62, 5.76)         | PDT                      |
| <b>1.54 (1.10, 2.17)</b> | <b>3.06 (1.11, 8.44)</b>  | <b>2.13 (1.28, 3.53)</b> | 0.87 (0.49, 1.56)        | 1.33 (0.50, 3.49)        | 0.77 (0.23, 2.61)        | <b>1.93 (1.11, 3.34)</b> | <b>3.21 (1.08, 9.60)</b>  | 0.98 (0.05, 18.52) | <b>3.68 (1.64, 8.25)</b>  | 1.95 (0.83, 4.62)        |
| 1.98 (0.50, 7.91)        | 3.93 (0.75, 20.47)        | 2.73 (0.66, 11.35)       | 1.12 (0.26, 4.84)        | 1.70 (0.32, 8.93)        | 0.99 (0.16, 6.08)        | 2.47 (0.60, 10.18)       | 4.12 (0.72, 23.51)        | 1.26 (0.05, 32.11) | <b>4.72 (1.08, 20.55)</b> | 2.51 (0.51, 12.24)       |
| 1.88 (0.67, 5.33)        | 3.74 (0.93, 15.10)        | 2.60 (0.88, 7.70)        | 1.06 (0.34, 3.32)        | 1.62 (0.41, 6.40)        | 0.94 (0.20, 4.49)        | 2.36 (0.78, 7.12)        | 3.93 (0.90, 17.17)        | 1.20 (0.05, 26.66) | <b>4.49 (1.27, 15.92)</b> | 2.39 (0.66, 8.67)        |
| 1.55 (0.41, 5.81)        | 3.07 (0.61, 15.45)        | 2.13 (0.54, 8.42)        | 0.87 (0.21, 3.58)        | 1.33 (0.27, 6.67)        | 0.77 (0.13, 4.55)        | 1.93 (0.49, 7.64)        | 3.22 (0.59, 17.55)        | 0.98 (0.04, 24.52) | <b>3.69 (0.95, 14.29)</b> | 1.96 (0.42, 9.13)        |
| 2.23 (0.47, 10.67)       | 4.43 (0.74, 26.42)        | 3.08 (0.65, 14.61)       | 1.26 (0.25, 6.36)        | 1.92 (0.32, 11.53)       | 1.12 (0.16, 7.78)        | 2.80 (0.58, 13.41)       | 4.66 (0.70, 30.81)        | 1.42 (0.05, 39.45) | 5.33 (0.97, 29.33)        | 2.83 (0.52, 15.56)       |
| 0.55 (0.25, 1.23)        | 1.09 (0.31, 3.81)         | 0.76 (0.31, 1.85)        | <b>0.31 (0.12, 0.80)</b> | 0.47 (0.14, 1.62)        | 0.27 (0.07, 1.15)        | 0.69 (0.27, 1.72)        | 1.14 (0.30, 4.37)         | 0.35 (0.02, 7.35)  | <b>1.31 (0.44, 3.90)</b>  | 0.69 (0.22, 2.16)        |
| 0.48 (0.24, 0.96)        | 0.94 (0.31, 2.85)         | 0.66 (0.38, 1.15)        | <b>0.27 (0.12, 0.62)</b> | 0.41 (0.13, 1.27)        | <b>0.24 (0.06, 0.92)</b> | 0.60 (0.30, 1.20)        | 0.99 (0.28, 3.52)         | 0.30 (0.02, 6.16)  | <b>1.14 (0.42, 3.05)</b>  | 0.60 (0.25, 1.47)        |
| <b>2.39 (1.11, 5.17)</b> | <b>4.75 (1.44, 15.72)</b> | <b>3.30 (1.46, 7.45)</b> | 1.35 (0.55, 3.30)        | 2.06 (0.63, 6.71)        | 1.20 (0.30, 4.83)        | <b>2.99 (1.29, 6.93)</b> | <b>4.99 (1.36, 18.37)</b> | 1.52 (0.07, 31.41) | <b>5.71 (2.00, 16.28)</b> | <b>3.03 (1.04, 8.85)</b> |
| <b>0.21 (0.06, 0.73)</b> | 0.42 (0.09, 1.98)         | 0.29 (0.08, 1.05)        | <b>0.12 (0.04, 0.37)</b> | <b>0.18 (0.04, 0.85)</b> | <b>0.11 (0.02, 0.50)</b> | <b>0.26 (0.07, 0.97)</b> | 0.44 (0.09, 2.25)         | 0.13 (0.01, 3.25)  | 0.50 (0.12, 2.11)         | 0.27 (0.06, 1.15)        |
| 0.68 (0.44, 1.05)        | 1.36 (0.51, 3.55)         | 0.94 (0.63, 1.41)        | <b>0.39 (0.21, 0.70)</b> | 0.59 (0.22, 1.56)        | 0.34 (0.10, 1.17)        | 0.85 (0.55, 1.34)        | 1.42 (0.45, 4.47)         | 0.43 (0.02, 8.42)  | 1.63 (0.73, 3.65)         | 0.87 (0.39, 1.93)        |

Note: Direct estimates are displayed above the comparison line, NMA estimates sit below. **Bold** = significant effect (p<.05) with estimates above 1 favouring intervention in the column, \*p<.1, \*\*p<.05 for significant inconsistency detected between direct and indirect evidence, ^ means no inconsistency comparison due to lack of indirect evidence. ACTST; Active Supportive Therapy (control); BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); PDT, Psychodynamic Therapy; SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control).

increasing the risk of spurious findings. However, our results were broadly consistent when we conducted a sensitivity analysis that included fewer nodes, and the proportion of nodes in our analyses (47.6%) comprised of three or fewer individual studies was similar or less

than other recent reviews.<sup>21,23,50</sup> Finally, we acknowledge that variations in the definition and application of TAU interventions may have threatened the transitivity of our results. However, the exclusion of studies with TAU arms would have resulted in the elimination of 11

|                          |                          |                          |                          |                   |                           |                           |                            |                           |                    |
|--------------------------|--------------------------|--------------------------|--------------------------|-------------------|---------------------------|---------------------------|----------------------------|---------------------------|--------------------|
| 0.58 (0.39, 0.87)        | 0.53 (0.19, 1.50)        |                          | 1.73 (0.64, 4.68)        |                   | 0.80 (0.04, 17.81)        |                           | 1.46 (0.60, 3.60)          |                           |                    |
| 4.20 (0.32, 55.41)*      |                          |                          |                          |                   | <b>2.12 (1.10, 4.06)*</b> |                           | 0.95 (0.59, 1.51)          |                           |                    |
| 0.93 (0.39, 2.23)        |                          |                          |                          |                   |                           |                           | <b>10.37 (3.06, 35.17)</b> |                           |                    |
| 0.59 (0.14, 2.47)        |                          |                          |                          |                   |                           |                           | <b>2.38 (1.01, 5.64)</b>   |                           |                    |
|                          |                          |                          |                          |                   |                           |                           | 3.89 (0.87, 17.49)         |                           |                    |
| 1.96 (0.61, 6.32)**      | 1.00 (0.05, 18.58)       |                          |                          |                   | 0.77 (0.18, 3.36)         |                           | 0.91 (0.55, 1.52)**        |                           |                    |
| 0.43 (0.13, 1.45)        |                          |                          |                          |                   |                           |                           |                            |                           |                    |
| 1.00 (0.05, 18.99)       |                          |                          |                          |                   |                           |                           |                            |                           |                    |
|                          |                          |                          | 1.38 (0.18, 10.38)**     |                   |                           |                           | 1.00 (0.27, 3.78)          |                           |                    |
| PE                       | 0.24 (0.04, 1.34)**      | 0.68 (0.21, 2.14)        | 0.24 (0.04, 1.36)**      |                   | 4.32 (0.89, 20.99)        | 1.62 (0.45, 5.92)         | 0.86 (0.35, 2.10)          | <b>2.73 (1.56, 4.77)</b>  |                    |
| 1.28 (0.33, 5.02)        | PE-SIT                   |                          | 0.99 (0.28, 3.53)        |                   |                           |                           |                            |                           |                    |
| 1.22 (0.45, 3.30)        | 0.95 (0.18, 5.11)        | PSYED                    |                          |                   |                           |                           |                            | 1.62 (0.24, 11.13)        |                    |
| 1.00 (0.27, 3.71)        | 0.78 (0.24, 2.59)        | 0.82 (0.16, 4.21)        | SIT                      |                   |                           |                           |                            |                           |                    |
| 1.45 (0.31, 6.85)        | 1.13 (0.15, 8.73)        | 1.19 (0.19, 7.34)        | 1.45 (0.19, 10.78)       | STAIR-PE          |                           |                           |                            | 3.27 (0.73, 14.70)^       |                    |
| <b>0.36 (0.16, 0.80)</b> | 0.28 (0.06, 1.33)        | 0.29 (0.08, 1.04)        | 0.36 (0.08, 1.62)        | 0.25 (0.04, 1.36) | TARGET                    |                           |                            | 1.04 (0.35, 3.06)         |                    |
| <b>0.31 (0.16, 0.60)</b> | 0.24 (0.05, 1.07)        | <b>0.25 (0.08, 0.82)</b> | 0.31 (0.07, 1.30)        | 0.21 (0.04, 1.09) | 0.87 (0.32, 2.37)         | TAU                       |                            |                           |                    |
| 1.55 (0.75, 3.21)        | 1.21 (0.26, 5.59)        | 1.27 (0.38, 4.28)        | 1.55 (0.35, 6.81)        | 1.07 (0.20, 5.69) | <b>4.37 (1.52, 12.58)</b> | <b>5.03 (1.98, 12.78)</b> | VRET                       | <b>5.46 (2.14, 12.42)</b> |                    |
| <b>0.14 (0.04, 0.47)</b> | <b>0.11 (0.02, 0.66)</b> | <b>0.11 (0.02, 0.54)</b> | <b>0.14 (0.02, 0.81)</b> | 0.09 (0.01, 0.66) | 0.38 (0.09, 1.63)         | 0.44 (0.11, 1.73)         | <b>0.09 (0.02, 0.36)</b>   | WET                       | 0.97 (0.06, 17.11) |
| <b>0.44 (0.30, 0.66)</b> | 0.35 (0.09, 1.38)        | 0.36 (0.13, 1.02)        | 0.44 (0.12, 1.68)        | 0.31 (0.07, 1.37) | 1.25 (0.55, 2.85)         | 1.43 (0.77, 2.68)         | <b>0.29 (0.14, 0.59)</b>   | 3.24 (0.94, 11.14)        | WL                 |

studies and a sample of studies disproportionately comprised of non-inferiority trials, so these studies were included for reasons of literature coverage and to attain a representative sample of studies.

There are several suggestions for future research in light of the outcomes from this NMA. A particular strength of

the network approach is that it can highlight where future comparisons are needed. The suboptimal connectivity illustrated by the network suggests that more direct studies (ie comparisons of psychotherapies head-to-head) are required. It is also evident that there is little utility in the continued use of control conditions (ie waitlist or ACTST),

TABLE 4 Ranking of network estimates of efficacy and acceptability compared to waitlist

| Efficacy | NMA estimate |                     |          |          |               | Acceptability |                   |       |       |      |
|----------|--------------|---------------------|----------|----------|---------------|---------------|-------------------|-------|-------|------|
|          | Condition    | NMA estimate (SMID) | CI lower | CI upper | Rank efficacy | Condition     | NMA estimate (OR) | Lower | Upper | Rank |
|          | MCT          | <u>2.32</u>         | 1.29     | 3.36     | 1             | WET           | 3.24              | 0.94  | 11.14 | 1    |
|          | CPT          | <u>1.67</u>         | 1.12     | 2.23     | 2             | NET           | 1.63              | 0.73  | 3.65  | 2    |
|          | WET          | <u>1.46</u>         | 0.70     | 2.22     | 3             | TAU           | 1.43              | 0.77  | 2.68  | 3    |
|          | DET          | <u>1.28</u>         | 0.02     | 2.54     | 4             | IPT           | 1.42              | 0.45  | 4.47  | 4    |
|          | PE           | <u>1.27</u>         | 0.97     | 1.57     | 5             | BET           | 1.36              | 0.51  | 3.55  | 5    |
|          | IPT          | <u>1.23</u>         | 0.11     | 2.34     | 6             | TARGET        | 1.25              | 0.55  | 2.85  | 6    |
|          | CT           | <u>1.19</u>         | 0.65     | 1.72     | 7             | CBT           | 0.94              | 0.63  | 1.41  | 7    |
|          | EMDR         | <u>1.19</u>         | 0.86     | 1.53     | 8             | PDT           | 0.87              | 0.39  | 1.93  | 8    |
|          | SIT          | <u>1.07</u>         | 0.20     | 1.95     | 9             | EMDR          | 0.85              | 0.55  | 1.34  | 9    |
|          | PE-SIT       | <u>1.05</u>         | 0.20     | 1.91     | 10            | ACTST         | 0.68              | 0.44  | 1.05  | 10   |
|          | BET          | <u>1.03</u>         | 0.10     | 1.97     | 11            | CT            | 0.59              | 0.22  | 1.56  | 11   |
|          | STAIR-PE     | 1.01                | -0.23    | 2.26     | 12            | SIT           | 0.44              | 0.12  | 1.68  | 12   |
|          | TARGET       | <u>0.99</u>         | 0.12     | 1.85     | 13            | PE            | <u>0.44</u>       | 0.30  | 0.66  | 13   |
|          | NET          | <u>0.98</u>         | 0.52     | 1.43     | 14            | MCT           | 0.43              | 0.02  | 8.42  | 14   |
|          | VRET         | <u>0.82</u>         | 0.22     | 1.42     | 15            | CPT           | <u>0.39</u>       | 0.21  | 0.70  | 15   |
|          | PSYED        | <u>0.73</u>         | 0.13     | 1.34     | 16            | PSYED         | 0.36              | 0.13  | 1.02  | 16   |
|          | CBT          | <u>0.72</u>         | 0.39     | 1.06     | 17            | PE-SIT        | 0.35              | 0.09  | 1.38  | 17   |
|          | ACTST        | <u>0.65</u>         | 0.31     | 0.99     | 18            | DET           | 0.34              | 0.10  | 1.17  | 18   |
|          | PDT          | 0.55                | -0.61    | 1.71     | 19            | STAIR-PE      | 0.31              | 0.07  | 1.37  | 19   |
|          | TAU          | 0.26                | -0.20    | 0.73     | 20            | VRET          | <u>0.29</u>       | 0.14  | 0.59  | 20   |

*n.b.* Bold and underlined indicates significance  $p < 0.05$ .

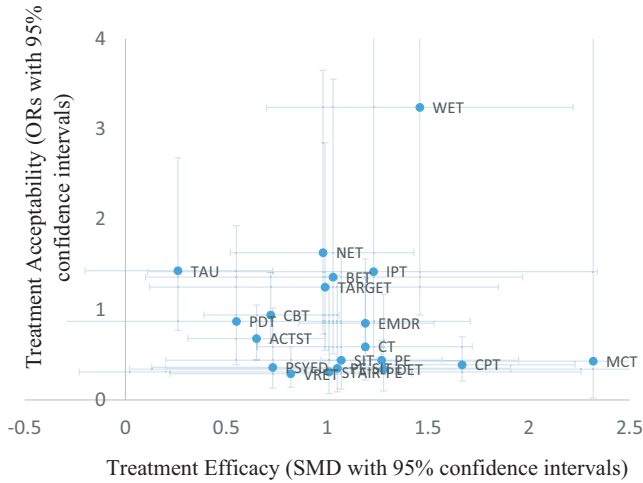
Abbreviations: Active Supportive Therapy (control); ACTST; BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PDT, Psychodynamic Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control).

given the large number of efficacious therapies available. New or emerging therapies need to demonstrate that they are as good or better than existing approaches, which would in turn strengthen the connectivity within the

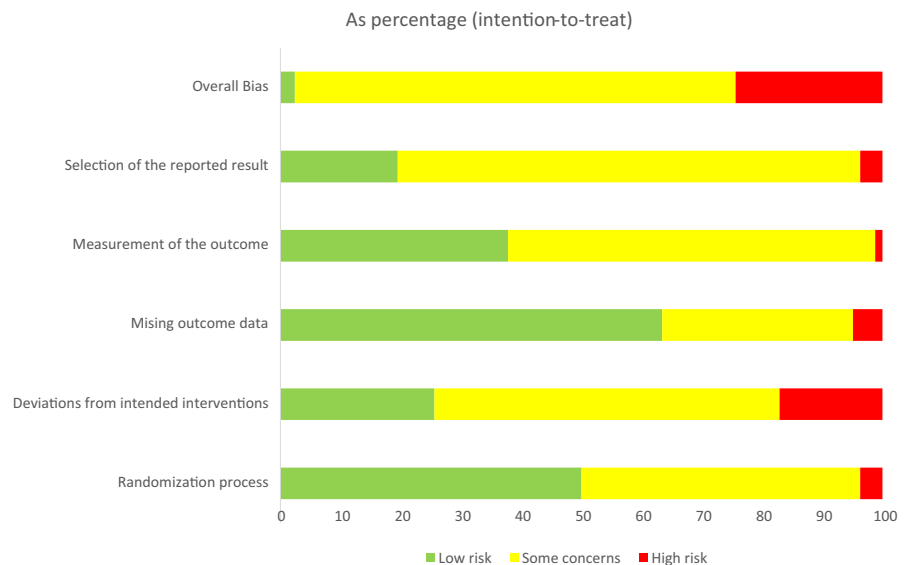
network of PTSD evidence. Moreover, while a consideration of long-term outcomes was beyond the scope of this project, a NMA of long-term follow-up of PTSD studies would also be useful to further assess the apparent equality of outcomes assumption, as well as promoting further comparisons of the long-term effects of psychotherapeutic intervention.

As additional dismantling studies continue to explore the efficacy of active components of therapy (eg trauma narrative writing, breathing retraining, in vivo exposure and psychoeducation), a component analysis would help disentangle the efficacy and acceptability of treatment components and to examine whether different *components* of psychotherapies result in comparable outcomes.

Our findings thus provide clarity on the PTSD psychotherapy literature that, until now, has not been examined with such granularity. The integration of direct and indirect evidence suggests that MCT is somewhat more efficacious than other psychotherapies in reducing PTSD symptoms; however, this finding is derived from only two studies which included MCT, an approach which seemingly has not been subjected to independent evaluation with respect to PTSD, and high rates of inconsistency and heterogeneity were noted with respect to our efficacy analyses. Written exposure and narrative therapies were also found to be the most tolerable and acceptable treatments. While the considerable heterogeneity and general quality of studies were poor, there was no evidence of violations of transitivity or overall network inconsistency assumption violations. These results should inform future research with head-to-head, non-inferiority and component dismantling studies being recommended for further exploration and integration of the PTSD evidence base.



**FIGURE 4** Ranking of efficacy and acceptability outcomes. ACTST; Active Supportive Therapy (control); BET, Brief Eclectic Therapy; CBT, Cognitive behavioural therapy; CPT, Cognitive Processing Therapy; CT, cognitive therapy; DET, Dialogical Exposure Therapy; EMDR, eye movement desensitization and reprocessing; IPT, Interpersonal Therapy; MCT, Metacognitive Therapy; NET, Narrative Exposure Therapy; PE, Prolonged Exposure; PE-SIT, Prolonged Exposure and Stress Inoculation Training; PSYED, Psychoeducation (control); PDT, Psychodynamic Therapy; SIT, Stress Inoculation Training; STAIR-PE, Skills training in affective and interpersonal regulation followed by prolonged exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; VRET, Virtual Reality Exposure Therapy; WET, Written Exposure Therapy; WL, Waitlist (control)



**FIGURE 5** Risk of bias judgements presented as percentages

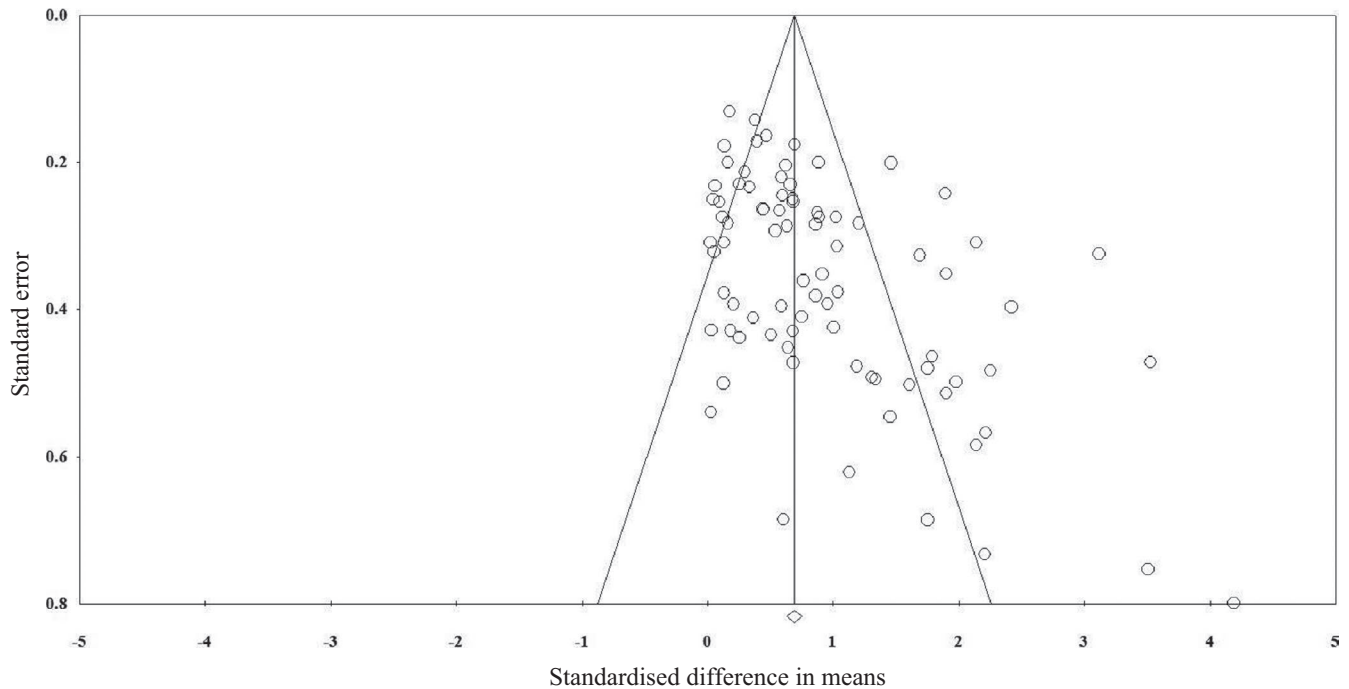


FIGURE 6 Funnel plot of small-study bias

#### ACKNOWLEDGEMENTS

The authors would like to thank Mr Matthew Bagg for his comments on an earlier draft. We would also like to thank Ms Fe Donaghue for her assistance with abstract review and risk of bias decisions. We also thank Associate Professor Kris Rogers for his assistance with statistical analysis and interpretation.

#### CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

#### PEER REVIEW

The peer review history for this article is available at <https://publons.com/publon/10.1111/acps.13366>.

#### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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### SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

**How to cite this article:** Jericho B, Luo A, Berle D. Trauma-focused psychotherapies for post-traumatic stress disorder: A systematic review and network meta-analysis. *Acta Psychiatr Scand*. 2021;00:1-24. <https://doi.org/10.1111/acps.13366>