Psychological treatments for post-traumatic stress disorder in adults: a network meta-analysis

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Abstract

Background: Post-traumatic stress disorder (PTSD) is a potentially chronic and disabling disorder affecting a significant minority of people exposed to trauma. Various psychological treatments have been shown to be effective, but their relative effects are not well established.

Methods: We undertook a systematic review and network meta-analyses of psychological interventions for adults with PTSD. Outcomes included PTSD symptom change scores post-treatment and at 1-4-month follow-up, and remission post-treatment.

Results: We included 90 trials, 6560 individuals and 22 interventions. Evidence was of moderate-to-low quality. Eye movement desensitisation and reprocessing [EMDR] (SMD -2.07; 95%CrI -2.70 to -1.44), combined somatic/cognitive therapies (SMD -1.69; 95%CrI -2.66 to -0.73), trauma-focused cognitive behavioural therapy [TF-CBT] (SMD -1.46; 95%CrI -1.87 to -1.05) and self-help with support (SMD -1.46; 95%CrI -2.33 to -0.59) appeared to be most effective in reducing PTSD symptoms post-treatment versus waitlist, followed by non-TF-CBT, TF-CBT combined with a selective serotonin reuptake inhibitor [SSRI], SSRIs, self-help without support, and counselling. EMDR and TF-CBT showed sustained effects at 1-4-month follow-up. EMDR, TF-CBT, self-help with support and counselling improved remission rates post-treatment. Results for other interventions were either inconclusive or based on limited evidence.

Conclusions: EMDR and TF-CBT appear to be most effective in reducing symptoms and improving remission rates in adults with PTSD. They are also effective in sustaining symptom improvements beyond treatment endpoint. Further research needs to explore the long-term comparative effectiveness of psychological therapies for adults with PTSD and also the impact of severity and complexity of PTSD on treatment outcomes.

INTRODUCTION

Worldwide, post-traumatic stress disorder (PTSD) has a lifetime prevalence of 3.9% in the general population, and 5.6% among those exposed to trauma (Koenen *et al.,* 2017). PTSD is associated with substantial levels of disability, poor quality of life and functional impairment (Alonso *et al.,* 2004). It is often comorbid with other mental disorders such as depression, anxiety, substance abuse (Kessler *et al.,* 1995), and has been associated with numerous physical health difficulties, including cardiovascular and metabolic disease (Ahmadi *et al.,* 2011).

Several psychological treatments are available for the management of PTSD in adults. Trauma-focused cognitive behavioural therapy (TF-CBT) is a broad class of psychological interventions that predominantly use trauma-focused cognitive, behavioural or cognitive-behavioural techniques and exposure approaches to treatment. Although some interventions place their main emphasis on exposure and others on cognitive techniques, most use a combination. There is considerable overlap in the proposed mechanisms underlying the effectiveness of the various versions of TF-CBT. TF-CBT includes therapies such as cognitive therapy (CT), cognitive processing therapy (CPT), exposure therapy/prolonged exposure, virtual reality exposure therapy, mindfulness-based CT and narrative exposure therapy. Other available treatments for PTSD include eye movement desensitisation and reprocessing (EMDR), interpersonal psychotherapy, present-centered therapy, self-help therapies such as internet-based TF-CBT and expressive writing, counselling, non-TF-CBT, which focuses on current symptoms of PTSD without re-visiting the trauma experience, and combined somatic/cognitive therapies such as emotional freedom techniques and thought field therapy; these are exposure-based therapies with both cognitive and somatic components that utilise the tapping of points on the body (Church *et al.*, 2013; Robson *et al.*, 2016).

A number of systematic reviews and meta-analyses have evaluated the effectiveness of psychological treatments for adults with PTSD (Bisson *et al.,* 2013; Cusack *et al.,* 2016; Forman-Hoffman *et al.,* 2018; Frost *et al.,* 2014; Gerger *et al.,* 2014; Khan *et al.,* 2018; Kuester *et al.,* 2016; Seidler and Wagner, 2006; Sijbrandij *et al.,* 2016; van Emmerik *et al.,* 2013). Commonly they find most robust evidence for the efficacy of individual TF-CBT and EMDR, and some evidence for non-TF-CBT, present-centered therapy and self-help. For other interventions (such as combined somatic/cognitive therapies) there has been more limited high quality research that did not always meet the inclusion criteria for these reviews, and therefore no robust conclusions on their effectiveness could be drawn. One review suggested that individual TF-CBT, EMDR and non-TF-CBT are more effective than other therapies for PTSD (Bisson *et al.,* 2013). Moreover, there was evidence to suggest superiority of EMDR over TF-CBT (Khan *et al.*, 2018). However, these findings were not confirmed in another review (Gerger *et al.*, 2014). With the exception of one review (Gerger *et al.,* 2014), these analyses have made limited comparisons across a narrow range of treatments using standard pairwise meta-analysis to synthesise evidence from randomised controlled trials (RCTs). This approach does not allow for the relative effectiveness across all treatments to be assessed, unless all possible comparisons have been evaluated in head-to-head trials.

Network meta-analysis (NMA) is a generalisation of pairwise meta-analysis to data structures that include, for example, A versus B, B versus C, and A versus C trials (Lu and Ades, 2004). NMA strengthens inferences concerning the relative effect of two treatments by including both direct and indirect treatment comparisons. This means that NMA allows estimation of the relative effects of treatments that may not have been directly compared in RCTs. Simultaneous estimation of all relative effects for any number of treatments is possible provided that treatments are connected in a single ‘network of evidence’ - that is, every treatment is linked to at least one of the other treatments under assessment through direct comparisons (Caldwell *et al.,* 2005; Mavridis *et al.,* 2015).

The objective of this study was to examine the relative effectiveness of psychological treatments for PTSD in adults using NMA techniques. The analyses presented here supported the updating of national guidance for PTSD in England (National Institute for Health and Care Excellence, 2018a). The guideline was developed by a guideline committee, an independent multi-disciplinary group of clinical academics, health professionals and service user and carer representatives with expertise and experience in the field of PTSD.

METHODS

Search strategy

A search for RCTs of treatments for people with clinically important post-traumatic stress symptoms was conducted in the following databases: MEDLINE, Embase, PsycINFO, CINAHL and The Cochrane Library. Databases were searched using relevant medical subject headings, free-text terms and a study design filter. The aim of the search was to update the evidence included in the previous National Institute for Health and Care Excellence (NICE) PTSD guideline, published in 2005. The search was undertaken in January/February 2017 with re-runs performed in January 2018. Online Supplementary Appendix 1 provides full details of the databases and search terms used. The reference lists of all relevant systematic reviews were hand-searched for any additional eligible studies. Clinical trial registries (ISRCTN and ClinicalTrials.gov) were also hand-searched to identify any relevant unpublished trials and authors were contacted to request study reports (where these were not available online). Primary authors of published included studies were also contacted to request outcome data where these could not be extracted.

Selection criteria for the systematic review and the network meta-analysis

A systematic review of psychological, psychosocial and other non-pharmacological interventions targeted at clinically important post-traumatic stress symptoms in adults more

than one month after a traumatic event was carried out in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Moher *et al.,* 2009). Eligible populations included adults with either a diagnosis of PTSD according to the Diagnostic and Statistical Manual of Mental Disorders (DSM), the World Health Organization (WHO) International Classification of Diseases (ICD) or similar criteria, or with the presence of clinically significant PTSD symptoms, as indicated by baseline scores above a pre-defined threshold on a validated PTSD symptom scale. If some, but not all, of a study's participants had clinically important PTSD symptoms, the study would be included if at least 80% of participants had clinically important PTSD symptoms or if disaggregated data only for those with PTSD could be extracted from the paper. If less than 80% of the participants had clinically important PTSD symptoms, or if disaggregated data only for those with PTSD were not available, then the mean baseline PTSD symptom score was used and a study was included in the review if this mean was above a pre-defined clinical threshold. Primary outcomes for the review included PTSD symptom endpoint or change scores on a validated PTSD scale; response to treatment; and recovery or remission defined either as the number of people no longer meeting diagnostic criteria for PTSD, or with PTSD symptom scores below the threshold on a validated scale.

For quality assurance of study identification, and in accordance with NICE guidance (National Institute for Health and Care Excellence, 2014), the titles and abstracts of identified studies were screened by two reviewers against inclusion criteria specified in the guideline review protocols until a good inter-rater reliability was observed (percentage agreement $\geqslant$ 90%). Initially, a random 10% of references were double-screened and inter-rater agreement was good; therefore, the remaining references were screened by one reviewer. All primary-level studies included after the first citation scan were acquired in full and re-evaluated for eligibility at the time of being entered into a study database (standardised template created in Microsoft Excel). At least 10% of data extraction (including data informing the risk of bias assessment) was double-coded. Discrepancies or difficulties with coding were resolved

through discussion between reviewers or the opinion of a third reviewer was sought. Data were extracted on study characteristics, intervention details, outcome data, and risk of bias.

For the NMA, we considered only first-line psychological treatments offered to adults with a diagnosis of PTSD or clinically important post-traumatic stress symptoms more than three months after trauma. Pharmacological and combined psychological and pharmacological treatments that were linked in the treatment network were also considered. Hypnotherapy, psychosocial interventions (meditation, mindfulness-based stress reduction, supported employment, peer and practical support) and physical interventions (exercise, yoga, acupuncture, bio-neuro-feedback and repetitive transcranial magnetic stimulation) were not included in the analysis as they were not considered to be alternative, first-line treatments for the management of PTSD in adults. Relaxation was included as a control intervention that provided additional indirect comparisons across interventions of interest.

Interventions in the TF-CBT class were not considered separately according to their type. Although the specific interventions that make up a class do not include exactly the same content or follow the same manual, they use the same broad approach and there is considerable overlap in the proposed mechanisms; the efficacy of interventions within the class was therefore considered to be equivalent. Hence, in the analyses presented here, TF-CBT is considered as an umbrella term and forms one node in the network. For the analyses that informed the NICE clinical guideline on PTSD, we divided the TF-CBT class by number of sessions and format of delivery and created different nodes in the network according to the intensity of TF-CBT, as these differences in resource use comprised practical considerations that informed the guideline economic analysis, and, subsequently, practice recommendations.

The guideline systematic review included two categories of RCTs: those that compared interventions or their combinations delivered as the sole treatment in a trial arm versus

waitlist or another inactive control or active intervention; and those comparing interventions added to treatment as usual (TAU) versus TAU alone or versus an inactive control added to TAU or versus another active intervention added to TAU. The definition of TAU varied widely across studies, including minimum contact comparison, a mixture of psychoeducation and supportive counselling, medication, substance misuse treatment, any treatment outside the research setting or any treatment except the intervention assessed in the study. To reduce heterogeneity attributable to the diversity of TAU across RCTs, comparisons involving TAU alone or combined with a control or with an intervention of interest were not included in the NMA even if they provided links in the network.

The NMA considered two outcomes: PTSD symptom change scores and remission. Data on these outcomes were mostly reported at treatment endpoint. Moreover, a number of studies reported data on one or both of these outcomes at 1-4-month follow-up. PTSD symptom change scores between baseline and 1-4-month follow-up were adequate to inform a NMA; in contrast, remission data at 1-4-month follow-up were very sparse (the network only included 10 studies, 7 interventions and 572 participants; the only active intervention that had been tested on more than 100 participants was TF-CBT). Beyond 1-4 months of follow-up, available data were very sparse for both outcomes. Based on the availability of data for the two outcomes of interest, three separate NMAs were conducted on the following outcomes and time points:

- PTSD symptom change scores between baseline and treatment endpoint
- PTSD symptom change scores between baseline and 1-4-month follow-up
- Remission at treatment endpoint

If both were available in the same study, PTSD symptom change scores derived from self-rated symptom scales were prioritised over those derived from clinician-rated symptom scales, because the former were deemed to better capture symptoms experienced by adults

with PTSD, according to the NICE guideline committee. Similarly, intention-to-treat (ITT) data, obtained after imputation of missing data, were prioritised over completer data, if both were available in the same study.

The guideline study protocol was published on the NICE website during consultation of the draft guidance with registered stakeholders (https://www.nice.org.uk/guidance/ng116/history). The systematic review protocol and the additional inclusion criteria applied for the NMA are provided in online Supplementary Appendix 2.

Statistical analysis

NMAs were conducted within a Bayesian framework using a generalised linear model (GLM) approach (Dias *et al.,* 2013a), estimated using Markov Chain Monte Carlo simulation techniques implemented in WinBUGS 1.4.3 (Lunn *et al.,* 2000; Spiegelhalter *et al.,* 2003). An overview of the approach and methods adopted is provided below. Details of the statistical analysis and WinBUGS codes used to synthesise changes in PTSD symptom scores and dichotomous remission data are reported in online Supplementary Appendix 3.

For the synthesis of continuous data (changes in PTSD symptom scores), a linear model with a normal likelihood and identity link was used (Dias *et al.,* 2018). Because the RCTs included in the NMAs used different continuous scales to report change in PTSD symptoms, relative effects were expressed in the form of the Standardised Mean Difference (SMD) between pairs of interventions. For the synthesis of dichotomous data (remission), a linear model with binomial likelihood and logit link was used (Dias *et al.,* 2013a; Dias *et al.,* 2018). The output of this analysis was the set of log-odds ratios (LORs) between pairs of interventions. The suitability of fixed and random effects models in terms of model fit was assessed and compared, and the most suitable model (fixed or random effects) was then selected for the analysis of each outcome.

For each analysis we report posterior mean relative effects (either SMD or LOR) with 95% credible intervals (CrI). We also report posterior mean ranks with 95%CrI for every treatment tested on at least 100 individuals in each analysis, where a rank of 1 indicates highest effectiveness. We only included interventions tested on at least 100 people in the ranking, as this was deemed the minimum adequate evidence to draw conclusions on effectiveness. Results were interpreted in terms of 'evidence of effect', rather than 'statistical significance' (Pike, 2019), and this was determined based on whether the 95%CrI crossed the line of no effect. Although no cut-off points were used in order to judge the magnitude of effect, in general a SMD value of 0.2 to 0.3 was deemed to indicate a small effect, a value around 0.5 a medium effect, and a value of 0.8 and above a large effect (Cohen, 1969).

Inconsistency checks

A basic assumption of NMA methods is that direct and indirect evidence estimate the same parameter, that is, the relative effect between A and B measured directly from an A versus B trial is the same as the relative effect between A and B estimated indirectly from A versus C and B versus C trials. In other words, it is assumed that there is agreement between the direct and indirect evidence informing the treatment contrasts (this has also been termed the similarity or transitivity assumption (Mavridis *et al.,* 2015)). Inconsistency arises when there is a conflict between direct evidence (from an A versus B trial) and indirect evidence (gained from A versus C and B versus C trials) and can only be statistically assessed when there are closed loops of evidence on 3 treatments that are informed by at least 3 distinct trials (van Valkenhoef *et al.,* 2016). The assumption of consistency between indirect and direct evidence was explored by undertaking global inconsistency tests (Dias *et al.,* 2010; Dias *et al.,* 2013b) and local tests through node-splitting (Dias *et al.,* 2013b; van Valkenhoef and Kuiper, 2016). When evidence of inconsistency was found, studies contributing to loops of evidence where there might be inconsistency were checked for data accuracy. Analyses were repeated if corrections in the data extraction were made. If evidence of inconsistency

was still present following data corrections, no studies were excluded from the analysis, as their results could not be considered to be less valid than those of other studies solely because of the inconsistency findings; nevertheless, the presence of inconsistency in the NMA was highlighted and results were interpreted accordingly.

Details of the methods used to test inconsistency and the WinBUGS codes of the inconsistency models are provided in online Supplementary Appendix 4.

Pairwise sub-analyses

For the purposes of the NICE clinical guideline, a number of sub-analyses of the pairwise meta-analyses were considered, including sub-analysis by specific intervention type for the TF-CBT comparisons, and sub-analyses by trauma type and multiplicity of index trauma for all interventions. It is beyond the scope of this paper to explore all sub-analyses but for illustrative purposes, exploratory sub-analyses have been conducted by specific TF-CBT intervention, method of analysis (ITT versus modified ITT versus completer) and multiplicity of index trauma (single or multiple) for the TF-CBT versus waitlist comparison for the PTSD symptom change scores between baseline and treatment endpoint outcome. This comparison and outcome were selected as it was the only pairwise meta-analysis with sufficient studies to enable meaningful comparison between subgroups. A sub-analysis by trauma type was not included because there were almost as many trauma types as studies and as such the analysis was not interpretable.

RESULTS

Studies and treatments

The systematic literature search identified 715 studies potentially eligible for the systematic review, 529 of which were excluded. Ninety-six more studies were excluded as they did not meet criteria for the NMA, leaving 90 eligible studies on 22 interventions (including two

inactive controls) that reported one or more outcomes of interest (Figure 1). In 64% of the included studies, the study population comprised adults with a diagnosis of PTSD; in the remaining 36% of the included studies, the study population consisted of adults with clinically significant PTSD symptoms, as indicated by baseline scores above a pre-defined threshold on a validated PTSD symptom scale. The characteristics of included studies are reported in online Supplementary Appendix 5. A list of excluded studies, with reasons for exclusion, is provided in online Supplementary Appendix 6. Online Supplementary Appendix 7 shows the full data included in each NMA.

Risk of bias assessment

All 90 included trials were assessed for risk of bias using the Cochrane risk of bias tool (Higgins and Green, 2011). Sequence generation and allocation concealment were adequately described in 36 and 29 trials, respectively. All trials were regarded as at high risk of bias for lack of participant and provider masking. In 20 studies, a clinician-rated scale was used, with assessors being unaware of treatment assignment. In seven trials it was unclear if the assessors were blinded, and in 63 studies a self-rated scale was used meaning that raters were non-blind but were less likely to have a conflict of interest in terms of detection bias. Attrition was high in 11 trials and unclear in 35 studies. However, we favoured ITT analysis and, for the remission outcome, we conservatively treated drop-outs as failing to remit. Of the studies that reported PTSD symptom change scores, approximately 60% reported ITT data, or ITT data were possible to estimate, with the remaining providing completer data only. Included trials reported a variety of outcomes. Only nine trials were registered on a trials database and reported all listed outcomes. Consequently, most studies were judged as being at high or unclear risk of reporting bias. Other potential biases were identified in seven studies; these included high risk of bias due to potential conflicts of interest or due to methodological limitations not otherwise captured. An overview of the trials' risk of bias assessment is provided in online Supplementary Appendix 8.

NMA model fit statistics

In all NMAs, the random effects model provided a better fit over the fixed effect model and fit the data well. However, the between-trial standard deviation (SD), which measures the heterogeneity of treatment effects estimated by trials within contrasts, was high when compared with the size of the intervention effect estimates across all three analyses (posterior median SD: 0.93 in the NMA of PTSD changes between baseline and treatment endpoint; 0.59 in the NMA of changes in PTSD symptom scores between baseline and 1-4-month follow-up; 1.05 in the NMA of remission at treatment endpoint).

Details of model fit statistics are provided in online Supplementary Appendix 9.

Inconsistency checks

No evidence of inconsistency between direct and indirect evidence was found in the NMAs of changes in PTSD symptom scores at treatment endpoint and at follow-up. The NMA of remission at endpoint showed evidence of inconsistency between pooled direct and indirect estimates comparing TF-CBT, EMDR, and self-help without support. Direct effects in these comparisons were implausibly large and with very wide 95%CrI (e.g. mean LOR of EMDR versus TF-CBT -2.01, 95%CrI -4.01 to -0.01), a finding likely attributable to the small number and size of RCTs involved in these comparisons; indirect/NMA estimates for these comparisons are therefore likely to be more trustworthy.

Results of inconsistency checks are provided in online Supplementary Appendix 10.

Treatment outcomes

Results of the three analyses are presented in Tables 1-3, as posterior mean effects with 95%CrI of each intervention versus waitlist, which served as the reference. In each analysis, interventions have been ordered from the most to the least effective, according to their posterior mean effect versus waitlist. The tables also show the number of participants

randomised to each intervention across RCTs included in each analysis, and the number of RCTs that assessed each intervention in each NMA. In each analysis, ranking is provided for all interventions tested on at least 100 individuals.

Changes in PTSD symptom scores between baseline and treatment endpoint

The network of changes in PTSD symptom scores between baseline and treatment endpoint was formed by 71 RCTs with 151 arms that assessed 19 interventions tested on a total of 4,700 participants (Figure 2a). The majority of the evidence was on TF-CBT (N=903 in 29 trials), followed by self-help without support (N=335 in 11 trials) and EMDR (N=260 in 11 trials). There was also good- or moderately good-sized evidence on counselling (N=278 in 9 trials), non-TF-CBT (N=209 in 7 trials), self-help with support (N=198 in 5 trials), combined somatic/cognitive therapies (N=237 in 4 trials), selective serotonin reuptake inhibitors [SSRIs] (N=166 in 5 trials), psychoeducation (N=152 in 2 trials) and TF-CBT combined with SSRIs (N=115 in 3 trials). All other interventions were tested on fewer than 100 participants each. Of the 71 trials, 26 recruited participants with a single trauma and 38 recruited participants with multiple traumas; the remaining 7 studies did not report this kind of information.

For interventions tested on N≥100 each with evidence of effect versus waitlist (i.e. 95%CrI that did not cross the line of no effect), the ranking (from the most to the least effective) was as follows: EMDR (mean SMD versus waitlist -2.07, 95%CrI -2.70 to -1.44), combined somatic/cognitive therapies (mean SMD versus waitlist -1.69, 95%CrI -2.66 to -0.73), TF-CBT (mean SMD versus waitlist -1.46, 95%CrI -1.87 to -1.05), self-help with support (mean SMD versus waitlist -1.46, 95%CrI -2.33 to -0.59), non-TF-CBT (mean SMD versus waitlist -1.22, 95%CrI -1.95 to -0.49), TF-CBT combined with a SSRI (mean SMD versus waitlist -1.21, 95%CrI -2.35 to -0.07), SSRIs (mean SMD versus waitlist -1.14, 95%CrI -2.09 to -0.19), self-help without support (mean SMD versus waitlist -0.91, 95%CrI -1.67 to -0.15) and counselling (mean SMD versus waitlist -0.73, 95%CrI -1.41 to -0.05) (Table 1).

Psychoeducation was the only intervention with an adequate evidence base (N=152) and inconclusive effect versus waitlist. Although results suggest a trend towards the superiority of EMDR over other active interventions, no evidence of differential effects between EMDR and other treatments with a large evidence base was found. Comparisons between active treatments suggested differences in effect only between EMDR and counselling (mean SMD -1.34, 95%CrI -2.19 to -0.49) and between TF-CBT and counselling (mean SMD -0.73, 95%CrI -1.37 to -0.09).

Metacognitive therapy (mean SMD -3.04, 95%CrI -5.09 to -0.98) and present-centered therapy (mean SMD -1.42, 95%CrI -2.45 to -0.40) also showed large effects versus waitlist with 95%CrI that did not cross the zero line; however, these effects were based on a more limited evidence base (N=10 and 99, respectively).

Overall, results were characterised by relatively wide 95%CrI around mean effects and ranks; for example, TF-CBT mostly ranked between the 2nd and 8th place in different iterations of the NMA model. High between-study heterogeneity may have contributed to the uncertainty around mean effects.

Changes in PTSD symptom scores between baseline and 1-4-month follow- up

The network of changes in PTSD symptom scores between baseline and 1-4-month follow-up included 28 RCTs, 2,315 participants and 15 interventions (Figure 2b). TF-CBT was again the intervention with the largest evidence base (N=753 in 13 trials); other interventions with moderately good-sized evidence base were counselling (N=205 in 4 trials), non-TF-CBT (N=123 in 4 trials), EMDR (N=121 in 4 trials) and psychoeducation (N=183 in 3 trials). All other interventions were tested on fewer than 100 participants each. Of the 28 trials, 10 and 15 recruited participants with a single and multiple trauma, respectively; 3 studies did not provide any information on participants' number of previous traumas.

Of the interventions tested on N≥100 each, only two showed evidence of effect versus waitlist: EMDR (mean SMD -1.12, 95%CrI -1.94 to -0.27) and TF-CBT (mean SMD -0.73, 95%CrI -1.23 to -0.25) (Table 2). Comparison between the two showed no evidence of difference in effect (mean SMD -0.39 favouring EMDR, 95%CrI -1.30 to 0.54). Interventions with N≥100 but inconclusive effects versus waitlist included psychoeducation, non-TF-CBT and counselling.

Of interventions with a limited evidence base (each tested on N<100), couple intervention, self-help with support and behavioural therapy also showed evidence of effectiveness against waitlist.

This analysis was also characterised by high between-study heterogeneity and uncertainty that was reflected in wide 95%CrI around mean effects and rankings across interventions.

Remission at treatment endpoint

The NMA of remission at treatment endpoint consisted of 34 studies, 2,249 participants and 16 interventions (Figure 2c). TF-CBT was tested on N=601 participants in 21 trials; other interventions with a moderately good-sized evidence base were counselling (N=150 in 6 trials); EMDR (N=132 in 5 trials); and self-help with support (N=105 in two trials). All other interventions were tested on fewer than 100 participants each. Of the 34 trials, 15 and 16 recruited participants with a single and multiple trauma, respectively; 3 studies did not provide any information on participants' number of previous traumas.

All interventions with an adequate evidence base (N≥100) showed evidence of large effects versus waitlist. Their order, from the most to least effective was: EMDR (mean LOR versus waitlist 3.38, 95%CrI 2.04 to 4.84), TF-CBT (mean LOR versus waitlist 2.46, 95%CrI 1.79 to 3.19), self-help with support (mean LOR versus waitlist 1.76, 95%CrI 0.03 to 3.49), and counselling (mean LOR versus waitlist 1.34, 95%CrI 0.20 to 2.51). Comparisons between

active treatments suggested differences in effect only between EMDR and counselling (mean LOR 2.04, 95%CrI 0.37 to 3.79) and between TF-CBT and counselling (mean LOR 1.12, 95%CrI 0.12 to 2.15).

Several interventions with limited evidence (each tested on N<100) showed large effects versus waitlist on the remission outcome; these included psychodynamic therapy, non-TF-CBT, relaxation, IPT and present-centered therapy.

As with previous outcomes, there was uncertainty in the results as suggested by very wide 95%CrI around mean effects and rankings across all interventions (Table 3). There was also very high between-study heterogeneity.

Results between all pairs of treatments examined in the NMAs and also results from indirect and, where available, direct (head-to-head) comparisons are reported in online Supplementary Appendix 11. For information, results of the NICE guideline analyses are shown in online Supplementary Appendix 12.

Pairwise sub-analyses

Exploratory sub-analyses of the pairwise meta-analysis comparing trauma-focused CBT and waitlist for PTSD symptom change scores between baseline and endpoint suggests no significant subgroup differences for different specific TF-CBT interventions (including CPT, cognitive therapy, prolonged exposure, narrative exposure therapy, brief eclectic psychotherapy, and non-branded individual and group CBT). There were also no significant subgroup differences between ITT, modified ITT and completer analysis, or for single compared to multiple incident index trauma. See online Supplementary Appendix 13 for forest plots of these sub-analyses.

DISCUSSION

Overview of findings

This study aimed to identify the relative treatment effects of various psychological treatments for PTSD. EMDR, combined somatic/cognitive therapies, TF-CBT and self-help with support appeared to have the greatest effects in reducing PTSD symptoms post-treatment, followed by non-TF-CBT, combined TF-CBT/SSRIs, SSRIs, self-help without support and counselling. No evidence of difference in effect post-treatment was identified between interventions, with the exception of EMDR and TF-CBT, both of which were found to be superior to counselling. Analysis of follow-up data suggested that EMDR and TF-CBT sustained this effect at 1-4 months. EMDR, TF-CBT, self-help with support, and counselling were also effective in achieving remission from PTSD at treatment endpoint. Results for other interventions were either inconclusive or based on limited evidence.

Commonalities across effective psychotherapies for PTSD include psychoeducation, imaginal exposure, and cognitive processing, restructuring and/or meaning making (Schnyder *et al.*, 2015). Moreover, all treatments found to be effective comprised structured therapies, delivered by healthcare professionals who have completed specialist training and who have access to regular supervision and undertake appropriate continuing professional development (CPD) accreditation. Combined somatic/cognitive therapies are exposure-based therapies with cognitive and somatic components, thus they share some characteristics with the TF-CBT class. All except one of the RCTs on self-help with support included in the NMA focused on computerised TF-CBT, consistent with TF-CBT delivered by a therapist. On the other hand, of the 13 trials on self-help without support, only 4 focused on computerised TF-CBT. Further to the presence or absence of the TF-CBT element in self-help interventions for PTSD, which may have been the driver of their effectiveness, there is evidence that facilitated self-help is more effective than self-help without support in the treatment of anxiety disorders and depression (National Institute for Health and Care Excellence, 2011).

Counselling was found to be amongst the least effective interventions. This can be attributed to counselling's non-directive person-centred approach, which is less likely to help the person overcome avoidance (which is one of the criteria for PTSD), and thus less likely to reduce PTSD symptoms. However, in 10 out of the 11 RCTs examining counselling across the 3 NMAs, counselling served as a control treatment to other active interventions, primarily TF-CBT, and therefore it is possible that counselling's effectiveness has been underestimated to some extent, due to researcher allegiance.

Comparison with findings of other reviews

The results of our analysis are consistent with those of other published reviews, according to which TF-CBT interventions and EMDR have the strongest evidence of effectiveness post-treatment and at short follow-up, both showing highest effects versus inactive controls compared with other psychological interventions (Bisson *et al.,* 2013; Cusack *et al.,* 2016; Forman-Hoffman *et al.,* 2018). This finding is also in line with five recently published PTSD clinical practice guidelines (as compared in Hamblen *et al*., 2019). Four of these five guidelines, including the NICE clinical guideline (International Society for Traumatic Stress Studies, 2019; National Institute for Health and Care Excellence, 2018a; Phoenix Australia Centre for Posttraumatic Mental Health, 2013; Departments of Veterans Affairs and Defense, 2017), make recommendations of equal strength for TF-CBT and EMDR for adults, whereas in one guideline (American Psychological Association, 2017) TF-CBT interventions are favoured with a strong recommendation while EMDR has been given a moderate rating. Conversely, Khan *et al*. (2018) suggests that EMDR may be more effective than TF-CBT, however this finding was not supported by another publication that employed NMA techniques (Gerger *et al.*, 2014). The latter review is in agreement with our findings, which show no evidence of difference between EMDR and TF-CBT. Further research is needed to establish any reliable difference between the efficacy of TF-CBT and EMDR.

There is some published evidence suggesting that non-TF-CBT (Bisson *et al.,* 2013), present-centered therapy (Frost *et al.,* 2014) and self-help (mainly internet-based TF-CBT and expressive writing therapy) (Kuester *et al.,* 2016; Sijbrandij *et al.,* 2016; van Emmerik *et al.,* 2013) are also effective options in the treatment of PTSD in adults. There are also recommendations for other psychotherapies in recently published clinical PTSD guidelines, although there was less consistency than for TF-CBT and EMDR (Hamblen *et al*., 2019). For instance, three of the guidelines included recommendations for non-trauma focused psychotherapies (International Society for Traumatic Stress Studies, 2019; Phoenix Australia Centre for Posttraumatic Mental Health, 2013; Departments of Veterans Affairs and Defense, 2017). This evidence, from both published reviews and clinical guidelines, is in line with our findings that suggest that non-TF-CBT, present-centered therapy and self-help (with or without support) are effective relative to waitlist for improving PTSD symptoms.

Our findings on the effectiveness of combined somatic/cognitive therapies are consistent with results reported in the systematic review by Forman-Hoffman *et al*. (2014), who carried out separate evaluations of the emotional freedom technique and thought field therapy (defined in the review as 'imagery rehearsal therapy') and found very limited evidence on both interventions which, nevertheless, indicated that these might be effective in the treatment of PTSD symptoms.

Another published NMA of treatments for adults with PTSD suggested that several interventions are effective in the management of PTSD (Gerger *et al.,* 2014). That study considered a more limited number of interventions than our analysis, including three types of TF-CBT (CBT, CT, exposure therapy) that were assessed separately but also as a TF-CBT class, EMDR, stress management (relaxation or biofeedback), supportive therapies (comprising psychotherapy placebos and counselling), and other psychological therapies (including psychodynamic, client-centered, gestalt and other forms). The authors reported that all assessed interventions were more effective than waitlist; TF-CBT interventions and

EMDR were more effective than stress management and supportive therapies, but no difference was observed between TF-CBT and EMDR. The robustness of evidence varied considerably between different interventions and between-trial heterogeneity was high. These findings are in line with our results. The study considered only PTSD symptom severity at end of treatment or at maximum of 1 month post-treatment, whereas our NMAs considered PTSD change scores at treatment endpoint and at 1-4-month follow-up and also remission at end of treatment. Therefore, our conclusions cover a wider range of interventions and outcomes and longer-term effects, where available.

Our findings are also broadly consistent with the results of a NMA of psychological interventions in children and young people with PTSD, which suggested that TF-CBT, in particular individual forms, was most effective in the management of PTSD in youth, whereas EMDR was effective but to a lesser extent; counselling did not appear to be effective compared with waitlist. Results in young populations also suggested a large positive effect for emotional freedom technique (a form of combined somatic/cognitive therapy), but this finding was based on very limited evidence (Mavranezouli *et al.*, 2020).

Overall, our results and conclusions are in agreement with previously published meta-analyses in this area. Small differences between our study results and those of other studies (which, nevertheless, led to very similar conclusions) have potentially arisen from differences in inclusion criteria relating to the population (e.g. we included only adult populations while some other studies did not apply any age restrictions or considered only children and young people with PTSD; we did not restrict to people with a formal diagnosis of PTSD while some other studies did), interventions (we used a wider range of interventions compared with other reviews and it is also possible that our categorisation into classes is different from that used in other studies), comparators (we excluded studies that used TAU as a comparator or as a component of an active arm), outcomes (we included continuous PTSD symptom change scores at endpoint and 1-4 month follow-up as well as dichotomous remission, whereas

some of the other studies included only continuous data and/or only treatment endpoint data) and study characteristics (we included studies with a sample size of at least 10 per arm, a criterion not applied in most, if not all, the other reviews), as well as differences in the method of analysis (we used NMA techniques whereas the vast majority of the other reviews in the area relied on pairwise meta-analysis of head-to-head comparisons).

Strengths and limitations of the analysis

To our knowledge, this is the first NMA of psychological treatments for adults with PTSD that was designed to inform a clinical guideline. The results of our NMAs further informed an economic analysis that assessed the cost-effectiveness of psychological interventions for adults with PTSD (Mavranezouli *et al., under review*). NMA techniques enabled evidence synthesis from both direct and indirect comparisons between interventions, and allowed simultaneous inference on all treatments examined in pairwise trial comparisons while respecting randomisation (Caldwell *et al.,* 2005; Lu and Ades, 2004). Inconsistency checks found no evidence of inconsistency between direct and indirect estimates in the NMAs of changes in PTSD symptoms post-treatment and at follow-up. This finding provides reassurance that the included studies were comparable across interventions, although it is acknowledged that, in agreement with the findings of other reviews, between-trial heterogeneity was high. On the other hand, we detected evidence of inconsistency in the NMA of remission post-treatment. However, we found that direct effects in this NMA were implausibly large and with very wide 95%CrI due to limitations in the direct evidence; therefore indirect/NMA evidence may be more trustworthy for the remission outcome. This means that results on this outcome (remission at treatment endpoint) should be treated with caution.

Between-trial heterogeneity was high across all analyses. This finding, which is consistent with previous reviews (Bisson *et al.*, 2013; Forman-Hoffman *et al.,* 2018; Gerger *et al.*, 2014), is likely to have been caused by heterogeneity across populations included in the

trials considered in our analysis, for example, in terms of the presence of a formal PTSD diagnosis, the baseline severity and complexity of PTSD symptoms, the type, extent and multiplicity of trauma exposure, the chronicity of symptoms and the presence of comorbidity. Moreover, the vast majority of the included studies did not distinguish between PTSD and complex PTSD, which ICD-11 (unlike DSM-5) now conceptualises as distinct diagnoses. This distinction is supported by evidence (Brewin *et al.*, 2017) but some disagreement about the validity of the construct amongst experts remains, as suggested by the discrepancy between the two classification systems (ICD-11 and DSM-5). We note that our review was undertaken before ICD-11 (and the distinction between PTSD and complex PTSD) was released (June 2018). Trials are likely to have varied widely in the proportion of participants with complex PTSD; this may have had an impact on the effectiveness of assessed interventions in each study and the heterogeneity across studies. Another factor potentially contributing to the high between-trial heterogeneity of our NMAs is the variability of interventions within each treatment node of the analysis (including different levels of intensity), and the difference across study settings, e.g. inpatient versus outpatient. This high between-trial heterogeneity may have contributed to the uncertainty in the mean relative effects, as reflected in the wide CrI for some comparisons in our analyses, and has limited our ability to draw firm conclusions on the relative effectiveness between interventions. However it is worth noting that, although exploratory in nature and limited to a single pairwise comparison, our sub-group analyses suggest that between-study heterogeneity cannot be accounted for solely by differences between specific TF-CBT interventions, based on the method of analysis (ITT versus completer), or by the multiplicity of index trauma (single versus multiple incident index trauma). This suggests that this heterogeneity is complex and further studies employing meta-regression techniques, ideally with access to individual patient data, are required to fully explore differences in effect estimates between studies.

We decided to analyse all TF-CBT interventions together, as a class, because, although they do not include exactly the same content or follow the same manual, they use the same broad approach; in grouping the interventions into a TF-CBT class we took the view that it is the core components of the treatments (e.g. exposure and cognitive restructuring) that make them effective. We also took into account that 'breaking' the solid evidence base for the TF-CBT class into smaller, separate pieces of evidence for specific interventions would unavoidably thin the evidence base and incur the risk of reducing the robustness of our conclusions on the effectiveness of interventions within the TF-CBT class relative to other types of treatment. Some reviews (for example Bisson *et al.*, 2013; Khan *et al.*, 2018) have followed our approach and have evaluated the overall effects of the TF-CBT class, rather than looking at the effects of specific interventions within the TF-CBT class separately. The Departments of Veterans Affairs and Defense (2017) guideline also grouped TF-CBT interventions together but chose to list the specific treatments for which there was the strongest support, which is a similar approach to the one taken by the NICE clinical guideline (Hamblen et al. 2019). There is now an emerging number of reviews that have attempted to evaluate the effects of distinct interventions within the TF-CBT class (e.g. American Psychological Association, 2017; Cusack *et al.*, 2016; Forman-Hoffman *et al.* 2018), with another review assessing the overall effect of the TF-CBT class, and also effects of individual forms within TF-CBT class where evidence was adequate to allow sub-group analysis (International Society for Traumatic Stress Studies, 2019). These reviews have carried out separate evaluations of various TF-CBT interventions such as CPT, CT, prolonged exposure and mixed TF-CBT which has elements of different types of CBT. The majority of these studies have found evidence on the effectiveness of all interventions within the TF-CBT class but none of the studies reported any evidence on differential effects between different types of TF-CBT. A previously published NMA in the area (Gerger *et al.*, 2014), which evaluated CBT, exposure and CT separately and made indirect comparisons between them, identified no differences in relative effects. The authors then merged CBT and CT into one category of CBT with a focus on cognitions and reanalysed the data; no

difference was found between CBT with focus on cognitions and exposure. These results suggest that there may be no difference in the effectiveness of different interventions within the TF-CBT class, and supports our decision to consider TF-CBT interventions together, as one class, in our analysis. It is worth noting here that our exploratory post-hoc sub-analysis by specific TF-CBT intervention for all studies including a waitlist control (see Appendix 13A) also suggests no significant sub-group difference between specific TF-CBT intervention types.

In our analyses we prioritised self-reported over clinician-rated scale data, where possible, as self-reported outcomes were deemed to better capture symptoms experienced by adults with PTSD, based on the NICE guideline committee's expert opinion. This approach is in line with a previously published NMA in the same area (Gerger *et al.*, 2014), although other reviews have conducted separate analyses for clinician-rated and self-reported outcome data (Bisson *et al.*, 2013; Forman-Hoffman *et al.*, 2018), or even prioritised clinician-rated outcomes over self-reported ones, where both were available, in the primary analysis (International Society for Traumatic Stress Studies, 2019). It is acknowledged that in other mental health areas, such as depression, it is recommended that both clinician-rated and self-reported outcomes be assessed as they have been shown to capture different aspects of treatment outcome (Cuijpers *et al.*, 2010; Uher *et al.*, 2012). A sub-group analysis conducted by Gerger *et al.* (2014) showed that the differences between effect sizes in trials reporting self-reported outcomes versus those reporting clinician-rated ones were small and non-significant (p=0.58) and within-trial heterogeneity was not affected by inclusion of only one type of outcome in the analysis. Therefore, we are confident that our choice of prioritising self-reported over clinician-rated outcomes has not had a negative impact on results.

In our NMA we did not include TAU, either alone or combined with a control or with an intervention of interest; this is because the definition of TAU varied considerably across

trials, so that inclusion of TAU in the networks was expected to considerably increase heterogeneity and reduce robustness of the results. Omission of studies that assessed interventions alone or combined with TAU versus TAU has limited the evidence base of our analyses. However, the number of included studies (which did not include TAU) was higher than the number of excluded studies that included TAU; included 'non-TAU' studies also considered a higher number of participants than the excluded 'TAU' studies. Therefore, our analyses have considered a significant amount of evidence without introducing heterogeneity attributable to the diversity of TAU.

The studies included in the NMAs were subject to risk of bias, in particular selection and reporting bias. In none of the studies were participants blinded, which was unavoidable due to the nature of the interventions. In most trials assessors were not blinded either. As described earlier, self-rated PTSD symptom scores were preferred to clinician-rated ones if both were reported in a study, as they were deemed to better capture symptoms experienced by people with PTSD. However, self-rated assessment cannot be blinded in trials of psychological interventions; on the other hand, raters were less likely to have a conflict of interest in terms of detection bias. The quality and limitations of RCTs included in the analyses need to be considered when interpreting the results.

For the change in PTSD symptom score outcome we prioritised ITT over completer data where possible, nevertheless, for approximately 40% of the studies we used completer data as only these were available. An exploratory sub-group analysis of the TF-CBT versus waitlist comparison for PTSD symptom change scores between baseline and treatment endpoint suggests no statistically significant subgroup difference between the results of studies using ITT, modified ITT and completer analysis (see Appendix 13B). This is also consistent with a sub-group analysis conducted in the context of a NMA of treatments for PTSD by Gerger *et al.* (2014) that showed that the differences between effect sizes in trials reporting ITT data versus those reporting completer data were small and non-significant

(p=0.47), although within-trial heterogeneity was somewhat reduced by inclusion of ITT data only (from τ^2=0.30 when both ITT and completer data were included in the analysis it fell at τ^2=0.21 when only ITT data were analysed). Our ITT approach for the dichotomous remission analysis meant that all participants were analysed in the group to which they had been randomised and that study non-completers were assumed to have failed to remit. This strategy provides a conservative estimate of treatment effects compared with completer analysis (Nüesch *et al.*, 2009), assuming that active interventions have a higher risk of drop-out compared with control conditions (this higher risk could be attributable to side effects, unacceptability of the active intervention, or to people discontinuing treatment early if their symptoms improve).

Evidence on the longer-term effectiveness of treatments for PTSD is limited, as follow-up data are sparse. Adequate evidence on remission rates at 1-4-month follow-up was only available for TF-CBT; for this reason we were not able to conduct any meaningful NMA of remission follow-up data. Available evidence suggests that TF-CBT and EMDR are effective in sustaining improvements in PTSD symptoms at 1-4-month follow-up. Evidence for other interventions was limited or inconclusive.

Implications for practice and need for further research

Results support current clinical practice within which TF-CBT and EMDR are the mainstream options offered to adults with PTSD. Our findings suggest that other treatments, such as supported self-help, combined somatic/cognitive therapies and non-TF-CBT are also effective and could be potential alternative treatment options, although amongst them only supported self-help has some limited evidence for sustained effects beyond treatment. This might have implications for clinical practice as services currently focus on provision of TF-CBT and EMDR. In contrast, although effective versus waitlist, counselling appears to be less effective than other treatment options and therefore should not be routinely offered if more effective options are available. In our review, we were not able to focus on complex

PTSD, which is currently less likely to be identified and managed effectively in routine practice. Further research is therefore needed to identify appropriate interventions specific to populations with complex PTSD.

Based on the results of the NMAs and the primary economic analysis (Mavranezouli *et al.*, under review; National Institute for Health and Care Excellence, 2018b), the NICE guideline on PTSD recommended EMDR and individual TF-CBT for the treatment of adults with PTSD presenting more than three months after trauma (National Institute for Health and Care Excellence, 2018a). Both interventions were effective in reducing PTSD symptoms post-treatment and demonstrated sufficient evidence to suggest sustainment of effect beyond treatment. The recommendation for EMDR was restricted to people with non-combat-related trauma, as evidence from sub-group pairwise meta-analysis suggested a non-significant effect on people with combat-related trauma, a finding that was confirmed by a recent systematic review and meta-analysis (Kitchiner *et al.*, 2019).

In addition, based on the available evidence and after taking account of the narrower evidence base, a weaker ('consider') recommendation was made for self-help with support and SSRIs for people who expressed a preference for these interventions, and, in the case of self-help, did not have severe PTSD symptoms and were not at risk of harm to themselves or others. A 'consider' recommendation was also made for non-TF-CBT targeted at specific symptoms, for people who are unable or unwilling to engage in a trauma-focused intervention or have residual symptoms after treatment. Finally, the guideline committee noted the positive evidence for combined somatic/cognitive therapies, but also considered their particularly limited evidence base beyond treatment endpoint and the lack of specific indications for these interventions, and decided not to recommend them but instead to make a recommendation for further research.

TF-CBT was the treatment with the largest evidence base on PTSD symptom severity and remission, both at the end of treatment and at 1-4-month follow-up. Further research is needed to establish the results for EMDR more firmly, in particular in relation to TF-CBT, as conclusions on its effectiveness are based on a more limited evidence base compared with TF-CBT and its relative effects versus TF-CBT were characterised by uncertainty. Similarly, research should further explore the effectiveness of other interventions, especially combined somatic/cognitive therapies, which demonstrated high effects at treatment endpoint, but also non-TF-CBT and self-help with support regarding remission and effectiveness beyond end of treatment, as relevant evidence is limited or lacking. Future research should also establish the effects of different types of TF-CBT relative to other types of treatment, but also relative to other types of TF-CBT, as evidence on comparative effectiveness is limited for some types of TF-CBT. In particular, evidence on sustainability of effects beyond treatment endpoint is sparse and only available for a few treatments; this lack of evidence is most evident for remission rates beyond treatment endpoint. This gap in evidence needs to be addressed by future trials, which should ideally include at least 12 months of follow-up, to explore the longer-term effectiveness of psychological therapies for PTSD.

CONCLUSION

EMDR and TF-CBT appear to be most effective in reducing symptoms and improving remission rates in adults with PTSD. They also appear to be effective in sustaining the reduction of PTSD symptoms beyond treatment endpoint. Other interventions, such as combined somatic/cognitive therapies, self-help, non-TF-CBT, SSRIs and counselling appear to be effective in reducing PTSD symptoms post-treatment; self-help with support and counselling appear to improve remission rates post-treatment, too. Counselling is likely to be less effective than EMDR and TF-CBT. Further research is needed to establish these findings for EMDR, as its evidence base is more limited compared with TF-CBT, and to better assess the relative effectiveness of interventions such as different types of TF-CBT, combined somatic/cognitive therapies, self-help with support and non-TF-CBT, in particular

regarding remission rates and effectiveness beyond end of treatment. Overall, there is a need for well-conducted RCTs to explore the long-term comparative effectiveness of psychological therapies for adults with PTSD.

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Table 1. Network meta-analysis of psychological treatments for PTSD in adults, changes in PTSD symptom scores between baseline and treatment endpoint: interventions, magnitude of evidence base and results

Changes in PTSD symptom scores between baseline and treatment endpoint N total = 4700; k total = 71; 151 study arms				
Intervention	**N**	**k**	**Mean SMD (95%CrI) vs waitlist**	**Mean rank (95%CrI)**
Metacognitive therapy	10	1	**-3.04 (-5.09 to -0.98)**	
Couple intervention	22	1	-2.67 (-5.41 to 0.06)	
EMDR	260	11	**-2.07 (-2.70 to -1.44)**	1.78 (1 to 5)
Combined somatic/cognitive therapies	237	4	**-1.69 (-2.66 to -0.73)**	3.64 (1 to 9)
Resilience-oriented treatment	20	1	-1.63 (-3.59 to 0.32)	
TF-CBT	903	29	**-1.46 (-1.87 to -1.05)**	4.51 (2 to 8)
Self-help with support	198	5	**-1.46 (-2.33 to -0.59)**	4.72 (1 to 10)
Present-centered therapy	99	3	**-1.42 (-2.45 to -0.40)**	
non-TF-CBT	209	7	**-1.22 (-1.95 to -0.49)**	6.07 (2 to 10)
TF-CBT + SSRI	115	3	**-1.21 (-2.35 to -0.07)**	6.14 (1 to 11)
Psychoeducation	152	2	-1.21 (-3.13 to 0.71)	6.19 (1 to 12)
IPT	55	2	-1.19 (-2.54 to 0.15)	
SSRI	166	5	**-1.14 (-2.09 to -0.19)**	6.55 (2 to 11)
Self-help without support	335	11	**-0.91 (-1.67 to -0.15)**	7.77 (3 to 11)
Relaxation	25	2	-0.73 (-2.15 to 0.70)	
Counselling	278	9	**-0.73 (-1.41 to -0.05)**	
Attention placebo	221	9	-0.39 (-1.42 to 0.63)	10.12 (5 to 12)
Waitlist	1312	43	Reference	11.61 (10 to 12)
Attention bias modification	83	3	2.14 (0.63 to 3.65)	
CrI: credible intervals; EMDR: eye movement desensitisation reprocessing; IPT: interpersonal psychotherapy; SMD: standardised mean difference; SSRI: selective serotonin reuptake inhibitor; TF-CBT: trauma-focused cognitive behavioural therapy k: number of randomised controlled trials (RCTs) that assessed each intervention; N: number randomised to each treatment across RCTs				

Negative values indicate a better effect for the intervention compared with the reference treatment (waitlist).

Only interventions tested on at least 100 people were considered in ranking

In bold effects where the 95%CrI do not cross the line of no effect (SMD=0)

Table 2. Network meta-analysis of psychological treatments for PTSD in adults, changes in PTSD symptom scores between baseline and 1-4-month follow-up: interventions, magnitude of evidence base and results

Changes in PTSD symptom scores between baseline and 1-4-month follow-up N total = 2,315; k total = 28; 57 study arms				
Intervention	**N**	**K**	**Mean SMD (95%CrI) vs waitlist**	**Mean rank (95%CrI)**
Couple intervention	21	1	**-2.04 (-3.72 to -0.36)**	
Self-help with support	85	3	**-1.27 (-2.12 to -0.42)**	
Self-help without support	40	2	-1.19 (-2.52 to 0.13)	
Behavioural therapy	47	2	**-1.19 (-2.16 to -0.21)**	
Combined somatic/cognitive therapies	23	1	-1.17 (-2.75 to 0.43)	
EMDR	121	4	**-1.12 (-1.94 to -0.27)**	1.50 (1 to 4)
TF-CBT	753	13	**-0.73 (-1.23 to -0.25)**	2.47 (1 to 4)
Psychoeducation	183	3	-0.51 (-1.47 to 0.44)	3.46 (1 to 6)
non-TF-CBT	123	4	-0.43 (-1.35 to 0.53)	3.80 (1 to 6)
IPT	32	1	-0.39 (-1.76 to 0.97)	
Counselling	205	4	-0.30 (-1.12 to 0.53)	4.31 (2 to 6)
Present-centered therapy	70	2	-0.15 (-1.29 to 1.01)	
Attention placebo	44	2	-0.02 (-1.35 to 1.33)	
Waitlist	496	14	Reference	5.46 (4 to 6)
Family therapy	72	1	0.15 (-1.13 to 1.43)	

CrI: credible intervals; EMDR: eye movement desensitisation reprocessing; IPT: interpersonal psychotherapy; SMD: standardised mean difference; TF-CBT: trauma-focused cognitive behavioural therapy

k: number of randomised controlled trials (RCTs) that assessed each intervention; N: number randomised to each treatment across RCTs

Negative values indicate a better effect for the intervention compared with the reference treatment (waitlist).

Only interventions tested on at least 100 people were considered in ranking.

In bold effects where the 95%CrI do not cross the line of no effect (SMD=0)

Table 3. Network meta-analysis of psychological treatments for PTSD in adults, remission at treatment endpoint: interventions, magnitude of evidence base and results

Remission at treatment endpoint N total = 2,249; k total = 34; 76 study arms				
Intervention	**N**	**k**	**Mean LOR (95%CrI) vs waitlist**	**Mean rank (95%CrI)**
Psychodynamic therapy	49	1	**4.61 (1.87 to 7.57)**	
EMDR	132	5	**3.38 (2.04 to 4.84)**	1.17 (1 to 3)
non-TF-CBT	65	2	**3.30 (1.48 to 5.29)**	
Relaxation	57	2	**2.65 (0.77 to 4.59)**	
IPT	72	2	**2.53 (0.71 to 4.40)**	
Present-centered therapy	75	2	**2.50 (0.75 to 4.36)**	
TF-CBT	601	21	**2.46 (1.79 to 3.19)**	2.15 (1 to 3)
Couple intervention	49	2	2.14 (-0.51 to 4.83)	
Self-help with support	105	2	**1.76 (0.03 to 3.49)**	3.07 (1 to 4)
TF-CBT + SSRI	57	1	1.65 (-0.61 to 4.00)	
Self-help without support	74	3	1.52 (-0.16 to 3.32)	
SSRI	87	2	1.42 (-0.45 to 3.42)	
Counselling	150	6	**1.34 (0.20 to 2.51)**	3.66 (3 to 4)
Attention placebo	23	1	1.09 (-1.97 to 4.24)	
Psychoeducation	28	1	-0.75 (-4.66 to 3.07)	
Waitlist	625	23	Reference	4.97 (4 to 5)

CrI: credible intervals; EMDR: eye movement desensitisation reprocessing; IPT: interpersonal psychotherapy; LOR: log-odds ratio; SSRI: selective serotonin reuptake inhibitor; TF-CBT: trauma-focused cognitive behavioural therapy

k: number of randomised controlled trials (RCTs) that assessed each intervention; N: number randomised to each treatment across RCTs

Positive values indicate a better effect for the intervention compared with the reference treatment (waitlist).

Only interventions tested on at least 100 people were considered in ranking.

In bold effects where the 95%CrI do not cross the line of no effect (LOR=0)