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**Psychological and psychosocial treatments for children and young people with post-traumatic stress disorder: a network meta-analysis**

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**Abstract**

**Background:** Post-traumatic stress disorder (PTSD) is a potentially chronic and disabling disorder that affects a significant minority of youth exposed to trauma. Previous studies have concluded that trauma-focused cognitive behavioural therapy (TF-CBT) is an effective treatment for PTSD in youth, but the relative strengths of different psychological therapies are poorly understood.

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

**Results:** We included 32 trials of 17 interventions and 2,260 participants. Overall, the evidence was of moderate-to-low quality. No inconsistency was detected between direct and indirect evidence. Individual forms of TF-CBT showed consistently large effects in reducing PTSD symptoms post-treatment compared with waitlist. The order of interventions by descending magnitude of effect versus waitlist was: cognitive therapy for PTSD (SMD -2.94, 95%CrI -3.94 to -1.95), combined somatic/cognitive therapies, child-parent psychotherapy, combined TF-CBT/parent training, meditation, narrative exposure, exposure/prolonged exposure, play therapy, Cohen TF-CBT/cognitive processing therapy (CPT), eye movement desensitisation and reprocessing (EMDR), parent training, group TF-CBT, supportive counselling, and family therapy (SMD -0.37, 95%CrI -1.60 to 0.84). Results for parent training, supportive counselling and family therapy were inconclusive. Cohen TF-CBT/CPT, group TF-CBT and supportive counselling had the largest evidence base. Results regarding changes in PTSD symptoms at follow-up and remission post-treatment were uncertain due to limited evidence.

**Conclusions:** TF-CBT, in particular individual forms, appears to be most effective in the management of PTSD in youth. EMDR is effective but to a lesser extent. Supportive counselling does not appear to be effective. Results suggest a large positive effect for emotional freedom technique, child-parent psychotherapy, combined TF-CBT/parent

training, and meditation, but further research is needed to confirm these findings as they were based on very limited evidence.

**Keywords:** post-traumatic stress disorder; network meta-analysis; intervention

## INTRODUCTION

More than half of children and young people are exposed to potentially traumatic events (Landolt, Schnyder, Maier, Schoenbucher, & Mohler-Kuo, 2013; McLaughlin et al., 2013) with a significant minority of exposed youth going on to develop post-traumatic stress disorder (PTSD) (Alisic et al., 2014). One twin study of UK youth suggested a population prevalence of 3% (Fisher et al., 2015). PTSD may be chronic (Morgan, Scourfield, Williams, Jasper, & Lewis, 2003; Yule et al., 2000) and have a significant impact on broader development, impairing social, academic and occupational functioning (Bolton, O'Ryan, Udwin, Boyle, & Yule, 2000). Given its chronicity and impact, it is not surprising that a variety of treatments have been proposed for this condition in youth, including different forms of trauma-focused cognitive behaviour therapy (TF-CBT), eye movement desensitisation and reprocessing (EMDR), child-parent psychotherapy, and parent training. A number of systematic reviews and meta-analyses have evaluated the effectiveness of psychological and psychosocial treatments for PTSD in children and young people (Cary & McMillen, 2012; Gutermann et al., 2016; Harvey & Taylor, 2010; Kowalik, Weller, Venter, & Drachman, 2011; Morina, Koerssen, & Pollet, 2016; Silverman et al., 2008). The consensus to date is that TF-CBT is an effective treatment for PTSD in children and young people, with some also concluding that EMDR is effective but to a lesser extent. These studies have made limited comparisons of a narrow range of treatments and used standard meta-analytic techniques to synthesise direct evidence from randomised controlled trials (RCTs). This approach does not allow the relative effectiveness between treatments to be assessed, unless these have been compared in a head-to-head trial.

Network meta-analysis (NMA) is a generalisation of standard pairwise meta-analysis to data structures that include, for example, A versus B, B versus C, and A versus C trials (Lu & Ades, 2004). NMA strengthens inference 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, Ades, & Higgins, 2005; Dias, Sutton, Ades, & Welton, 2013a; Mavridis, Giannatsi, Cipriani, & Salanti, 2015).

The objective of this study was to examine the relative effectiveness of psychological, psychosocial and other non-pharmacological treatments of PTSD in children and young people using NMA.

## METHODS

The analyses presented here supported the updating of national guidance for the management of PTSD in England, published by the National Institute for Health and Care Excellence (NICE) (National Institute for Health and Care Excellence, 2018). 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.

### *Search strategy*

A search for RCTs of treatments for people with clinically important post-traumatic stress symptoms was conducted in the databases MEDLINE, Embase, PsycINFO, CINAHL and The Cochrane Library. Databases were searched using relevant medical subject headings, free-text terms and study type filters where appropriate. Studies published in languages other than English were excluded following NICE guidance (National Institute for Health and Care Excellence 2014); evidence suggests that use of language restrictions in systematic review-based meta-analyses in conventional medicine does not introduce systematic bias (Morrison et al., 2012). The aim of the search was to update the evidence included in the previous NICE PTSD guideline, published in 2005. The search was undertaken in

January/February 2017 with re-runs being performed in January 2018. Online Appendix 1 provides full details of the databases and the search terms used.

***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 children and young people (aged under 18 years) more than one month after a traumatic event was carried out according to Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). Clinically important post-traumatic stress symptoms were defined by 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 clinically significant PTSD symptoms, indicated by baseline PTSD symptom scores above threshold on a validated scale. Critical outcomes included PTSD symptom endpoint or change scores on a validated PTSD scale; response; and recovery or remission defined either as number of the people no longer meeting DSM, ICD or similar diagnostic criteria for PTSD, or with PTSD symptom scores below threshold on a validated scale.

For quality assurance of study identification, the titles and abstracts of identified studies were screened by two reviewers for inclusion against criteria specified in the guideline review protocols, until a good inter-rater reliability was observed (percentage agreement $\geqslant$ 90% or Kappa statistic K>0.60). Initially 10% of references were double-screened; as inter-rater agreement was good for this initial 10%, the remaining references were screened by one reviewer. All primary-level studies included after the first scan of citations 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 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 treatments tested on children and young people with clinically important post-traumatic stress symptoms more than three months after a traumatic event. Treatments that were not connected to the treatment network were excluded from the NMAs.

The NMA assessed different interventions within the TF-CBT class. 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 (e.g. imaginal reliving, producing a written narrative or in vivo exposure) and others on cognitive techniques (e.g. restructuring of trauma-related appraisals), most use a combination. Interventions included in the TF-CBT class, such as cognitive therapy for PTSD, TF-CBT largely based on the Cohen manual (Cohen, Mannarino, & Deblinger, 2006) and cognitive processing therapy, narrative exposure, exposure/prolonged exposure, and group TF-CBT, were analysed as separate treatments in the network, in order to explore any differences in effectiveness among them. The sole study of cognitive processing therapy was collapsed into a group with TF-CBT largely based on the Cohen manual, given the degree of overlap between these therapies (e.g. structured format, psychoeducation, production of a trauma narrative, cognitive restructuring). Combined somatic/cognitive therapies only included emotional freedom technique, as evidence was only available for this treatment. Treatment as usual (TAU), according to study descriptions, ranged from providing information on post-traumatic symptom patterns and encouragement to access therapy, to any care required, including psychotherapy, medication or psychoeducational family counselling, as judged by the clinician. Waitlist and no treatment arms were included in the same node and analysed together, as there were very few no treatment arms (2) compared with waitlist (14) and

keeping them separate was considered to add no value in the analyses. Nevertheless, we undertook a sensitivity analysis in which we kept waitlist and no treatment in separate nodes, to explore the impact of our decision to merge and analyse these two controls together on the results.

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 PTSD symptom change scores at 1-4-month follow-up; in contrast, remission data at 1-4-month follow-up were only available for the comparison of group TF-CBT versus waitlist. Beyond 1-4 months of follow-up, available data were very sparse for both outcomes. Based on the availability of data on the two outcomes of interest, three separate NMAs were conducted using data for 3 outcomes, respectively:

- 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

PTSD symptom change scores derived from self-rated symptom scales were prioritised over those derived from clinician-rated symptom scales if both were available in the same study, as they were deemed to better capture symptoms experienced by children and young people with PTSD. Intention-to-treat (ITT) data, obtained after imputation of missing data, were prioritised over completers' data, if both were available in the same study.

The 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 guideline systematic review protocol and the additional inclusion criteria applied for the NMA are provided in online Appendix 2.

***Statistical analysis***

NMAs were conducted within a Bayesian framework using Markov Chain Monte Carlo simulation techniques implemented in WinBUGS 1.4.3 (Lunn, Thomas, Best, & Spiegelhalter, 2000; Spiegelhalter, Thomas, Best, & Lunn, 2003). An overview of the approach and methods adopted is provided below. Full details of the statistical analysis and the WinBUGS codes used to synthesise changes in PTSD symptom scores and dichotomous remission data are reported in online 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, Sutton, Ades, & Welton, 2013a; Dias, Ades, Welton, Jansen, & Sutton, 2018). Because the RCTs included in the NMAs used different continuous scales to report change in PTSD symptoms, results were expressed in the form of the Standardised Mean Difference (SMD) between pairs of interventions. For the synthesis of dichotomous data (remission), a generalised linear model with binomial likelihood and logit link was used (Dias et al., 2013a, 2018). The output of this analysis was the log-odds ratios (LORs) between pairs of interventions. The suitability of fixed and random effects models (model fit) was assessed and compared and the most suitable model (fixed or random effects) was selected for the analysis of each of the three outcomes.

For each analysis we report mean relative effects (either SMD or LOR) with 95% credible intervals (CrI). We also report mean ranks with 95% CrI for every treatment in each analysis, where a rank of 1 indicates highest 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, i.e. the evidence is consistent (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 assessed when there are closed loops of evidence on 3 treatments that are informed by at least 3 distinct trials (van Valkenhoef, Dias, Ades, & Welton, 2016). The assumption of consistency between indirect and direct evidence was explored by undertaking global inconsistency tests (Dias et al., 2013b) and node-split testing (Dias et al., 2013b; van Valkenhoef & Kuiper, 2016). When evidence of inconsistency was found, studies contributing to loops of evidence where there might be inconsistency were checked for data accuracy and analyses were repeated if corrections in the data extraction were made. However, if evidence of inconsistency was still present following data corrections, no studies were excluded from the analysis, as their results could not be considered as 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 code for the inconsistency model are provided in online Appendix 4.

### **Threshold analysis**

Threshold analysis was undertaken to test the robustness of treatment recommendations based on the NMA to potential biases or sampling variation in the included evidence (Phillippo et al., 2019). The results of threshold analysis describe how much each data point could change (for example if adjusted for bias) before the conclusion changes and what the

revised conclusion would be. Threshold analyses were carried out at two levels: (i) at a study level, assessing the influence of individual study estimates on the conclusion of the analysis and (ii) at a contrast level, where the influence of the combined evidence on each treatment contrast was considered (Caldwell et al., 2016; Phillippo, Dias, Ades, Didelez & Welton, 2018; Phillippo et al., 2019). Full methods used for threshold analysis are provided in online Appendix 5.

## RESULTS

### Studies and treatments

The systematic literature search identified 141 studies potentially eligible for the systematic review, 104 of which were excluded. Five more studies were excluded as they did not meet criteria for the NMA, leaving 32 eligible studies that reported one or more outcomes of interest (Figure 1). The characteristics of included studies are reported in online Appendix 6, while a list of excluded studies, with reasons for exclusion, is provided in online Appendix 7.

The NMA of changes in PTSD symptom scores between baseline and treatment endpoint was informed by 29 RCTs that assessed 17 interventions tested on 1960 participants. The NMA of changes in PTSD symptom scores between baseline and 1-4-month follow-up included 10 RCTs, 608 participants and 12 interventions. The NMA of remission at treatment endpoint considered 9 studies, 485 participants and 7 interventions.

The three respective networks are shown in Figure 2. Full data utilised in each NMA are shown in online Appendix 8.

#### *Risk of bias assessment*

All 32 included trials were assessed for risk of bias using the Cochrane risk of bias tool (Higgins & Green, 2011). Sequence generation and allocation concealment were adequately described in eleven and seven trials, respectively. Trials were regarded at high risk of bias

for lack of participant and provider masking. In four studies, a clinician-rated scale was used and assessors were unaware of treatment assignment, in three trials it was unclear if the assessors were blinded, in two studies a non-blind clinician-rated scale was used, and in 23 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 two trials and unclear in eleven studies. However, we favoured ITT analysis and, for the remission outcome, we conservatively treated drop outs as failing to remit (rather than as remitters). Included trials reported a variety of outcomes. Only four trials were registered on a trials database and reported all listed outcomes. Consequently, most studies were judged as being at unclear risk of reporting bias. Other potential biases were only identified in one study which was rated as high risk due to a potential conflict of interest. An overview of the trials' risk of bias assessment is provided in online Appendix 9.

***NMA model fit statistics***

In the NMA of changes in PTSD symptom scores between baseline and treatment endpoint, the random effects model provided a better fit over the fixed effect model; however, the between-trial standard deviation (sd), which measures the heterogeneity of treatment effects estimated by trials within contrasts, was moderate-to-high when compared with the size of the intervention effect estimates (posterior median sd 0.56, 95% CrI 0.37 to 0.89).

In the NMA of changes in PTSD symptom scores between baseline and 1-4-month follow-up, the random effects model provided a better fit over the fixed effect model; however, due to limited evidence, the posterior distribution for the between-trial heterogeneity was implausibly wide. Therefore, an informative prior distribution on the logged between-study variance was used (Rhodes, Turner, & Higgins, 2015) (see online Appendix 3), which resulted in a moderate-to-high between-study heterogeneity compared with the size of treatment effects (posterior median sd 0.46, 95% CrI 0.10 to 1.20).

In the NMA of remission at treatment endpoint, both fixed and random effects models provided good fit; therefore, the simpler, fixed effect model was chosen.

Full details of model fit statistics are provided in online Appendix 10.

***Treatment outcomes***

Results of each analysis are presented in Table 1, as 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 mean ranking. The table also shows 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 of the 3 NMAs.

*Changes in PTSD symptom scores between baseline and treatment endpoint*

All individual forms of TF-CBT (cognitive therapy, narrative exposure therapy, exposure/prolonged exposure therapy, Cohen TF-CBT/CPT) showed large effects compared with waitlist, with the mean SMD ranging from -2.94 [95% CrI -3.94 to -1.95] for cognitive therapy to -1.17 [95% CrI -1.78 to -0.54] for Cohen TF-CBT/CPT, although for a number of interventions effects were characterised by considerable uncertainty, as indicated by wide 95% CrI; nevertheless, 95% CrI did not cross the line of no effect for any of the individual forms of TF-CBT, suggesting evidence of effect. Cognitive therapy for PTSD appeared to be the most effective intervention; however, this finding was based on a very narrow evidence base (N=25), focused on single-trauma PTSD. Cohen TF-CBT/CPT showed the smallest positive effect amongst individual forms of TF-CBT but had the largest evidence base (N=349) and its effect was characterised by relatively narrow CrI. Group TF-CBT showed evidence of a positive effect, albeit lower than that of individual forms of TF-CBT (mean SMD -0.91, 95% CrI -1.48 to -0.34).

Other interventions with large effects versus waitlist and 95% CrI that did not cross the line of no effect were, by order of mean ranking, combined somatic/cognitive therapies (mean SMD -2.14, 95% CrI -3.34 to -0.92, ranked second best intervention), child-parent psychotherapy, combined TF-CBT/parent training, meditation, play therapy and EMDR (mean SMD -0.99, 95% CrI -1.76 to -0.23). However, these interventions were tested on a small number of individuals (N<100 for each intervention), which may explain the wide 95% CrI characterising their effects and rankings. Parent training, supportive counselling and family therapy showed smaller and inconclusive effects, as 95% CrI crossed the line of no effect in comparisons with waitlist; with the exception of supportive counselling (N=180) these findings were based on limited evidence (N<100 for each of the other two interventions).

The large uncertainty in the results for most interventions is also indicated by the wide 95% CrI around mean rankings, for example, combined somatic/cognitive therapies could plausibly be ranked between the 1st and 11th place according to the NMA model.

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

Combined somatic/cognitive therapies showed the largest effect versus waitlist (mean SMD -1.80, 95% CrI -3.01 to -0.58), followed by Cohen TF-CBT/CPT, group TF-CBT, and combined TF-CBT/parent training (mean SMD -1.49, 95% CrI -2.90 to -0.07). Of the remaining interventions, narrative exposure was the only one for which there was evidence of effect compared with waitlist, as suggested by 95% CrI that did not cross the line of no effect (mean SMD -0.94, 95% CrI -1.84 to -0.04). With the exception of group TF-CBT (N=112), all other interventions were tested on small numbers of participants, and this is reflected in the wide 95% CrI around effects and rankings (Table 1).

*Remission at treatment endpoint*

All individual forms of TF-CBT showed better effects than waitlist and 95% CrI that did not cross the line of no effect. Narrative exposure showed the highest mean effect (mean LOR 2.81, 95% CrI 0.87 to 5.13), followed by cognitive therapy for PTSD, exposure/prolonged exposure therapy, and Cohen TF-CBT/CPT (mean LOR 0.89, 95% CrI 0.15 to 1.64). Supportive counselling showed a small and inconclusive effect versus waitlist (mean LOR 0.15, 95% CrI -0.98 to 1.28). With the exception of Cohen TF-CBT/CPT (N=158), all other interventions were tested on a small number of trial participants (N<100), and this is reflected in the uncertainty of the results as indicated by wide 95% CrI around effects and rankings.

Detailed results between all pairs of treatments examined in the NMAs as well as results from available direct (head-to-head) comparisons are reported in online Appendix 11. It can be seen that the NMA and pairwise results were in agreement in all cases, as indicated by the overlapping of credible/confidence intervals.

***Inconsistency checks***

No evidence of inconsistency between direct and indirect evidence was found in either NMA of changes in PTSD symptom scores. The network of remission at treatment endpoint had no closed loops of evidence, therefore inconsistency checks were not applicable. Results of inconsistency checks are provided in online Appendix 12.

***Results of threshold analysis***

TF-CBT treatments in individual form tended to be the first recommended treatment based on a decision rule of recommending the most efficacious treatments that have been studied on at least 50 trial participants (as this was considered the minimum adequate evidence that could support a treatment recommendation). For PTSD symptom change scores between baseline and treatment endpoint, the treatment recommendation of narrative exposure was sensitive to imprecision; this means that changes in the point estimate within its 95% CrI

would result in play therapy or exposure/prolonged exposure being recommended. For PTSD symptom change scores between baseline and 1-4 months follow-up, the recommendation of group CBT was also sensitive to imprecision, and narrative exposure would be recommended instead. Finally, in terms of remission, the recommendation of exposure/prolonged exposure was sensitive to imprecision, and Cohen TF-CBT/CPT would be recommended instead. Results of the threshold analysis are provided in online Appendix 13.

***Sensitivity analysis: waitlist and no treatment analysed in separate nodes***

This analysis was only relevant for two outcomes: changes in PTSD symptom scores between baseline and treatment endpoint; and changes in PTSD symptom scores between baseline and 1-4-month follow-up. No studies included in the NMA of remission had a 'no treatment' control. The NMA modes used were the same as for the base-case analyses. Networks, datasets and results of these sensitivity analyses are provided in online Appendix 14.

In the sensitivity analysis of changes in PTSD symptom scores between baseline and treatment endpoint, no treatment showed a small and uncertain positive effect compared with waitlist. Relative effects of all treatments versus waitlist were similar to those obtained from the base-case analysis and ranking was identical. Relative effects versus no treatment were characterised by wide 95% CrI which, for most interventions, crossed the line of no effect. The only interventions with evidence of effect versus no treatment were cognitive therapy for PTSD, combined somatic/cognitive therapies, and narrative exposure. These findings suggest that the base-case analysis may have overestimated the effects of active interventions at treatment endpoint.

In the sensitivity analysis of changes in PTSD symptom scores between baseline and 1-4-month follow-up, no treatment showed a moderate and uncertain negative effect compared

with waitlist. Relative effects versus waitlist were sensitive for some interventions, which resulted in changes in ranking compared with the base-case analysis; notably, Cohen TF-CBT/CPT ranked in the first place, followed by combined TF-CBT/parent training, whereas combined somatic/cognitive therapies fell at the 3rd place in mean ranking. All interventions showed very large effects versus no treatment, with wide 95% CrI that did not cross the line of no effect with the exception of EMDR and TAU. These results suggest that the base-case estimates of the effects of active interventions at 1-4-month follow-up may have been conservative.

## DISCUSSION

TF-CBT, in particular individually delivered forms such as cognitive therapy, narrative exposure, exposure/prolonged exposure, and Cohen TF-CBT/CPT, appear to be most effective in reducing PTSD symptoms and achieving remission in children and young people with PTSD at end of treatment. Cognitive therapy for PTSD was shown to be the most effective intervention in reducing PTSD symptoms at treatment endpoint (albeit based on small samples and only single-event trauma), followed by combined somatic/cognitive therapies, child-parent psychotherapy, combined TF-CBT/parent training, and meditation; however, results for these interventions were also based on a very limited evidence base (each tested on N<50 across trials). Play therapy showed similar effects to exposure/prolonged exposure. EMDR and group TF-CBT also appeared to be effective in reducing PTSD symptoms in children and young people with PTSD at treatment endpoint, but with smaller effects compared with other interventions. Parent training alone, supportive counselling and family therapy showed smaller effects in reducing PTSD symptoms and 95% CrI that crossed the line of no effect in comparisons with waitlist. Supportive counselling appeared to have no effect in achieving remission compared with waitlist. Cohen TF-CBT/CPT had the largest evidence base, followed by supportive counselling and group TF-CBT. All other interventions had a narrow evidence base which was reflected, in most cases, in the uncertainty around the results, which should therefore be treated with caution. The

results of the threshold analyses reflected these findings, where recommendations of TF-CBT forms were sensitive to imprecision or uncertainty in estimates contributing to the NMA.

At 1-4-month follow-up, combined somatic/cognitive therapies appeared to be the most effective in retaining improvement in PTSD symptoms followed by Cohen TF-CBT/CPT, group CBT, and combined TF-CBT/parent training. Narrative exposure also appeared to be effective, to a lesser degree, in retaining effects at follow-up. Results for other interventions were inconclusive as 95% CrI of effects crossed the line of no effect. The results of this analysis should be treated with caution due to the narrow evidence base.

To our knowledge, this is the first known NMA of treatments for children and young people with PTSD that was designed to inform a clinical guideline. The NMAs that utilised PTSD symptom change scores further informed the guideline economic analysis, described in a companion paper (Mavranezouli et al., submitted). NMA techniques enabled evidence synthesis from both direct and indirect comparisons between interventions, and allowed simultaneous inference on all treatments examined in pair-wise trial comparisons while respecting randomisation (Caldwell et al., 2005; Lu & Ades, 2004). Inconsistency checks found no inconsistency between direct and indirect evidence in the two NMAs of changes in PTSD symptom scores. This finding provides reassurance that the included studies were comparable across interventions, although it is acknowledged that between-trial heterogeneity was moderate-to-high. Inconsistency checks were not possible for the NMA of remission, as there were no closed loops of evidence within the network. Threshold analyses found that, among treatments studied on at least 50 patients, forms of TF-CBT are recommended based on efficacy, yet these recommendations are sensitive to imprecision. The alternative recommended treatments were play therapy or other forms of TF-CBT treatments.

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 interventions, and in most cases it was unclear whether assessors were blinded. 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 children and young people with PTSD. However, self-rated assessment cannot be blinded in trials of psychological and psychosocial 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. The ITT approach that we adopted for analyses 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, 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).

We evaluated outcomes at treatment endpoint and, for PTSD symptom change scores, also at 1-4-month follow-up. Evidence on the long-term effectiveness of treatments for PTSD in youth is very limited, in particular for the outcome of remission. It is important that future trials address this gap in evidence.

The description of TAU was not always clear and its content varied across studies; the diversity of TAU across RCTs is likely to have contributed to the heterogeneity observed in the analyses. Waitlist and no treatment arms were analysed together, as there were only two ‘no treatment’ arms and keeping them separate was considered to add no value in the analyses. However, it is acknowledged that the baseline effect of waitlist may be lower than that of ‘no treatment’ (Furukawa et al., 2014), resulting in the relative effects of active

interventions having been potentially exaggerated in waitlist-controlled studies compared with their expected effects versus a 'no treatment' control. We tested this assumption in sensitivity analyses that treated waitlist and no treatment as separate interventions and found that in the base-case analyses effects of treatments may have been overestimated at treatment endpoint but may have been underestimated at 1-4-month follow-up. Nevertheless, overall conclusions were not materially different. It is noted that no treatment was only tested on 32 trial participants and had limited connections into the 1-4-month follow-up network, therefore introducing considerable uncertainty into these sensitivity analyses, which need to be treated with caution.

**Clinical implications**

The support for TF-CBT demonstrated in these NMAs is consistent with the findings of earlier meta-analytic reviews. Moreover, the use of an NMA design revealed further noteworthy results that would not be possible to obtain with standard forms of meta-analysis. The lack of any significant difference between supportive counselling and waitlist shown here warns against the use of this intervention as a "fall-back" option, for example where a therapist trained in a TF-CBT approach is not available or a client has refused to engage with TF-CBT; these findings may also bring into question the suitability of this intervention as a control treatment in future trials. While the few studies to have compared TF-CBT with EMDR have not shown any significant differences, the overall pattern of evidence incorporated in these NMAs suggests that EMDR, while more effective than waitlist or no treatment, is likely to have a lower effect than most individual forms of TF-CBT. Results, therefore, support routine use of different forms of TF-CBT for children and young people with TF-CBT, and, potentially, EMDR as an alternative treatment option. Results show a positive effect for a number of other treatment approaches, such as emotional freedom technique, child-parent psychotherapy, combined TF-CBT/parent training, and meditation, but further research is needed to establish their efficacy in this population.

## CONCLUSION

TF-CBT, in particular individually delivered forms, appears to be most effective in the management of PTSD in youth. Results from the threshold analyses for the most part support this finding, with play therapy potentially being effective in managing PTSD symptoms at treatment endpoint. EMDR is effective but to a lesser extent. Supportive counselling does not appear to be effective in this population. Results suggest a large positive effect for emotional freedom technique, child-parent psychotherapy, combined TF-CBT/parent training, and meditation, but further research is needed to confirm these findings as they were based on very limited evidence. There is a need for well-conducted head-to-head RCTs that examine the relative effectiveness of interventions with promising evidence, including comparative assessment of their longer term effects, in order to establish their long-term relative clinical and cost-effectiveness.

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**Key points**

- PTSD is a potentially chronic and disabling disorder that affects a significant minority of youth exposed to trauma.
- A number of psychological and psychosocial therapies are available for the treatment of PTSD in youth.
- NMA techniques enable evidence synthesis from direct and indirect comparisons between interventions, and allow simultaneous inference on all treatments that form a network of evidence while respecting randomisation.
- TF-CBT, in particular individually delivered forms, appears to be most effective in the management of PTSD in youth. EMDR is effective but to a lesser extent. Supportive counselling does not appear to be effective in this population.
- Results support routine use of different forms of TF-CBT for youth with TF-CBT, and, potentially, EMDR as an alternative treatment option.
- Results suggest a large positive effect for emotional freedom technique, child-parent psychotherapy, combined TF-CBT/parent training, and meditation, but further research is needed to confirm these findings as they were based on very limited evidence.

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**Table 1. Network meta-analyses of psychological and psychosocial treatments for PTSD in children and young people: interventions, magnitude of evidence base and results**

| **Changes in PTSD symptom scores between baseline and treatment endpoint**<br>**N total = 1960; k total = 29; 63 study arms** | | | | |
|---|---|---|---|---|
| **Intervention** | **N** | **k** | **Mean SMD (95% CrI) vs waitlist** | **Mean ranking (95% CrI)** |
| [TF-CBT] cognitive therapy | 25 | 2 | **-2.94 (-3.94 to -1.95)** | 1.58 (1 to 4) |
| Combined somatic/cognitive therapies | 20 | 1 | **-2.14 (-3.34 to -0.92)** | 3.77 (1 to 11) |
| Child-parent psychotherapy | 36 | 1 | **-2.16 (-4.02 to -0.26)** | 4.13 (1 to 13) |
| TF-CBT & parent training | 12 | 1 | **-1.79 (-3.15 to -0.45)** | 5.40 (1 to 14) |
| Meditation | 38 | 1 | **-1.67 (-2.94 to -0.41)** | 5.96 (1 to 14) |
| [TF-CBT] narrative exposure | 73 | 3 | **-1.49 (-2.25 to -0.74)** | 6.57 (3 to 12) |
| [TF-CBT] exposure/PE | 83 | 4 | **-1.34 (-2.15 to -0.51)** | 7.51 (3 to 12) |
| Play therapy | 83 | 2 | **-1.35 (-2.48 to -0.20)** | 7.60 (2 to 14) |
| [TF-CBT] Cohen TF-CBT/CPT | 349 | 8 | **-1.17 (-1.78 to -0.54)** | 8.69 (5 to 13) |
| EMDR | 85 | 3 | **-0.99 (-1.76 to -0.23)** | 10.14 (5 to 15) |
| Parent training | 49 | 2 | -0.96 (-2.32 to 0.41) | 10.28 (3 to 17) |
| [TF-CBT] group CBT | 171 | 6 | **-0.91 (-1.48 to -0.34)** | 10.72 (6 to 15) |

| | | | | |
|---|---|---|---|---|
| Supportive counselling | 180 | 6 | -0.59 (-1.29 to 0.12) | 12.96 (9 to 16) |
| Family therapy | 75 | 1 | -0.37 (-1.60 to 0.84) | 13.59 (5 to 17) |
| EMDR & TAU | 10 | 1 | -0.28 (-1.96 to 1.40) | 13.65 (4 to 17) |
| TAU | 158 | 5 | -0.31 (-1.16 to 0.56) | 14.51 (10 to 17) |
| Waitlist/no treatment | 513 | 16 | Reference | 15.96 (14 to 17) |
| **Changes in PTSD symptom scores between baseline and 1-4-month follow-up<br><br>N total = 608; k total = 10; 25 study arms** | | | | |
| **Intervention** | **N** | **k** | **Mean SMD (95% CrI) vs waitlist** | **Mean ranking (95% CrI)** |
| Combined somatic/cognitive therapies | 20 | 1 | **-1.80 (-3.01 to -0.58)** | 3.02 (1 to 9) |
| [TF-CBT] Cohen TF-CBT/CPT | 19 | 1 | **-1.74 (-3.09 to -0.42)** | 3.37 (1 to 10) |
| [TF-CBT] group CBT | 112 | 3 | **-1.51 (-2.48 to -0.61)** | 4.09 (1 to 9) |
| TF-CBT & parent training | 12 | 1 | **-1.49 (-2.90 to -0.07)** | 4.33 (1 to 10) |
| EMDR & TAU | 12 | 1 | -1.10 (-3.51 to 1.23) | 6.06 (1 to 12) |
| Parent training | 20 | 1 | -1.04 (-2.91 to 0.80) | 6.30 (1 to 11) |
| [TF-CBT] narrative exposure | 87 | 3 | **-0.94 (-1.84 to -0.04)** | 6.85 (3 to 11) |
| [TF-CBT] exposure/PE | 33 | 2 | -0.92 (-2.25 to 0.37) | 6.97 (3 to 11) |
| Supportive counselling | 34 | 2 | -0.74 (-1.41 to 0.06) | 7.94 (4 to 11) |
| EMDR | 43 | 1 | -0.59 (-2.12 to 0.97) | 8.48 (2 to 12) |
| TAU | 25 | 2 | -0.35 (-2.26 to 1.60) | 9.52 (3 to 12) |

| | | | | |
|---|---|---|---|---|
| Waitlist/no treatment | 191 | 7 | Reference | 11.08 (8 to 12) |
| **Remission at treatment endpoint**<br>**N total = 485; k total = 9; 18 study arms** | | | | |
| **Intervention** | **N** | **k** | **Mean LOR (95% CrI) vs waitlist** | **Mean ranking (95% CrI)** |
| [TF-CBT] narrative exposure | 13 | 1 | **2.81 (0.87 to 5.13)** | 1.69 (1 to 4) |
| [TF-CBT] cognitive therapy | 26 | 2 | **2.66 (1.28 to 4.22)** | 1.72 (1 to 3) |
| [TF-CBT] exposure/PE | 50 | 2 | **1.62 (0.22 to 3.04)** | 2.81 (1 to 4) |
| [TF-CBT] Cohen TF-CBT/CPT | 158 | 4 | **0.89 (0.15 to 1.64)** | 3.90 (3 to 5) |
| Supportive counselling | 93 | 4 | 0.15 (-0.98 to 1.28) | 5.64 (4 to 7) |
| Waitlist | 103 | 4 | Reference | 5.95 (5 to 7) |
| TAU | 42 | 1 | -0.21 (-1.48 to 1.03) | *6.30 (5 to 7)* |

CPT: cognitive processing therapy; CrI: credible intervals; EMDR: eye movement desensitisation reprocessing; LOR: log-odds ratio; SMD: standardised mean difference; PE: prolonged exposure; TAU: treatment as usual; TF-CBT: trauma-focused cognitive behavioural therapy

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

Negative values for the SMD and positive values for the LOR indicate a better effect for the intervention compared with the reference treatment (waitlist/no treatment).

**In bold** effects where the 95% CrI do not cross the line of no effect (SMD=0 or LOR=0, as relevant)

**Figure 1. Flow diagram of study selection for the systematic review and the network meta-analysis**

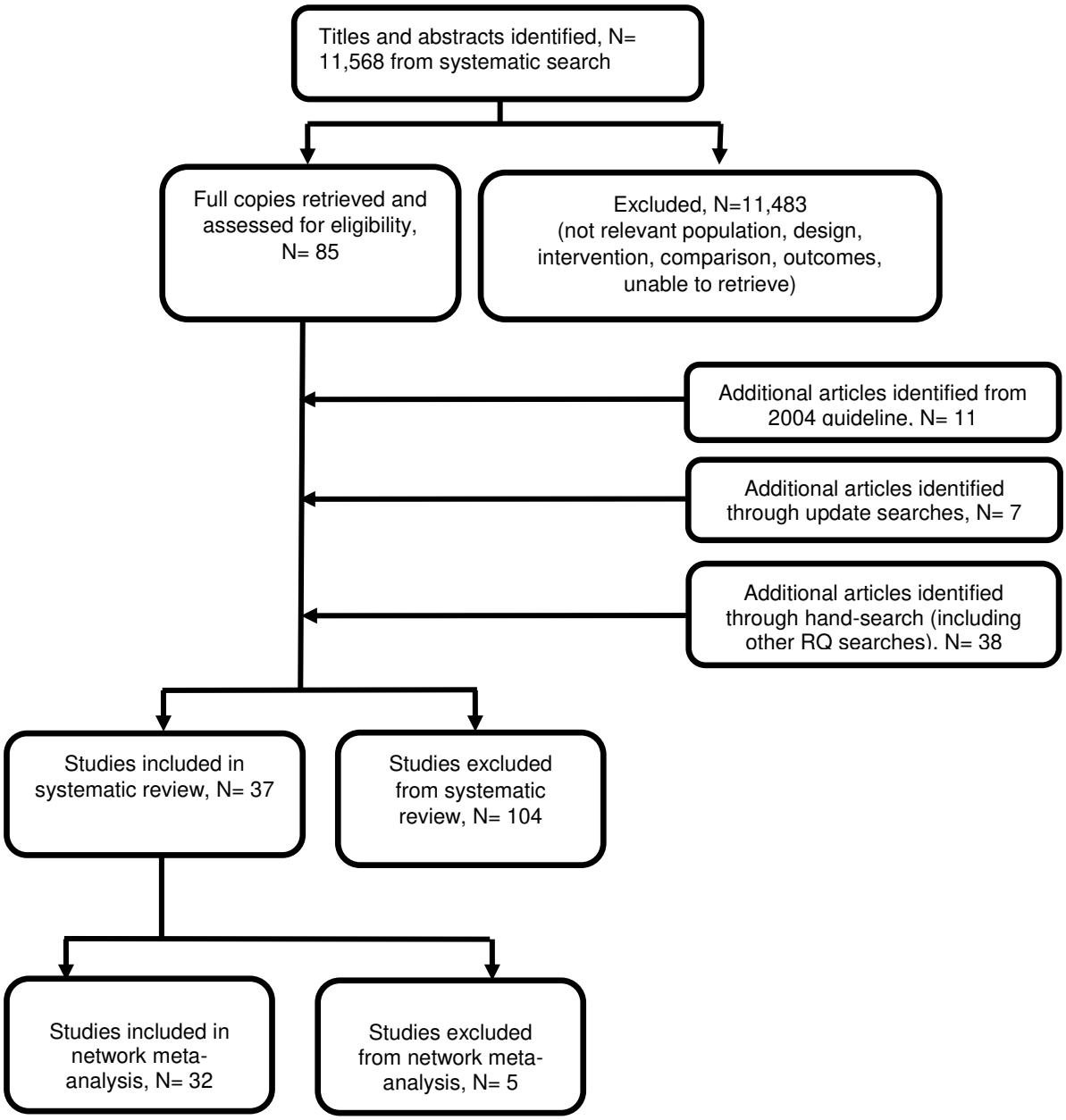
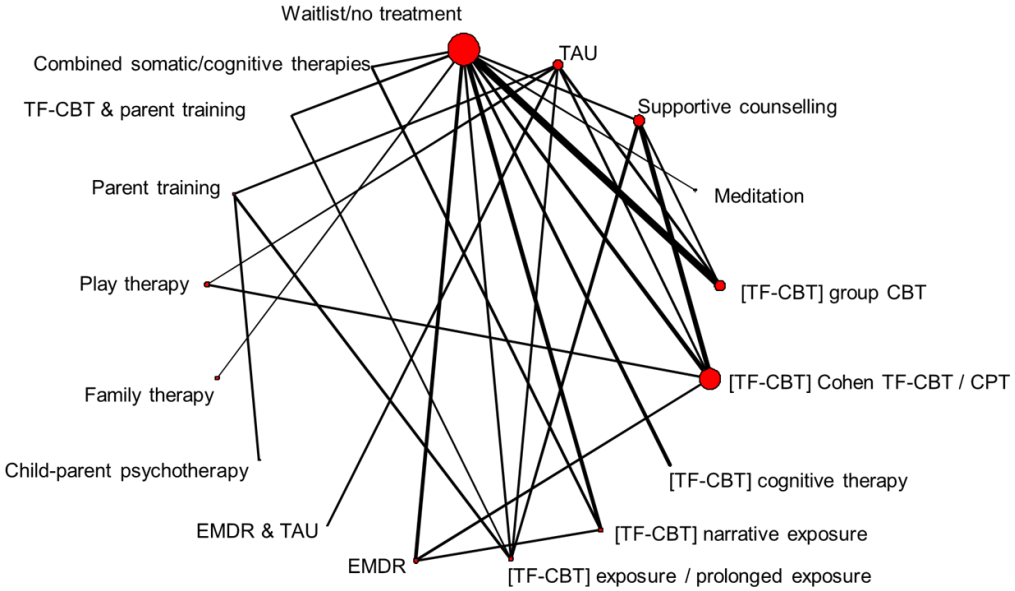


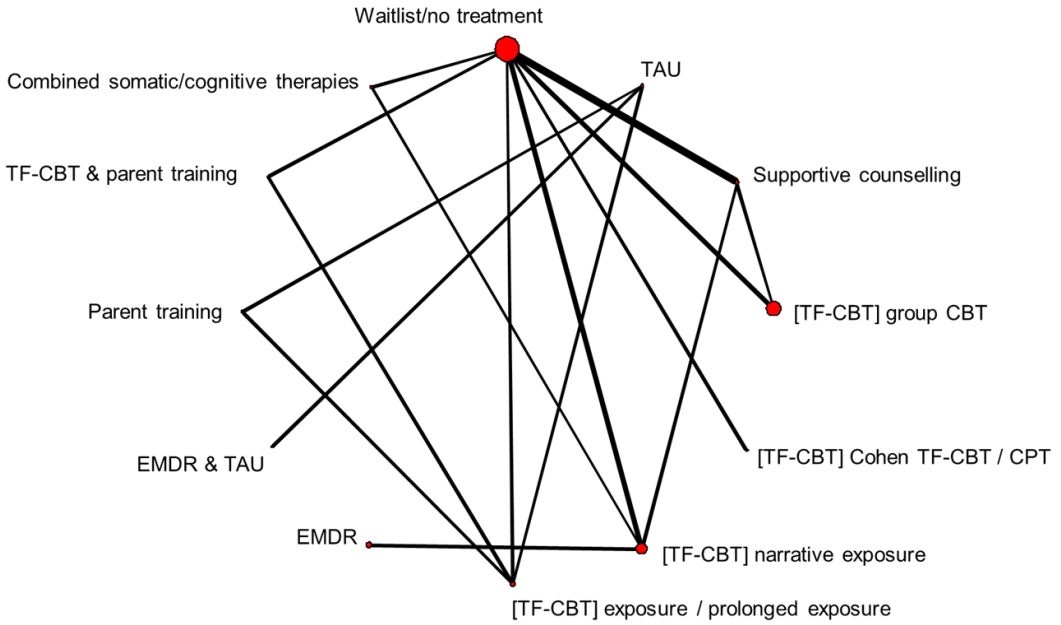
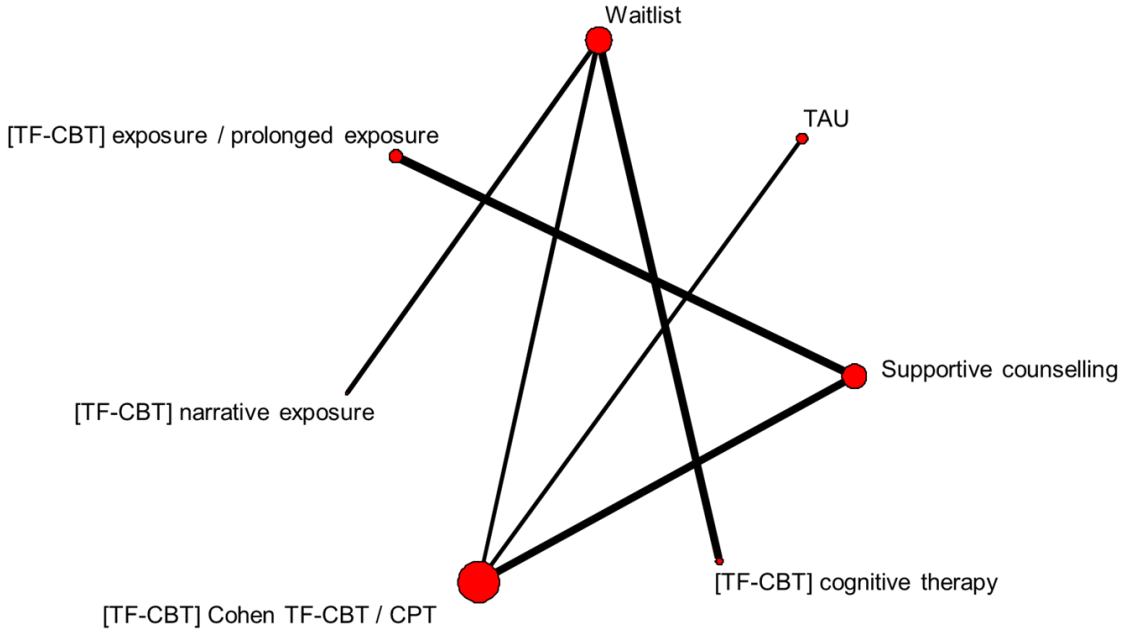
**Figure 2. Network of interventions for children and young people with PTSD**

**The width of lines is proportional to the number of trials in which each direct comparison is made. The size of each circle (treatment node) is proportional to the number of people who received each treatment.**

**a. Changes in PTSD symptom scores between baseline and treatment endpoint**




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



**c. Remission at treatment endpoint**