Efficacy and moderators of efficacy of cognitive behavioural therapies with a trauma focus in children and adolescents: an individual participant data meta-analysis of randomised trials

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Summary

Background Existing clinical trials of cognitive behavioural therapies with a trauma focus (CBTs-TF) are underpowered to examine key variables that might moderate treatment effects. We aimed to determine the efficacy of CBTs-TF for young people, relative to passive and active control conditions, and elucidate putative individual-level and treatment-level moderators.

Methods This was an individual participant data meta-analysis of published and unpublished randomised studies in young people aged 6–18 years exposed to trauma. We included studies identified by the latest UK National Institute of Health and Care Excellence guidelines (completed on Jan 29, 2018) and updated their search. The search strategy included database searches restricted to publications between Jan 1, 2018, and Nov 12, 2019; grey literature search of trial registries ClinicalTrials.gov and ISRCTN; preprint archives PsyArXiv and bioRxiv; and use of social media and emails to key authors to identify any unpublished datasets. The primary outcome was post-traumatic stress symptoms after treatment (<1 month after the final session). Predominantly, one-stage random-effects models were fitted. This study is registered with PROSPERO, CRD42019151954.

Findings We identified 38 studies; 25 studies provided individual participant data, comprising 1686 young people (mean age 13·65 years [SD 3·01]), with 802 receiving CBTs-TF and 884 a control condition. The risk-of-bias assessment indicated five studies as low risk and 20 studies with some concerns. Participants who received CBTs-TF had lower mean post-traumatic stress symptoms after treatment than those who received the control conditions, after adjusting for post-traumatic stress symptoms before treatment (b=–13·17, 95% CI –17·84 to –8·50, p<0·001, τ^2=103·72). Moderation analysis indicated that this effect of CBTs-TF on post-traumatic stress symptoms post-treatment increased by 0·15 units (b=–0·15, 95% CI –0·29 to –0·01, p=0·041, τ^2=0·03) for each unit increase in pre-treatment post-traumatic stress symptoms.

Interpretation This is the first individual participant data meta-analysis of young people exposed to trauma. Our findings support CBTs-TF as the first-line treatment, irrespective of age, gender, trauma characteristics, or carer involvement in treatment, with particular benefits for those with higher initial distress.

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Introduction

Trauma exposure in children and adolescents remains high, with global prevalence estimates ranging from 31%[1] in England and Wales to 62% in the USA.[2] According to a 2014 meta-analysis,[3] one in six young people exposed to trauma develops post-traumatic stress disorder. Often, this condition is comorbid with depression, pathological grief, anxiety, behavioural difficulties, and, in adolescents, increased suicidality, self-harm, and substance use.[1,4] For young people who develop post-traumatic stress disorder, spontaneous recovery beyond 6 months is unlikely,[5] and untreated symptoms and associated difficulties can persist well into adulthood.[6]

Clinical practice guidelines recommend cognitive behavioural therapies with a trauma focus (CBTs-TF) as the first-line treatment for post-traumatic stress disorder.[7–9] This recommendation is based on previous aggregate-data meta-analyses in young people showing that CBTs-TF are effective in reducing psychological

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Research in context

Evidence before this study

We considered clinical practice guidelines, aggregate-data meta-analyses, and individual studies of cognitive behavioural therapies with a trauma focus (CBTs-TF). Clinical practice guidelines recommend CBTs-TF as the first-line treatment for post-traumatic stress disorder. Several aggregate-data meta-analyses in young people supported this evaluation and showed that CBTs-TF were effective in reducing psychological distress. However, individual-level and treatment-level factors might attenuate or enhance treatment effects. Aggregate-data meta-analyses that rely on summary data are suboptimal for investigating moderating factors defined at the participant level. Furthermore, previous individual studies exploring moderators are limited by sample characteristics or size. The current literature indicates that although the overall efficacy of CBTs-TF is well established, findings on moderators of efficacy are limited by sample size or confounded by analysis method.

Added value of this study

This is the first individual participant data meta-analysis on the efficacy of CBTs-TF in young people exposed to trauma. We combined 25 randomised studies from around the world with various CBTs-TF, control conditions, and participant characteristics such as age, gender, trauma type, and trauma history. We applied state-of-the-art statistical methods to investigate moderators of efficacy at the individual level and treatment level. Our findings support the efficacy of CBTs-TF across post-traumatic stress symptoms, depression, and anxiety. The moderation analyses suggested that the efficacy of CBTs-TF, relative to control conditions, was amplified in participants with higher pre-treatment levels of post-traumatic stress symptoms, depression, and anxiety. There was little evidence of moderating effects of any participant characteristic or the involvement of caregivers in CBTs-TF. The effect of duration of treatment (ie, number of CBTs-TF sessions) needs further evaluation.

Implications of all the available evidence

Our investigation in a representative sample of school-aged young people (aged 6–18 years) exposed to trauma highlighted the efficacy of CBTs-TF irrespective of age, gender, and trauma characteristics. Moreover, our findings suggest that young people with greater initial distress especially benefit from CBTs-TF. The involvement of caregivers in CBTs-TF does not seem crucial for treatment success. Further studies evaluating the impact of number of sessions on treatment efficacy might inform the balance of sufficient support with resource allocation. Future mediation analyses within the individual participant data meta-analysis context is a promising next step to evaluate mechanisms of action of CBTs-TF.

distress[10] and are superior to control conditions.[11,12] Within the context of these overall benefits, important individual-level and treatment-level factors are likely to attenuate or enhance treatment effects. An understanding of such factors is crucial to personalise and refine treatment. Indeed, an aggregate-data meta-analysis suggested that individual-level factors (trauma type and gender) modulate outcomes for post-traumatic stress symptoms in young people exposed to trauma, whereas treatment-level factors (study design and treatment setting) influence treatment outcomes for depression.[13] However, meta-analyses that rely on aggregate data are necessarily based on group-level analyses and need to be interpreted with caution when seeking to understand individual-level factors that moderate outcomes.[14,15] Relatedly, existing individual clinical trials of CBTs-TF typically have inadequate statistical power to examine moderators because of limitations in sample characteristics (ie, insufficient variation of characteristics to investigate modifiers) or sample size. Consequently, there is a compelling case for combining individual participant data from multiple trials in an individual participant data meta-analysis to examine these key moderation effects.[16] We aimed to determine the efficacy of CBTs-TF compared with passive and active control conditions in young people and to examine individual-level and treatment-level factors that potentially moderate treatment effects.

We had two hypotheses. The first hypothesis was that CBTs-TF produce a reduction in a primary outcome of post-traumatic stress symptoms in young people, compared with either no intervention, treatment as usual, individual non-trauma-focused psychosocial interventions, or other individual trauma-focused psychosocial (non-CBT) interventions. The second hypothesis was that the relative efficacy of CBTs-TF in reducing post-traumatic stress symptoms compared with control conditions is moderated by individual-level factors, including age at the start of treatment, gender, trauma type of index event, trauma history, severity of post-traumatic stress symptoms before treatment, and predefined treatment-level factors available before treatment, including intended duration of CBTs-TF (number of sessions), and intended involvement of caregivers in CBTs-TF. The second hypothesis was non-directional owing to the mixed previous findings.

Methods

Search strategy and selection criteria

Only randomised intervention studies published in English were included in this individual participant data meta-analysis. Unpublished data were actively sought; hence, non-peer-reviewed studies were also included. The population of interest was children and adolescents aged 6–18 years who had been exposed to trauma, with a clinically relevant degree of severity of post-traumatic stress symptoms at trial baseline. This was determined

either by them scoring above a validated cutoff point on a traumatic stress symptom rating scale or by meeting criteria for traumatic stress disorder. We included studies that used any manualised CBT-TF, delivered either in-person or online. The following exclusion criteria were applied in this order: duplicate study; no applicable age range data extractable; no manualised CBT-TF; group format; single-session treatment; no assessment post-treatment; no standardised outcome measure to assess post-traumatic stress symptoms; no clinically relevant post-traumatic stress symptom data extractable; and comparison condition being outside the protocol.

We included studies identified by the UK National Institute of Health and Care Excellence (NICE) in its latest guideline for post-traumatic stress disorder in children and young people based on a search completed on Jan 29, 2018.[8] To update the list of studies identified by NICE, we searched the same databases (PsycInfo via Ebsco, MEDLINE and Embase via Ovid, Cochrane Central Register of Controlled Trials, and CINAHL) for content published between Jan 1, 2018, and Nov 12, 2019, using keywords, synonyms, and appropriate subject headings. The basic structure of the strategy was (("trauma*" OR "stress*") AND ("cognitive therap*" OR "psychotherap*") AND ("trial*" or "review*")). The full strategies for all databases are described in the protocol.[17] Initial agreements on abstract and full-text level for the literature search were high (99·6% for abstracts and 96·1% for full-text articles).

A second independent rater confirmed the results of the grey literature search of trial registries ClinicalTrials.gov and ISRCTN; preprint archives PsyArXiv and bioRxiv; and reference lists of included studies and relevant meta-analyses. We contacted key authors by email to request any unpublished datasets and used social media to raise awareness of the individual participant data meta-analysis. Disagreements among raters were resolved via discussion with RM-S, MAL, and TD.

Some studies recorded "age last birthday" (eg, 7 years, 8 months was recorded as 7 years), and some studies recorded age in rounded years (ie, nearest whole number of years, eg, 7 years, 8 months was recorded as 8 years), so we included studies with young people aged between 5 years and 6 months and 18 years and 11 months. Owing to different procedures across studies, sex and gender were treated interchangeably. Trauma types for the index event were combined into the following categories: accidental trauma (accidental events and natural disasters) and interpersonal trauma (war trauma and interpersonal events). Index traumas that did not match either of these two categories were indexed as missing.

Two raters (AdH and SDP) independently evaluated the risk of bias in reports of post-traumatic stress symptoms using the revised Cochrane Risk of Bias tool (RoB 2).[18] Disagreements among raters were resolved via discussion with TD.

The PRISMA-IPD checklist,[19] PICOS characteristics of included studies, and ethical committee approvals for each randomised trial are shown in appendix 1 (pp 2–6, 15–17).

Data extraction and analysis

Where multiple studies used the same source dataset, that dataset was only included once in our individual participant data meta-analysis. For published studies, key variables were re-analysed to identify potential inconsistencies in the supplied data. Inconsistencies were reported to study authors and resolved. Subsequently, data were harmonised as far as possible for definitions and scales of outcomes; timings of measurements; and definitions, scales, or subgroups used as covariates. Uncertainties were discussed with study authors.

The primary outcome was child-reported post-traumatic stress symptoms based on standardised self-report immediately after treatment completion (<1 month after the final session). We planned to analyse proxy reports by teachers, parents, and caregivers separately.

Secondary outcomes included child-reported post-traumatic stress symptoms 1–3 months after treatment completion; 4–6 months after treatment completion (irrespective of whether this was the first or second follow-up); 7–12 months after treatment completion (irrespective of whether first, second, or third follow-up); as well as at 18 months and 24 months after treatment completion. Further secondary outcomes were post-traumatic stress disorder diagnosis and symptoms of comorbid disorders such as depression and anxiety-related and externalising problems after treatment.

Post-traumatic stress symptoms measures were included for the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), DSM-5, and the tenth revision of the International Classification of Diseases (ICD-10) symptoms. Where broader stress-related measures had been administered, we included only the post-traumatic stress symptom subscale. We included any depression, anxiety (excluding obesessive compulsive disorder subscales), and externalising problems scales after treatment (<1 month after the final session) within relevant analyses. Obsessive compulsive disorder subscales were excluded to better align the anxiety measures because, first, DSM-5 and ICD-11 no longer classify obsessive compulsive disorder as an anxiety disorder, and, second, only a few anxiety measures included an obsessive compulsive disorder subscale.

Analyses followed the most recent recommendations for individual participant data meta-analysis.[20,21] We analysed overall treatment efficacy with a one-stage random-effects model with random intercept for study and random slope for intervention (CBTs-TF *vs* control conditions), adjusting for pre-treatment levels of outcomes, which was measured immediately before treatment start (<1 month before the first session; randomisation had to have taken place after this assessment). We used forest plots to present individual

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See Online for appendix 1

study results for each outcome. We subsequently adjusted for a prespecified set of covariates (age, gender, trauma type, trauma history, and pre-treatment post-traumatic stress symptoms) in the one-stage random-effects model. In line with protocol, we checked whether sufficient data on any additional individual-level factors (eg, pre-treatment comorbidity, pre-treatment levels of dysfunctional post-traumatic cognitions, pre-treatment IQ, and pre-treatment parental mental health) or treatment-level factors (eg, predefined mode of administration, profession of therapists, and pre-treatment treatment expectancy) were available from a representative number of studies. Pre-treatment level of dysfunctional post-traumatic cognitions was added as an exploratory individual-level factor. Information on data categorisation is available in appendix 1 (p 7). For the outcomes depression, anxiety, and externalising problems, we additionally adjusted for their respective pre-treatment levels. All covariates were entered simultaneously.

No adjustments for multiple testing were made. The analysis of CBTs-TF versus control conditions on post-traumatic stress symptoms (without covariate adjustment other than pre-treatment post-traumatic stress symptoms) was the prespecified primary analysis, whereas other analyses were considered exploratory.

In an exploratory analysis, we compared CBTs-TF with specific types of control conditions. We applied a two-stage network meta-analysis because it accounted for studies that provided multiple comparisons. For each study, we first extracted the effect of intervention (CBT-TF *vs* specific control condition) on the outcomes and adjusted for pre-treatment levels. We then compared the effect sizes of all four control conditions against CBTs-TF.

Heterogeneity was quantified using τ^2 and obtained by modelling a random slope for the variable of interest. Heterogeneity was then interpretable as the variance of the random-effects distribution on the observed effect of the variable, such that τ^2 reflected the between-study variance in the effect.[22] A value of 0 indicated no heterogeneity. Mean differences between CBTs-TF and control conditions served as measures of effect. Because we standardised the measures of the primary and secondary outcomes of the studies to uniform scales, we treated them as standardised mean differences (*b*) with 95% CIs.

See Online for appendix 2

Individual-level factors were centred for each study to separate within-study and across-study effects. Interaction terms between intervention status (CBT-TF *vs* control condition) and individual-level factors were specified. Within-study interactions were created out of the main effects of intervention (CBT-TF *vs* control condition) and the individual deviation from the study mean (eg, individual age minus mean age in a specific study). Across-study interactions were derived from the main effects of intervention (CBT-TF *vs* control condition) and the study mean. We report within-study interactions; across-study interactions were included to adjust for aggregation bias. Both the three main effects (intervention, individual deviation from study mean, and study mean) and respective pre-treatment levels were included as fixed effects.

We assessed whether the overall effect of CBTs-TF was moderated by the predefined intended duration of CBTs-TF or by predefined intended involvement of caregivers in CBTs-TF (both treatment-level factors at the study level). Two-stage meta-regression analysis was used to investigate the effect of the intended number of CBTs-TF treatment sessions on the overall treatment effect of CBTs-TF. For each study, we first extracted the effect of intervention (CBT-TF *vs* control condition) on the outcomes, adjusted for pre-treatment levels. In a second step, we regressed this effect on the intended number of CBTs-TF treatment sessions. Two-stage network meta-analysis was applied to examine the role of predefined intended involvement of caregivers in CBTs-TF because it accounted for studies that provided multiple comparisons. For each study, we first extracted the effect for each contrast on the outcomes, adjusted for pre-treatment levels. In a second step, we compared these three groups against each other.

We did not adjust for multiple testing for the moderation analyses of the primary outcome of post-traumatic stress symptoms after treatment. Consequently, the interpretation of the results of modifiers of this primary outcome effect focuses on strength and direction of effect rather than on statistical significance.

Multiple imputation was used to account for missing data. The imputation model took the clustered data structure into account (ie, clustered by study). Detailed information on the data harmonisation, imputation model, and sensitivity analyses are presented in appendix 1 (pp 7–10). SPSS software (version 27.0) was used for data extraction, data checks, and data harmonisation. R software (version 4.2.2) was used for data analysis (appendix 1 p 11). The R script is provided in appendix 2.

The study is registered with PROSPERO, CRD42019151954.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

38 studies met the inclusion criteria and were queried for individual participant data (figure 1). The study results or protocols were published between 1996 and 2023. Of the 38 studies, 25 provided individual participant data.[23–47] Reasons for not providing individual participant data were restrictions due to ethics (six studies), no access to the original data (four studies), and no time to provide the data (two studies; figure 1). One research group did not respond to multiple contact attempts (see appendix 1 p 12 for individual reasons per study). We were able to

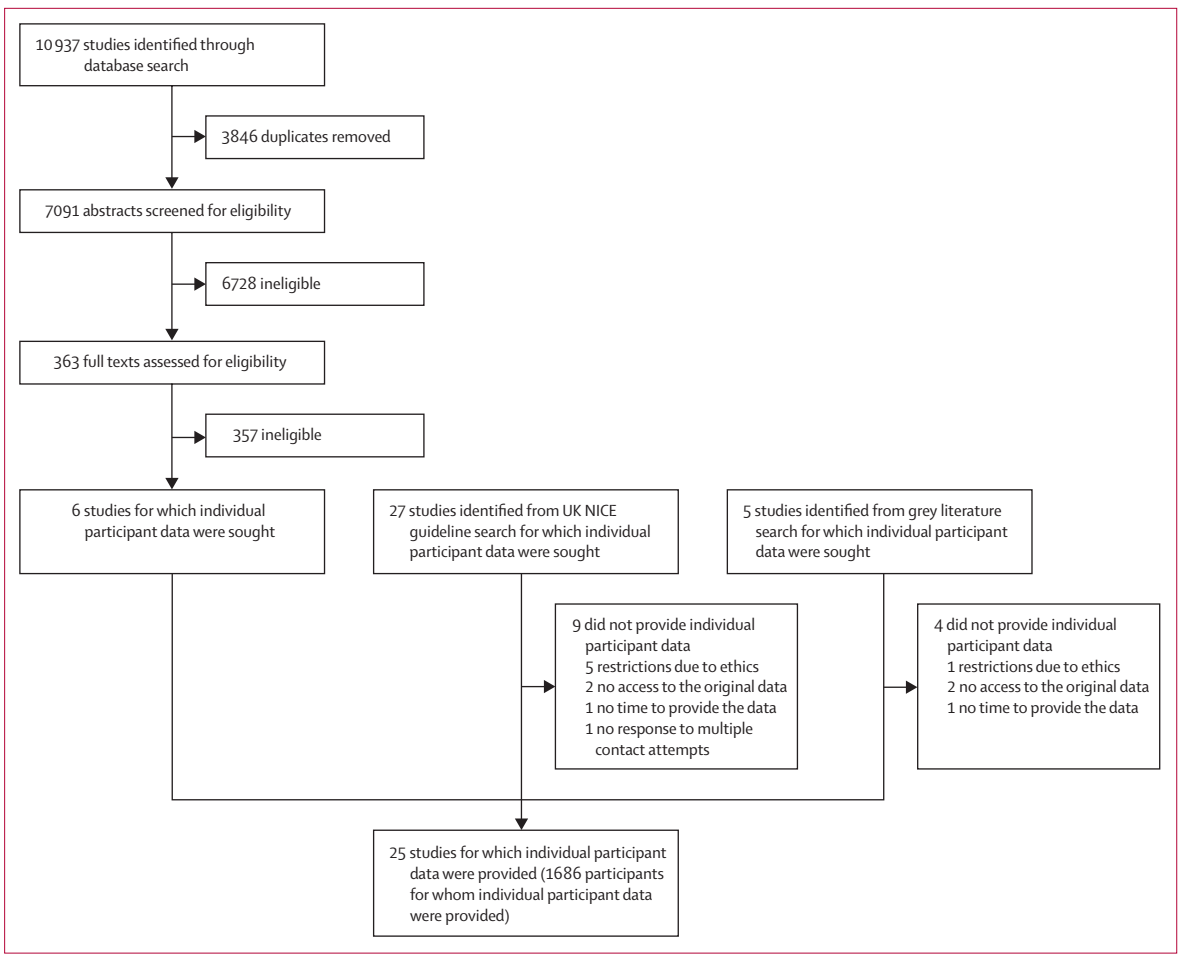

Figure 1: **Study selection**
The individual reasons per study why individual participant data were not provided are given in appendix 1 (p 12). NICE=National Institute for Health and Care Excellence.

use the published data for nine of those 13 studies that did not provide individual participant data to compare risk-of-bias ratings and aggregate-level treatment effect sizes with the 25 included studies that did provide individual participant data; risk-of-bias ratings did not significantly differ (x^2[1]=2·11, p=0·15; see appendix 1 pp 13–14 for individual study ratings), and no significant difference was seen in aggregate-level treatment effects (t[28]=–0·22, p=0·83).

The final dataset comprised 25 studies with 1686 young people aged 6–18 years (mean age 13·65 years [SD 3·01]) from countries with both high-income and low-middle income status (Australia, Democratic Republic of the Congo, Finland, Germany, Indonesia, Iran, Iraq, Israel, Norway, South Africa, Sri Lanka, Sweden, the Netherlands, Uganda, the UK, the USA, and Zambia; appendix 1 pp 15–17). Study characteristics are shown in appendix 1 (pp 15–17). Eight studies had administered the Child Post-Traumatic Cognitions Inventory (CPTCI)[48] and three studies the Post-Traumatic Cognitions Inventory (PTCI).[49] 1060 (62·9%) of 1686 participants were female. 1045 (62·0%) reported an interpersonal trauma as the index event and 185 (11·0%) an accidental trauma, with missing information for 456 (27·0%) participants. 967 (57·4%) participants had experienced other traumas in addition to the index event, and 138 (8·2%) reported no further trauma exposure, with missing information for 581 (34·5%) participants. All treatments were administered in person. 802 (47·6%) participants had CBTs-TF. Types of CBT-TF belonged to the following broad categories, often adapted for young people: abuse-focused or trauma-focused CBT, CBT, cognitive therapy, cognitive behavioural writing therapy, cognitive processing therapy, narrative exposure therapy, prolonged exposure therapy, and trauma affect regulation. The intended duration of treatment for CBTs-TF varied from four to 30 sessions (mean 11·76 [SD 5·54]). 240 (14·2%) participants, including those on waitlists, received no intervention. 341 (20·2%) participants received treatment as usual, which was delivered in the routine setting of any social, psychological, or pharmacological intervention that was not a CBT-TF. 175 (10·4%) participants received

individual non-trauma-focused psychosocial interventions that were formal control conditions with manualised protocols; these interventions ranged from meditation relaxation, supportive counselling, relational supportive therapy to time-limited psychodynamic psychotherapy. 128 (7·6%) participants received other individual trauma-focused non-CBT psychosocial interventions that were formal control conditions with manualised protocols; these interventions included eye movement desensitisation and reprocessing (EMDR) and emotional freedom techniques.

Five studies were identified as having a low risk of bias. For 20 studies, concerns arose mainly due to domain four "measurement of the outcome" (self-report or unmasked assessors) and domain five "selection of the reported results" (no pre-registered analysis protocols available; appendix 1 p 13).

In a deviation from protocol, we combined child self-report (19 studies), clinician-rated child report (five studies), and proxy report (one study) for the primary outcome of post-traumatic stress symptoms. This was necessary because there was not enough of each reporting type to consider them separately. Sensitivity checks indicated that these studies could sensibly be combined (see appendix 1 p 7 for information on data harmonisation). We also repeated every analysis with the subsample of the 19 studies that provided child self-reported post-traumatic stress symptoms after treatment (including 1527 participants) and found the results to be very similar to results from the total sample (appendix 1 pp 9–10). Appendix 1 (p 18) provides information on the secondary outcomes of post-traumatic stress symptoms at 3-month, 6-month, and 12-month follow-ups, and of depression, anxiety, and externalising problems after treatment. Too few studies provided data on post-traumatic stress disorder diagnosis and post-traumatic stress symptoms at 18-month and at 24-month follow-up assessments to facilitate the planned analyses.

In the primary outcome analysis adjusted for post-traumatic stress symptoms before treatment, CBTs-TF had lower mean post-traumatic stress symptoms after treatment than the control conditions (b=–13·17, 95% CI –17·84 to –8·50, SE 2·38, t[1547·71]=–5·53, p<0·001; figure 2). Between-study heterogeneity was large (τ^2=103·72).

Analyses of post-traumatic stress symptoms, adjusted for pre-treatment levels, showed similar effects in favour of CBTs-TF at follow-up assessments at 1–3 months, 4–6 months, and 7–12 months (ranging from b=–12·09 [SE 2·36] to –9·72 [2·12], all p<0·001). Slightly smaller

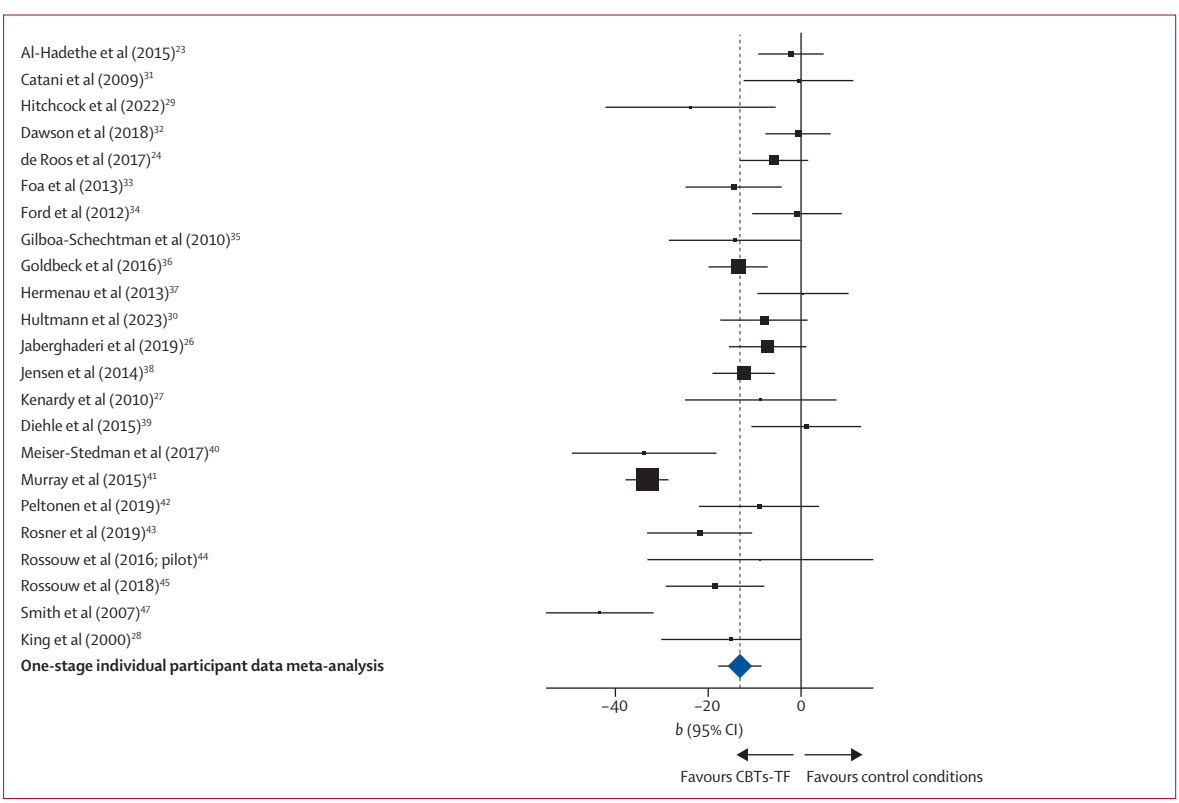

Figure 2: **Effect of CBTs-TF versus control conditions on post-traumatic stress symptoms after treatment, adjusted for post-traumatic stress symptoms before treatment**

Because of their study designs, the studies by Ertl and colleagues[25] and Robjant and colleagues[46] are not shown. Marker size reflects study sample size. The lozenge shows the pooled estimate from the one-stage analysis (between-study heterogeneity τ^2=103·72). b is the standardised mean difference, and error bars indicate 95% CIs. CBTs-TF=cognitive behavioural therapies with a trauma focus.

effects in favour of CBTs-TF were found for depression after treatment (–6·63 [1·69], p<0·001) and anxiety after treatment (–7·77 [1·97], p<0·001; appendix 1 pp 19, 21–25). We found no evidence of an effect of CBTs-TF on externalising problems after treatment (*b*=–2·76 [SE 1·67], p=0·098; appendix 1 pp 19, 26).

When adjusting for covariates (age, gender, trauma type, trauma history, post-traumatic stress symptoms, and dysfunctional post-traumatic cognition severity before treatment), the effect of CBTs-TF remained similar to the unadjusted result for post-traumatic stress symptoms after treatment and at follow-up assessments (ranging from *b*=–13·16 [SE 2·38] to –9·68 [2·11], all p<0·001; appendix 1 p 27). The same was true for depression (*b*=–6·73 [SE 1·68], p<0·001), anxiety (–7·89 [1·97], p<0·001), and externalising problems (–2·64 [1·72], p=0·13) after treatment, additionally adjusted for respective pre-treatment levels (appendix 1 pp 27–28).

CBTs-TF was associated with lower mean post-traumatic stress symptoms after treatment compared with no intervention and treatment as usual (figure 3A). There was a slightly smaller effect in favour of CBTs-TF than with non-trauma-focused psychosocial interventions. We found no evidence of a difference in post-treatment post-traumatic stress symptoms between CBTs-TF and trauma-focused non-CBT psychosocial interventions. Post-traumatic stress symptoms showed similar patterns at 1–3, 4–6, and 7–12 month follow-up assessments, and for depression and anxiety after treatment (appendix 1 pp 29–31).

For externalising problems, CBTs-TF was associated with lower mean externalising problems after treatment compared with no intervention and treatment as usual (figure 3B), but there was no evidence of a difference in post-treatment externalising problems between CBTs-TF and non-trauma-focused psychosocial interventions. Notably, however, trauma-focused non-CBT psychosocial interventions were associated with lower mean externalising problems after treatment compared with CBTs-TF.

Post-traumatic stress symptoms before treatment had a moderating effect on the effect of CBTs-TF on post-traumatic stress symptoms after treatment. Moderation analysis indicated that the beneficial effect of CBTs-TF on post-traumatic stress symptoms increased by 0·15 units for each unit increase in pre-treatment post-traumatic stress symptoms, suggesting that the efficacy of CBTs-TF, relative to control conditions, was amplified in those with higher pre-treatment post-traumatic stress symptoms (appendix 1 p 33). Similar moderating effects were observed for depression severity before treatment on depression severity after treatment, and anxiety severity before treatment on anxiety severity after treatment, suggesting that the efficacy of CBTs-TF, relative to control conditions, was amplified for these respective outcomes in those with higher pre-treatment depression or anxiety

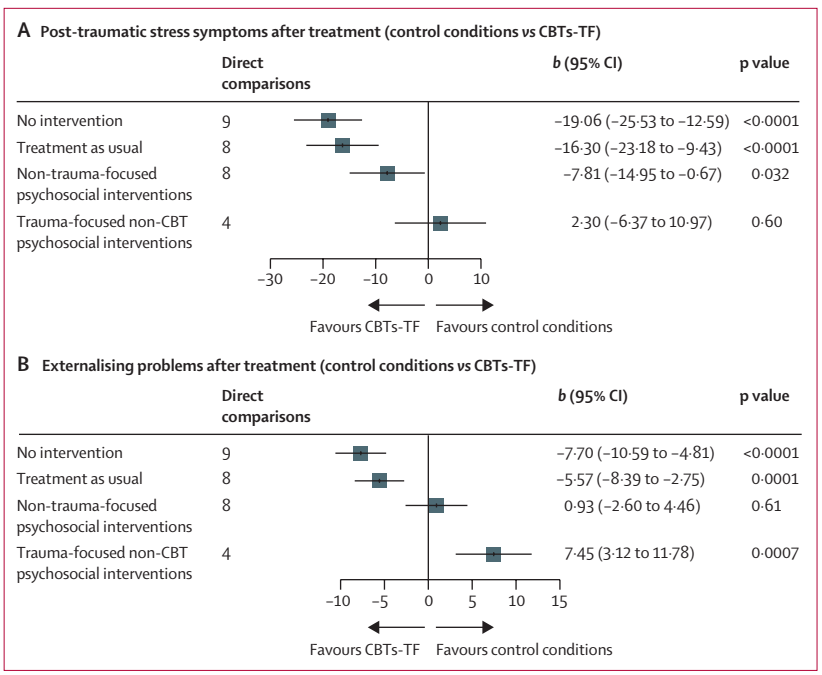

***Figure* 3: Comparison of standard mean differences in efficacy on post-traumatic stress symptoms (A) and externalising problems (B) after CBTs-TF versus control conditions, adjusting for respective pre-treatment levels**

b is the standardised mean difference, and error bars indicate 95% CIs. CBTs-TF=cognitive behavioural therapies with a trauma focus.

(appendix 1 p 33). However, there was no evidence of a moderating effect of pre-treatment externalising problems for externalising problems after treatment (appendix 1 p 33). Moreover, there was no evidence of moderating effects of any of the other individual-level factors, including age, gender, trauma type, trauma history, and dysfunctional post-traumatic cognitions, for post-traumatic stress symptoms after treatment or for secondary outcomes (appendix 1 p 33).

In a meta-regression analysis of the effect of predefined intended duration of CBT-TF treatment, a greater number of intended CBT-TF treatment sessions was associated with a larger effect in favour of CBTs-TF (appendix 1 p 34) for the primary outcome of post-treatment post-traumatic stress symptoms after treatment (the beneficial effect of CBTs-TF on post-traumatic stress symptoms after treatment increased by 0·92 units for each unit increase in number of intended CBT-TF treatment sessions). Similar results were observed for all secondary outcomes (appendix 1 p 34). However, on average, the number of intended CBT-TF treatment sessions varied relative to different control conditions, making interpretation difficult. We therefore fitted a one-stage model with random intercept for study and respective pre-treatment adjustment to explore the effect of intended duration of treatment only for those participants who received CBTs-TF (n=802). Here, we found no evidence that

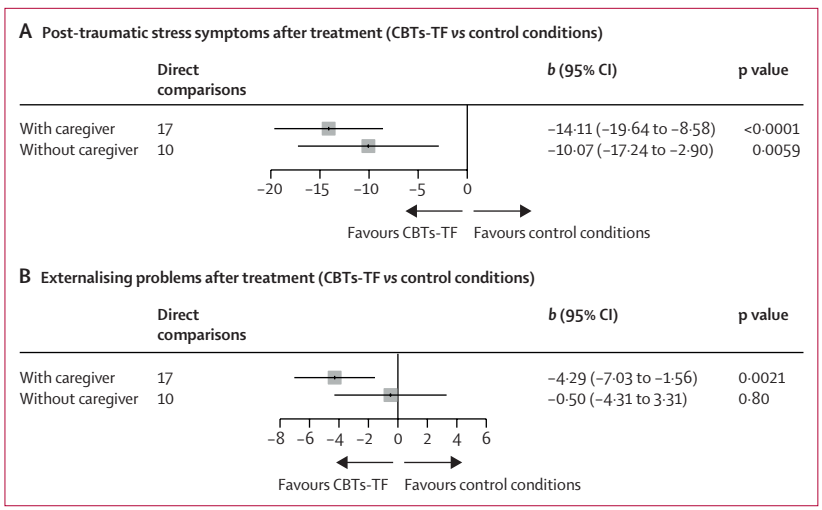

Figure 4: **Comparison of standard mean differences in efficacy of CBTs-TF (with and without intended caregiver involvement) versus control conditions on post-traumatic stress symptoms (A) and externalising problems (B), adjusting for respective pre-treatment levels**

b is the standardised mean difference, and error bars indicate 95% CIs. CBTs-TF=cognitive behavioural therapies with a trauma focus.

intended duration of treatment influenced post-traumatic stress symptoms after treatment or any secondary outcome (appendix 1 p 34).

There was no evidence of a moderating effect of predefined intended involvement of caregivers in CBTs-TF for the primary outcome of post-traumatic stress symptoms after treatment (*b*=4·04, 95% CI −4·65 to 12·74, p=0·36) or for any of the secondary outcomes (ranging from 1·26 to 3·80, all p≥0·094; appendix 1 pp 35–38). Post-traumatic stress symptoms after treatment were lower in participants receiving CBTs-TF with intended caregiver involvement and with no caregiver involvement than participants given control conditions (figure 4A). Similar (if not slightly smaller) effects in favour of CBTs-TF were found for the secondary outcomes, except for externalising problems after treatment (appendix 1 pp 35–38). There was a difference in post-treatment externalising problems between CBTs-TF with intended caregiver involvement and control conditions, but no difference in post-treatment externalising problems between CBTs-TF without intended caregiver involvement and control conditions (figure 4B).

Discussion

Results of this individual participant data meta-analysis suggest that CBT-TF is an efficacious treatment for young people with post-traumatic stress symptoms. CBTs-TF were superior to both active and passive control conditions in reducing post-traumatic stress symptoms, and these benefits were maintained for 12 months. Moreover, CBTs-TF showed superior efficacy relative to control conditions for reducing depression and anxiety, consistent with the results of recent aggregate-data meta-analyses.[11–13]

When exploring differential effects across types of control condition, CBTs-TF were superior to control conditions that included no intervention, treatment as usual, or non-trauma-focused psychosocial interventions. We found little evidence of a difference in effects between CBTs-TF and trauma-focused non-CBT psychosocial interventions such as EMDR and emotional freedom techniques for post-traumatic stress symptoms, depression, and anxiety, in line with findings of previous aggregate-data meta-analyses.[11,12] EMDR entails the activation and reprocessing of the traumatic memory, whereas emotional freedom techniques include exposure and cognitive restructuring. Although conceptually different, CBT-TF, EMDR, and emotional freedom techniques are varieties of trauma-focused protocols. Indeed, International Society for Traumatic Stress Studies (ISTSS) guidelines "strongly recommend"[7] both EMDR and CBT-TF as first-line treatments for paediatric post-traumatic stress disorder. Other guidelines, however, such as the latest NICE guidance,[8] state that EMDR should be considered for young people with persistent post-traumatic stress disorder only if they do not respond to or engage with CBT-TF. Only a small number of randomised studies have compared trauma-focused non-CBT approaches and CBTs-TF in young people. Determining which treatment should be offered first to young people with post-traumatic stress symptoms might be a promising avenue of future research.

Use of individual participant data meta-analysis enabled a thorough examination of putative treatment-moderating factors. In terms of individual-level predictors of treatment efficacy, we found some evidence of moderating effects of pre-treatment levels of post-traumatic stress symptoms, depression, and anxiety, such that the efficacy of CBTs-TF relative to control conditions for those respective outcomes at post-treatment appeared amplified when pre-treatment levels were higher. Although of moderate size, these moderation effects suggest that CBT-TF might be especially effective for young people with higher initial distress levels. Conversely, we found no evidence of moderating effects of participants' characteristics (age, gender, trauma type, and trauma history), supporting clinical recommendations to administer CBT-TF to all young people irrespective of age, gender, and trauma characteristics. Our findings make a strong case that even the relatively short-term CBT-TF included in the current dataset (mean of 12 CBT-TF sessions) can be successfully administered in young people exposed to multiple traumas, and they contradict concerns that short-term CBT-TF is a therapy format that only works for patients with a single incident of trauma exposure.[50,51] The weak evidence of moderating effects of participants' characteristics does contrast with previous individual clinical trials and aggregate-data meta-analyses. For example, previous aggregate-data meta-analyses suggest trauma type, gender, and age as moderators.[10,13] This is an indication of the necessity to disentangle within-study

and across-study interactions,[15,20] which is only possible in individual participant data meta-analyses. Significant across-study interactions might arise due to potential differences in covariate distribution between studies (ie, some studies might be mostly male or mostly female), and from these differences correlating with other study-level factors so that the interaction effect is at risk of study-level confounding.

In terms of treatment-level moderating factors, greater number of intended CBT-TF sessions was associated with a larger effect in favour of CBT-TF for all clinical outcomes. However, a limitation of the interpretability of this result is that the number of intended CBT-TF sessions differed in comparison to different control conditions. Our analyses on the effect of intended duration of CBT-TF treatment on treatment efficacy was therefore probably confounded by type of control condition. Indeed, among those participants who received CBTs-TF, there was no evidence that intended duration of treatment influenced any clinical outcome. Future studies that purposefully vary the number of intended CBT-TF sessions across trial groups, or match the number of planned sessions across treatment types, might clarify this issue. However, duration of treatment is probably dependent on study setting (eg, refugee camp *vs* clinical routine setting) and the health-care system's defaults.

Across all outcomes, our findings provide little evidence of a differential effect by caregiver involvement in CBT-TF compared with control conditions, with the exception of the outcome of externalising problems. This is potentially good news in settings and family constellations in which involving caregivers in trauma-focused therapy is either not possible or unwanted by the young person. Notably, we explored the role of intended involvement of caregivers (ie, the actual involvement in therapy might have been different) and did not have any further information on the quality and quantity of caregiver involvement. A recent aggregate-data meta-analysis suggests differential effects of number of sessions and duration of sessions on treatment effect.[52] Although future work might indicate individual-level factors where a caregiver should be involved, current evidence suggests that involvement of a caregiver will not significantly change the efficacy of CBT-TF in treating post-traumatic stress symptoms and comorbid symptoms.

We found mixed results for the efficacy of CBTs-TF on externalising problems after treatment. From a methodological point of view, variance between studies might be a reason. Compared with the other outcomes (ie, post-traumatic stress symptoms, depression, and anxiety), we included more proxy reports and used a broader construct. From a clinical point of view, treating externalising problems without involving a caregiver might miss the interactional component of externalising problems in daily life.[53] This might explain why only CBTs-TF involving a caregiver were superior to control conditions.

A key strength of our study is the use of individual participant data, which allowed us to align inclusion criteria, outcome measures, individual-level factors, and treatment-level factors, and to disentangle across-study from within-study effects, thus overcoming limitations of previous moderation analyses. For the primary outcome, we chose post-traumatic stress symptoms rather than post-traumatic stress disorder diagnosis. This is a sensitive approach because it allows us to harmonise data across children and adolescents (as some children manifest clinically significant post-traumatic stress symptoms and need treatment but do not meet the full post-traumatic stress disorder criteria);[54] different diagnostic classification systems (eg, differences between ICD and DSM in regard to how many symptoms need to be met to fulfil a post-traumatic stress disorder diagnosis); and findings across various settings, including those in which conducting clinical interviews might not be possible. As in every meta-analysis, we combined different post-traumatic stress symptoms measures. The use of individual participant data allowed us to better align the scales and content (eg, where broader stress-related measures had been administered, we included only the post-traumatic stress symptoms subscale) than would have been possible in an aggregate-data meta-analysis.

However, using individual participant data takes considerably longer than an aggregate-data meta-analysis. Considering the large number of trials and the variety and complexity of statistical analyses in our individual participant data meta-analysis, up to 24 months can be expected for data collection, cleaning, and harmonisation, and up to 12 months for the statistical analyses.[21] This accounts for why the search was completed at the end of 2019. By including completed but unpublished studies[29,30] at the time of the search, we were able to stay up to date. Notably, as with all secondary data analyses, we were constrained by the data provided. This precluded us from exploring additional factors of putative interest, including profession of therapists, treatment expectancy, and parental mental health. Moreover, we were not able to differentiate further within the categories of interpersonal trauma and accidental trauma. Most participants reported an interpersonal trauma as the index event and had experienced other additional traumas. Whether experience of interpersonal versus non-interpersonal trauma might substantially affect treatment effects is therefore unclear. Further clinical trials will improve our ability to answer these questions in future meta-analyses. Finally, although we did not receive individual participant data for all identified studies, the studies from which we could not include data did not differ in aggregate analyses from the 25 included studies in terms of effect size or risk-of-bias rating. Hence, we are confident that our results provide a representative picture of the current state of evidence. Childhood trauma has been reported as a transdiagnostic

risk factor[1,55] and models of transdiagnostic mechanisms have been proposed.[56] Future analyses applying mediation analyses within the individual participant data meta-analysis context to evaluate transdiagnostic processes and mechanisms of action of CBTs-TF such as cognitive and behavioural processes, actual number of CBT-TF sessions, and actual involvement and actual number of CBT-TF sessions for caregivers seem like a promising next step.

In conclusion, CBTs-TF are efficacious in treating young people with post-traumatic stress symptoms. Moreover, the results suggest a sustained effect up to 12 months and a transdiagnostic value for depression and anxiety. Importantly, these effects seem to be amplified for young people with higher pre-treatment distress levels across post-traumatic stress symptoms, depression, and anxiety. More research is needed to explore whether CBTs-TFs need to be tailored more for children with externalising problems, as the small number of studies and methodological differences between those studies limit our conclusions. There was no evidence that the effects were moderated by participants' characteristics, supporting CBTs-TF as the first-line treatment for all children and adolescents worldwide. Hence, increasing access to CBTs-TF across the world seems an important next step. The results indicate that CBT-TF can be successfully administered even if caregivers are not available to take part. However, future examination of the ideal treatment features of CBT-TF will need to further explore the impact of intended duration of treatment (for young people and caregivers) on treatment efficacy to balance of sufficient support with resource allocation.

Contributors

AdH, RM-S, MAL, CHi, and TD designed the project. IK did the literature search. AdH, MJB, KK, and SDP completed study screening, with input from RM-S, MAL, and TD. AdH and SDP did the risk-of-bias rating, with input from TD. RM-S, AMF, CC, KD, RAB, CdR, VE, EBF, JDF, EG-S, DT, KH, TH, OH, UA, NJ, TKJ, SMO, JK, RJLL, JD, LKM, JCK, KP, SK, KR, AK, RR, JR, PS, BJT, CHi, and TD provided datasets and advised on data harmonisation. AdH and CHi accessed and verified the data. AdH completed data analysis with input from CHa, CHi, and TD, and statistical advice from DJF, OCU, and BGJ. AdH wrote the first draft of the manuscript with input from CHi and TD. All authors critically reviewed and approved the final manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

RM-S received personal payment for teaching on the delivery of cognitive therapy for post-traumatic stress disorder for children and young people at various UK universities and training bodies, and he is an unpaid council member of the UK Trauma Council. EBF received payment for contributing to a post-traumatic stress disorder manual and workbook and for post-traumatic stress disorder workshops, lectures, and meetings. JDF served as a consultant for Advanced Trauma Solutions Professionals. SK received minor side income from lecturing in a clinical training program for Narrative Exposure Therapy (University of Turku, Turku, Finland). PS received a share of royalties from Routledge publishers from publication of a cognitive therapy for post-traumatic stress disorder manual for young people; he was an unpaid member of the research committee of the Children and War Foundation (a non-profit based in Norway) and an unpaid trustee of the Children and War UK (a non-profit based in the UK). CHi received personal payment for writing an article regarding treatment of therapy for post-traumatic stress disorder in preschool-aged children from the Aeon Media Group. TD received personal payment for teaching on the delivery of cognitive therapy for post-traumatic stress disorder for children and young people at various UK universities and training bodies. All other authors declare no competing interests.

Data sharing

The R script is provided in appendix 2. The data cannot be made available to others because of ethical restrictions.

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