



The early course and treatment of posttraumatic stress disorder in very young children: diagnostic prevalence and predictors in hospital-attending children and a randomized controlled proof-of-concept trial of trauma-focused cognitive therapy, for 3- to 8-year-olds

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Background: The introduction of developmentally adapted criteria for posttraumatic stress disorder (PTSD) has improved the identification of ≤ 6 -year-old children with clinical needs. Across two studies, we assess predictors of the development of PTSD in young children (PTSD-YC), including the adult-led acute stress disorder (ASD) diagnosis, and provide proof of principle for cognitive-focused therapy for this age range, with the aim of increasing treatment options for children diagnosed with PTSD-YC. **Method:** Study 1 ($N = 105$) assessed ASD and PTSD-YC diagnosis in 3- to 8-year-old children within one month and at around three months following attendance at an emergency room. Study 2 ($N = 37$) was a preregistered (www.isrctn.com/ISRCTN35018680) randomized controlled early-phase trial comparing CBT-3M, a cognitive-focused intervention, to treatment-as-usual (TAU) delivered within the UK NHS to 3- to 8-year-olds diagnosed with PTSD-YC. **Results:** In Study 1, the ASD diagnosis failed to identify any young children. In contrast, prevalence of acute PTSD-YC (minus the duration requirement) was 8.6% in the first month post-trauma and 10.1% at 3 months. Length of hospital stay, but no other demographic or trauma-related characteristics, predicted development of later PTSD-YC. Early (within one month) diagnosis of acute PTSD-YC had a positive predictive value of 50% for later PTSD-YC. In Study 2, most children lost their PTSD-YC diagnosis following completion of CBT-3M (84.6%) relative to TAU (6.7%) and CBT-3M was acceptable to recipient families. Effect sizes were also in favor of CBT-3M for secondary outcome measures. **Conclusions:** The ASD diagnosis is not fit for purpose in this age-group. There was a strong and encouraging signal of putative efficacy for young children treated using a cognitive-focused treatment for PTSD, and a larger trial of CBT-3M is now warranted. **Keywords:** Posttraumatic stress disorder; young children; cognitive behavioral therapy; randomized control trial.

Introduction

Recent editions of diagnostic manuals for mental health disorders include an increased focus on identifying posttraumatic stress disorder (PTSD) in preschool children aged 6 years or younger (e.g. the PTSD Preschool diagnosis in the Fifth edition of the Diagnostic and Statistical Manual: DSM-5 (American Psychiatric Association, 2013); PTSD in the Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood (Zero to Three, 2016)) using developmentally appropriate symptom algorithms. This shift emerged following pioneering research demonstrating that traumatic stress diagnoses derived from adult-led

PTSD criteria fail to identify many young children with clinical needs in contrast to a developmentally sensitive 'alternative algorithm' (Scheeringa, Myers, Putnam, & Zeanah, 2012). Developmentally tailored PTSD diagnoses for young children (PTSD-YC) are now in widespread use (e.g. De Young, Kenardy, & Cobham, 2011; Meiser-Stedman, Smith, Glucksmann, Yule, & Dalgleish, 2008; Scheeringa et al., 2012; see De Young & Landolt, 2018, for a review), with a growing number of trials demonstrating that cognitive behavioral therapy (CBT) can efficaciously treat PTSD symptoms in this younger age range (e.g. Haag et al., 2020; Salloum et al., 2016; Scheeringa, Weems, Cohen, Amaya-Jackson, & Guthrie, 2011). Here, across two studies, we aimed to further advance understanding of the course and treatment options for PTSD-YC diagnosis by exploring (a) early post-trauma predictors of the course of DSM-5

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PTSD-YC and specifically whether the current DSM-5 version of the acute stress disorder diagnosis may also need developmental modification, and (b) providing proof of concept in 3- to 8-year-olds for a cognitive-focused therapy for PTSD which has been shown to be effective in older children and adolescents via an early-stage randomized controlled trial.

Study 1: DSM-5 acute stress disorder and PTSD-YC in trauma exposed young children following emergency room attendance

Many young people show natural attenuation of posttraumatic stress symptoms in the months following exposure (Hiller et al., 2016; Le Brocque et al., 2020). In terms of very young children, to date, there have been a small number of longitudinal studies charting the course of PTSD symptoms and/or of the PTSD-YC diagnosis using the alternative algorithm (e.g. De Young et al., 2011; Le Brocque et al., 2020; Meiser-Stedman et al., 2008; Scheeringa, Zeanah, Myers, & Putnam, 2005). In addition, wait-list control arms of prior CBT studies (e.g. Scheeringa et al., 2011) have tracked the untreated course of PTSD symptoms in this age-group. To our knowledge, there have been no studies evaluating the early course of the DSM-5 PTSD-YC, as opposed to severity of symptoms, in very young children.

In older youth, several predictive factors reliably distinguish children who recover from those who go on to develop PTSD (only diagnosable at 1 month post-trauma) (Meiser-Stedman, McKinnon, et al., 2017; Meiser-Stedman, Smith, et al., 2017; Trickey, Siddaway, Meiser-Stedman, Serpell, & Field, 2012). However, we know far less about predictors in very young children (Le Brocque et al., 2020; Meiser-Stedman et al., 2008). The first aims of Study 1 were therefore to examine both the course of, and predictors of, DSM-5 PTSD-YC in very young children.

One such putative predictor is meeting criteria for DSM-5 acute stress disorder (ASD) within the first month post-trauma. ASD was introduced in the DSM-IV to identify in the acute stage those at higher risk of later PTSD. In 8- to 16-year-olds, the presence of ASD markedly increases the likelihood of later PTSD (odds ratio = 26.9; Meiser-Stedman, McKinnon, et al., 2017). However, despite the significant update to the PTSD criteria to accommodate very young children in the DSM-5 there has been no corresponding change in the ASD criteria which remain grounded in the adult literature. The further aims of Study 1 were therefore to examine the utility of the DSM-5 ASD criteria in very young children both in detecting early cases of young children in clinical need and in predicting later PTSD-YC.

One alternative to the current DSM-5 ASD criteria for very young children would be to use the current developmentally sensitive DSM-5 PTSD-YC criteria in the first month post-trauma (i.e. with the usual PTSD duration criterion removed) in the form of an

'acute DSM-5 PTSD-YC' diagnosis. In one study in children aged 2–6 years, meeting acute PTSD-YC criteria (based on the alternative algorithm (AA); Scheeringa et al., 2012) in the month post-trauma significantly predicted increased risk of later AA-PTSD-YC (Meiser-Stedman et al., 2008). Our final aim for Study 1 was therefore to examine the utility of an acute DSM-5 PTSD-YC diagnosis in identifying cases and predicting later DSM-5 PTSD-YC.

Previous research has suggested that the PTSD-YC diagnosis may be a more appropriate conceptualization of PTSD beyond the preschool range for children up to 8 years of age (Danzi & La Greca, 2017; Hitchcock et al., 2021; Meiser-Stedman et al., 2008). For this reason, the present study also reports prevalence estimates for children both up to 6 years and up to 8 years.

Study 1 therefore addressed five questions: (1) What is the course of DSM-5 PTSD-YC symptoms in 3- to 6-year-olds (and 3- to 8-year-olds) over the first 3 months post-trauma following attendance at an Emergency Room? (2) What trauma-related and demographic factors predict later DSM-5 PTSD-YC? (3) What is the prevalence of DSM-5 ASD in young children? (4) Does the DSM-5 ASD diagnosis – designed to aid early identification of those at risk – have prognostic utility in this age-group? and (5) Is 'acute PTSD-YC' a superior alternative?

Method

Participants. National Health Service ethics approval (12/EE/0458) was obtained. Participants were 3- to 8-year-old children and caregivers ($N = 105$) attending 3 emergency rooms (ER) in East Anglia, UK, during recruitment phases between 2014 and 2017. Participants were eligible for inclusion if they were aged 3–8 years and if the event that led to attendance at the ER met criteria for a traumatic event according to the DSM-5 (though see De Young & Landolt, 2018, for a discussion of the complexities around this criterion in younger children). We only included children with a single-event trauma, that is, for whom no other DSM-5 criterion A trauma was identified by their parents. Exclusion criteria were lack of English fluency in either the child or the caregiver, moderate-to-severe brain injury, and the presence of a child protection issue.

ER records were screened for trauma event details to determine eligibility before approaching families. Eligible families were given study information upon or after discharge and gave informed consent prior to participation. Approximately 27% of approached families agreed to participate. This rate is similar to that in our prior RCTs for childhood PTSD (e.g. Meiser-Stedman, Smith, et al., 2017). Reasons for nonparticipation included caregivers not interested (37%), caregivers had no time (35%), could not make contact (25%), and exclusion criterion identified at first contact (2%). The substantial lack of parental engagement and perceived lack of time for mental health research recruiting from ER attendance highlight an important feasibility issue for future research.

Diagnostic assessments. Assessments were conducted via telephone by trained research staff within the first month (Time 1) and at around three months (Time 2) after ER attendance. Diagnoses of DSM-5 ASD (within the first month post-trauma) and DSM-5 PTSD-YC and adult-algorithm DSM-

5 PTSD (three months post-trauma) were made via clinical interview with a parent using the Diagnostic Infant and Preschool Assessment (DIPA; Scheeringa & Haslett, 2010), adapted (through correspondence with the DIPA lead author) for the DSM-5 to cover the preschool PTSD diagnosis as well as to include criteria for acute stress disorder and with minor adjustments for oppositional defiance disorder. We also generated an 'acute PTSD-YC' diagnosis at Time 1 (ignoring the duration criterion) to evaluate whether this had better predictive value than the ASD diagnosis. The DIPA is a psychometrically robust parental-report semistructured interview which was delivered and scored by an Assistant Psychologist, with scoring for 100% of interviews second-rated using the original audio files by a registered Clinical Psychologist with extensive experience treating children with PTSD. Symptoms were scored as present or absent. Agreement was obtained on 100% of interviews.

Of the 105 children screened at Time 1, 26 did not respond to repeated attempts to contact at Time 2.

Analytic approach. Multiple imputation: We used multiple imputation to deal with missing data at Time 2, using multivariate imputation by chained equations (MICE) (Van Buuren, 2018) implemented in SPSS v.25. We imputed 25 datasets using a fully conditional specification whereby all Time 2 variables with missing data were included in the chained regression models (logistic or linear for categorical and continuous variables, respectively), alongside Time 1 variables for which we had complete data, and residual variance was added to the parameter estimates using a Bayesian approach. This meant that for any given analysis involving imputed data, the imputation model for those data had included variables with complete data that were not themselves included in the analysis (Van Buuren, 2018).

Prediction of Time 2 diagnostic outcomes: To examine prediction of PTSD-YC at Time 2 from baseline sample characteristics, we compared those children who developed PTSD-YC at Time 2 to those who did not, on Time 1 variables of age, sex, ethnicity, type of trauma, whether the child lost consciousness, whether pain killing medication was administered, whether there was an admission to hospital, and number of days in hospital, with analyses pooled across the 25 imputed datasets.

The predictive utilities of the different diagnostic criteria at Time 1 for the diagnoses at Time 2 were examined using positive/negative predictive values, where a positive predictive value represents the likelihood that a child meeting PTSD-YC criteria at Time 1 would have PTSD-YC at Time 2 and a negative predictive value represents the likelihood that a child without the diagnosis at Time 1 would not have the diagnosis at Time 2. Analyses were pooled across the imputed datasets.

Results

Sample characteristics and prevalence. Sample characteristics are presented in Table 1. Observed prevalence rates are presented separately for 3- to 6-year-olds and 3- to 8-year-olds. At Time 1, in both 3- to 6-year-olds and 3- to 8-year-olds, strikingly DSM-5 ASD criteria did not identify any children. Using acute PTSD-YC criteria, prevalence estimates rose to 9.1% (7/77) in 3- to 6-year-olds and to 8.6% (9/105) in 3- to 8-year-olds.

At Time 2, the standard DSM-5 PTSD criteria identified 5.3% (3/57) of 3- to 6-year-olds, and this doubled to 10.5% (6/57) when using DSM-5 PTSD-YC. For 3- to 8-year-olds, use of PTSD-YC identified

Table 1 Sample characteristics at Time 1 for Study 1

	Age ≤6 years (n = 77 unless otherwise noted)	Age ≤8 years (n = 105 unless otherwise noted)
Age (mean (SD))	4.38 (1.10) range 3–6	5.19 (1.73) range 3–8 ^e
Female	56.9% ^a	38.1% ^f
White/European origin	83.9% ^b	85.2% ^g
Trauma type	^a	^h
Accidental injury	54.2%	55.3%
Road traffic accident	12.5%	14.9%
Acute medical emergency	18.1%	17.0%
Burn	13.9%	11.7%
Other	1.4%	1.1%
Painkillers administered	21.4% ^c	18.9% ^g
Loss of consciousness	12.9% ^c	11.0% ⁱ
Admitted to hospital	56.9% ^a	56.4% ^f
Number of days in hospital (mean (SD))	1.66 (2.36), range 0–10 ^d	1.65 (2.31), range 0–10 ^j

Table shows observed data.

^an = 72.

^bn = 62.

^cn = 70.

^dn = 71.

^en = 102.

^fn = 94.

^gn = 81.

^hn = 90.

ⁱn = 91.

^jn = 92.

10.1% (8/79) with PTSD, relative to 6.3% (5/79) according to the DSM-5 adult criteria.

At Time 1, of those who did not meet criteria for the full 'acute PTSD-YC' diagnosis, 57 (53.8%) did meet the re-experiencing criterion, 42 (39.6%) the avoidance criterion, and 25 (25.3%) the hyperarousal criterion. At Time 2, of those who did not meet full PTSD-YC criteria, 30 (28.6%) did meet the re-experiencing criterion, 16 (15.2%) the avoidance criterion, and 16 (15.2%) the hyperarousal criterion.

Predictors of PTSD-YC at Time 2. Data were compiled across 3- to 8-year-olds for these analyses to increase power. Analyses are reported for multiply imputed data (Van Buuren, 2018). Sensitivity analyses on complete cases revealed no differences in the pattern of results.

We first compared the Time 1 variables (listed in Table 1) between those children who went on to develop PTSD-YC at Time 2 to those who did not. Neither trauma type (Fisher's exact $p = .34$), age (Mann-Whitney test: $d = 0.14$, 95% CI $[-0.41, 0.71]$, $p = .62$), sex (Fisher's exact $p = .70$), ethnicity (Fisher's exact $p = 1.00$), admission to hospital (Fisher's exact $p = .41$), whether the child lost consciousness

(Fisher's exact $p = .59$), or administration of painkillers (Fisher's exact $p = .61$) at Time 1 was associated with PTSD-YC at Time 2. A greater number of days in hospital (Mann-Whitney test: $d = 0.92$, 95% CI $[-0.32, 1.51]$, $p = .002$) at Time 1 were significantly associated with Time 2 development of PTSD-YC.

As no children at Time 1 met criteria for DSM-5 ASD, this had no calculable predictive value for later PTSD-YC. Of the nine children diagnosed with acute PTSD-YC at Time 1, 4 met DSM-5 PTSD-YC criteria at Time 2, 4 did not meet criteria at Time 2, and one was lost to attrition. Of the 95 children not diagnosed with acute PTSD-YC at Time 1, four were diagnosed with PTSD-YC at Time 2. There was a modest positive predictive value of 50% and a high negative predictive value of 90%, using the imputed data, comparable to the predictive value of DSM-IV ASD in older youth (Dalglish et al., 2008).

Discussion

Consistent with a recent review (De Young & Landolt, 2018), application of the developmentally appropriate DSM-5 PTSD-YC criteria in an ER-attending sample doubled the prevalence estimate for PTSD relative to adult DSM-5 PTSD criteria, at 3 months post-trauma. PTSD-YC appeared to have clinical utility up to 8 years of age, replicating prior research (Meiser-Stedman et al., 2008), and this reinforces suggestions that the developmental stage of all youth, including older children, should be taken into consideration when optimizing the conceptualization of posttraumatic stress, as opposed to a simple binary distinction with the cutoff at 6 years (De Young & Landolt, 2018).

No young children met DSM-5 ASD criteria (which importantly remain adult-based in the DSM-5) in the acute post-trauma phase. In contrast, DSM-5 PTSD-YC criteria applied in this acute phase (minus the duration criterion) – acute PTSD-YC – suggested that ~9% of young children had diagnosable levels of immediate distress. This is not dissimilar to rates reported in older children (Kassam-Adams et al., 2012) and in the small number of studies of younger children in this acute phase (e.g. Haag & Landolt, 2017; Meiser-Stedman et al., 2008). Half of these children meeting criteria for acute PTSD-YC in the first month went on to develop PTSD-YC at three months. Prevalence estimates for PTSD-YC at 3 months were ~10%, and this is not dissimilar to other studies looking at PTSD-YC at around this time point post-trauma (e.g. Scheeringa et al., 2005). No other demographic, trauma-related, or clinical factors were significantly predictive of later PTSD-YC other than amount of time in hospital (although other factors not measured, such as parental factors, may have shown a different pattern; e.g. Le Brocq et al., 2020).

There are a number of potential limitations to this study. A low prevalence of children with ASD and

acute PTSD-YC at Time 1 meant we were not able to fully explore predicting factors. A large percentage of families also declined participation. As we were unable to collect PTSD measures from nonparticipating families, it may be that those experiencing more difficulty were more likely to volunteer for research, impacting our prevalence estimates. Finally, diagnoses, necessarily in this age-group, relied upon clinical interviews using parent report.

However, with the participating sample, we were able to gain important understanding of the course of PTSD-YC in the early months following trauma. Study findings further validate the introduction of PTSD-YC into the DSM-5, but suggest that the current adult-based DSM-5 ASD diagnosis is not fit for purpose as an acute prognostic algorithm for young children and requires revision or replacement. It may be that particular ASD symptoms are insensitive in young children (Dalglish et al., 2008) or that the current thresholds for diagnosis in the DSM-5 are inappropriate (Kassam-Adams et al., 2012). Given this, it is difficult to recommend ASD for future study in this age-group.

Study 2: A randomized controlled proof-of-principle trial of a trauma-focused cognitive therapy for young children with PTSD-YC

International guidelines recommend individual cognitive behavior therapy (CBT) with a trauma focus for the treatment of PTSD in adults and older youth (Australian Centre for Posttraumatic Mental Health, 2007; Bisson et al., 2019; National Institute for Health & Care Excellence, 2018; World Health Organization, 2013). However, these guidelines offer no explicit recommendation for the treatment of PTSD in young children aged under 5 years. Prior trials have been very encouraging, suggesting that developmentally tailored CBT can reduce symptoms of PTSD in children aged 2–8 years who experience elevated posttraumatic stress but who do not necessarily meet criteria for a PTSD diagnosis (Deblinger, Stauffer, & Steer, 2001; Salloum et al., 2016; Scheeringa et al., 2011). Parent-directed CBT-based intervention has also been effective in accelerating recovery from acute stress symptoms in 1- to 6-year-olds following accidental injury (Haag et al., 2020). There is therefore a promising evidence base for variations of CBT in treating young children.

The availability of multiple evidence-based treatments for a condition offers sufferers and their families an important degree of choice. Based on our prior clinical trials with older children (e.g. Meiser-Stedman, Smith, et al., 2017), we were interested in whether a CBT for PTSD intervention that is more cognitive in its formulation compared to that used in extant trials may also be adaptable for this younger sample. Our trauma-based cognitive therapy protocol for young children – CBT-3M (Goodall et al., 2017) – includes a strong focus on three Ms:

cognitive restructuring of trauma *Memories*, challenging maladaptive cognitive appraisals (*Meanings*), and remediating unhelpful coping strategies employed by children and parents/caregivers (*Management*). The manual also includes much less of an emphasis on exposure relative to other protocols, as some therapists can be hesitant to use exposure with young children (Whiteside, Deacon, Benito, & Stewart, 2016). Instead, the CBT-3M protocol focuses predominantly on restructuring and updating the trauma *memory* narrative (through drawings, play, and talking) with new information that challenges or contradicts the maladaptive *meanings* associated with the trauma that are embedded in the narrative (see Goodall et al., 2017, for a detailed case study).

We therefore built upon prior work by (a) developing a CBT-3M manual building on the protocol used by Scheeringa et al. (2011) but enriching the cognitive elements based on our work with older youth (Smith, Dalgleish, & Meiser-Stedman, 2018) as outlined above; (b) conducting a proof-of-principle randomized controlled trial (RCT) to explore whether CBT-3M (versus treatment-as-usual; TAU) is likely to deliver remission from PTSD-YC in young children. This is therefore not a definitive evaluation of CBT-3M but an earlier stage RCT to provide a point estimate of putative efficacy as a platform for later phase trials (Dalgleish et al., 2015); and (c) providing important information about acceptability and feasibility of CBT-3M and of the feasibility of a later-stage trial.

The RCT represents the first UK trial of a CBT intervention for PTSD-YC and is the first to include only those children who meet criteria for a DSM-5 PTSD-YC diagnosis, as opposed to elevated symptom levels, where recovery from diagnosis is the primary outcome – a factor that may be important for healthcare systems where diagnosis acts as a gateway to care.

As a result of the findings from Study 1 showing that PTSD-YC identifies children with PTSD up to age 8 years who are missed by the standard PTSD diagnosis alongside the other similar data that prompted the age cutoff in Study 1 (Danzi & La Greca, 2017; Hitchcock et al., 2021; Meiser-Stedman et al., 2008), and in accordance with the slightly wider age range recruited in some prior CBT trials providing treatment to young children experiencing PTSD (e.g. Salloum et al., 2016), we recruited young children with PTSD-YC up to 8 years of age.

Method

Trial design and procedure. The RCT was preregistered (www.isrctn.com/ISRCTN35018680) and ethically approved (Cambridge South: MREC 12/EE/0458). Full details of design, measures, and recruitment are in the published protocol (Dalgleish et al., 2015). All participants were recruited in the East of England from a variety of sources including ERs (including participants from Study 1 who had PTSD at 3 months post-trauma), schools, general medical practices,

secondary care child mental health services, social services, and via self-referral. Figure 1 shows the CONSORT diagram prior to cross-over at post-treatment. Recruitment took place from December 2013 until April 2018. There were periods of time when recruitment was stalled or significantly slowed (around 9 months in total) due to staffing changes and the necessity for retraining, and/or part-time working in the trial team. Initial recruitment rates were also slower due to the need to establish a recruitment network. Once recruitment pathways were established and fully resourced, recruitment rates were around 3–4 young people per month of whom around 1 in 3 met inclusion criteria and for whom the parent(s) agreed to take part in the trial.

Inclusion criteria were being aged 3–8 years and having experienced a single incident trauma according to the DSM-5 definition (see Study 1) and diagnosis of DSM-5-Preschool PTSD-YC assessed via clinical interview using the DIPA. Exclusion criteria were the presence of head trauma (Glasgow Coma Score < 8); learning disability, but not specific learning difficulties; a diagnosis of autism; another primary psychiatric diagnosis that warrants treatment using a psychological therapy ahead of the traumatic stress response; inability to speak English within the family; ongoing exposure to threat; and a history of organic brain damage. Victims of chronic sexual or physical abuse were invited into the trial because of the need to involve specialist services.

A wider range of trauma compared to Study 1 were experienced by the 37 participants including a burn ($n = 1$), accidental injury (e.g. dog attack; $n = 9$), acute medical emergency ($n = 2$), home invasion ($n = 4$), road traffic accident ($n = 3$), physical or sexual assault or other interpersonal event involving threat of injury/life ($n = 9$), or witnessing an event in which a family member (parent, sibling, or grandparent) experienced threat to life/serious injury ($n = 9$).

Participants were randomized to treatment with stratification for age, gender, and symptom severity (based on the DIPA), by an independent statistician. The treating clinical psychologist was informed of allocation after the baseline assessment via email from the statistician. All assessments were completed by trained research staff, who were blind to treatment allocation. Outcomes were assessed pretreatment, within two weeks of post-treatment and, for those in the CBT-3M arm, at three-month follow-up. Upon completion of the post-treatment assessment, children in TAU who still met PTSD-YC criteria were offered CBT-3M. The planned twelve-month follow-up for the CBT-3M arm was unfeasible given lower than anticipated completion rates at three-month follow-up. No adverse events were reported.

Outcomes

Primary outcome. The primary outcome was recovery from DSM-5 PTSD-YC at post-treatment, using the parent-report DIPA (Scheeringa & Haslett, 2010). As in Study 1, a registered Clinical Psychologist agreed on diagnosis for 100% of the interviews, which were completed by trained research staff who were blind to treatment allocation.

Secondary outcomes. Secondary outcomes were comorbid diagnoses of major depressive disorder (MDD), attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), generalized anxiety disorder (GAD), specific phobia and separation anxiety disorder (SAD) on the DIPA, and changes on the parent-completed Young Child PTSD Checklist (Scheeringa, 2010) (Cronbach's $\alpha = .85$ for this study) to index symptoms of

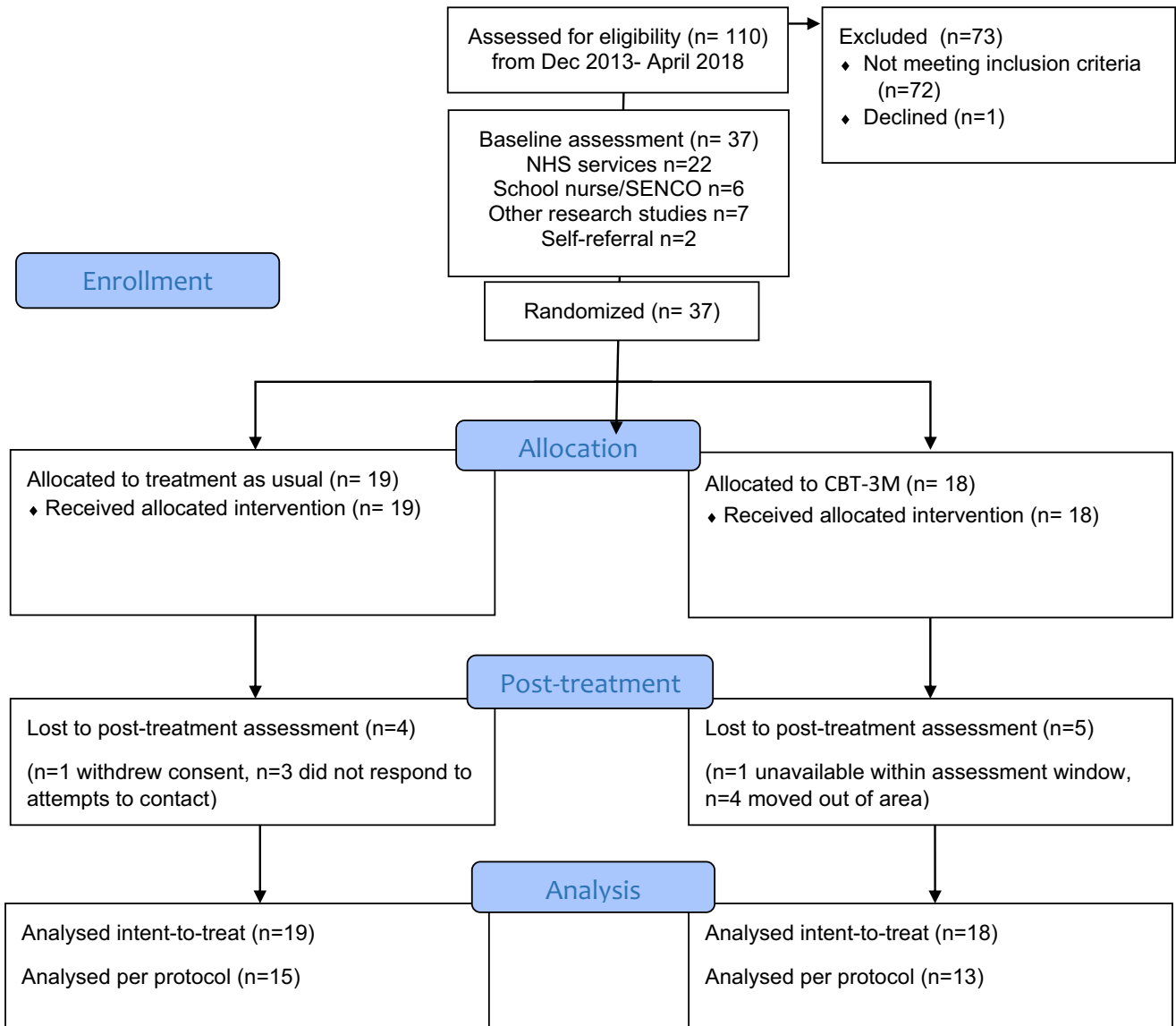


Figure 1 CONSORT diagram for randomized controlled trial of CBT-3M versus treatment-as-usual (TAU), prior to cross-over post-treatment

PTSD, the parent-completed Pediatric Emotional Distress Scale (to index general distress; Saylor, Swenson, Stokes Reynolds, & Taylor, 1999) (Cronbach's $\alpha = .84$ for this study), and parent-completed Preschool Feelings Checklist (to index emotional functioning; Luby, Heffelfinger, Koenig-McNaught, Brown, & Spitznagel, 2004) (Cronbach's $\alpha = .74$ for this study).

Feasibility and acceptability. Attrition at each assessment point indicated trial and intervention feasibility and acceptability. A random 50% of families (to reduce participant burden) completing CBT-3M were also asked to rate, out of ten, whether (1) 'this kind of treatment seems to make sense', (2) 'I think this treatment is going to help us', (3) 'I would tell a friend to try this treatment with their child', and (4) 'the therapist is keen to help my child'. Additional formal acceptability measures outlined in the trial

protocol (Dalglish et al., 2015) – for example, the Therapeutic Alliance Scale (Shirk, Karver, & Brown, 2011) – were withdrawn in order to reduce clinician and participant burden.

Interventions. *CBT-3M:* The CBT-3M treatment manual is available online (<https://c2ad.mrc-cbu.cam.ac.uk/resources/>). The intervention was adapted from our 12-session intervention for older youth (Meiser-Stedman, Smith, et al., 2017; Perrin et al., 2017; Smith et al., 2007) and the prior trial protocol from Scheeringa (Scheeringa et al., 2011). As noted in the Introduction, the protocol is more cognitive than that used in prior trials and targets three key mechanisms: trauma *Memories*, maladaptive appraisals (*Meanings*), and adaptive coping (*Management*). Twelve sessions, delivered weekly, involve a combination of the therapist and child alone, therapist and parent alone, and parent and

child with the therapist, with each session involving a combination of these three elements. Treatment fidelity and adherence was maintained through supervision with manual authors (Dalglish and Smith).

Treatment-as-usual: Given that PTSD-YC as a diagnosis has no explicit treatment guidelines in the United Kingdom, TAU was expected to vary from no intervention, to diverse forms of psychosocial support. Caregivers in both trial arms were given some basic psychoeducation about PTSD symptoms in young children in the initial assessment. Comparison against TAU allowed us to assess what intervention young children with PTSD commonly receive through the UK NHS. Participants allocated to TAU who did not receive a multi-session psychological intervention were assessed for 'post-treatment' at 13–15 weeks postbaseline to maximize comparability with CBT-3M.

Overview of analyses. Analyses were completed by an independent statistician who was blind to treatment allocation. We tested for between-arm differences using the nonparametric Quade's test (Quade, 1967) to account for the modest sample size. This represents a deviation from our protocol where we discussed using parametric analyses (Dalglish et al., 2015). Intent-to-treat (ITT) analysis was completed following multiple imputation of post-treatment variables across 40 datasets using the same MICE and imputation modeling approach as that outlined for Study 1 (Bodner, 2008; van Buuren, 2018) such that baseline variables with complete data, alongside the trial arm variable, were included in the imputation models.

As an early-phase proof-of-principle trial, the RCT was not powered to detect statistically significant effects on outcomes but rather to derive point estimates of effect size for the efficacy of CBT-3M to inform later fully powered definitive trial investigations (see trial protocol paper; Dalglish et al., 2015).

In addition to the reported data, we collected information on health service usage on the complete cases to evaluate feasibility for collecting such data to inform health economics analyses in later-stage trials.

Results

Baseline characteristics, treatment completion, and acceptability. The baseline characteristics of the sample are presented in Table 2.

Of the nineteen children allocated to TAU, four did not complete post-treatment assessments (21% attrition): one family pursued treatment elsewhere and withdrew and three were uncontactable. Within TAU, only one child received any form of psychological intervention; the rest received no specific

Table 2 Baseline clinical characteristics for Study 2

	TAU (<i>n</i> = 19)		CBT-3M (<i>n</i> = 18)	
	Mean	(<i>SD</i>)	Mean	(<i>SD</i>)
Number female (%)	10	53%	9	50%
Age (range 3–8)	6.5	(1.9)	6.0	(1.7)
Time since trauma (months)	9.22	(9.30)	11.88	(8.50)
Young Child PTSD Checklist	33.97	(14.63)	33.54	(15.66)
Preschool Feelings Checklist	28.71	(11.19)	29.73	(9.68)
Pediatric Emotional Distress Scale	51.40	(8.42)	51.71	(10.05)
Comorbid MDD ^a	7	39%	8	47%
Comorbid ADHD ^b	5	26%	3	19%
Comorbid ODD ^b	10	53%	10	63%
Comorbid specific phobia ^b	10	53%	11	69%
Comorbid social phobia ^c	2	11%	3	18%
Comorbid GAD ^a	0	0%	2	12%
Comorbid separation anxiety ^b	10	53%	8	50%

Comorbid diagnoses scored using the DIPA. ADHD, attention deficit hyperactivity disorder; GAD, generalized anxiety disorder; MDD, major depressive disorder; ODD, oppositional defiant disorder.

^a*n* = 18 for TAU and *n* = 17 for CBT-3M.

^b*n* = 16 for CBT-3M.

^c*n* = 17 for CBT-3M.

trauma-related support. Following the TAU period, caregivers of four of those children who still met criteria for PTSD declined treatment with CBT-3M; one child had received treatment elsewhere, two reported that it was no longer required, and one did not respond to efforts to contact. The remainder received the intervention.

For CBT-3M, in all but one case the parent who attended with their child was the mother. Within the CBT-3M arm, all participants completed the 12 intervention sessions (where participants were unable to attend, sessions were rescheduled in order to deliver the full dose of the intervention). Sessions took place at the local general practice, child mental health clinic, at the university treatment center, or in the child's home. Five CBT-3M participants did not attend the post-treatment assessment (29% attrition); one was unavailable in the assessment window, and four could not be contacted as they had moved away from the area. There was no significant difference for gender (TAU: Fisher's exact = 1.55, *p* = .21; CBT-3M: Fisher's exact = 1.29, *p* = .26), age (TAU: *t* = 0.26, *p* = .80; CBT-3M: *t* = 1.01, *p* = .37), symptoms on the YCPC (TAU: *t* = 1.28, *p* = .22; CBT-3M: *t* = 1.25, *p* = .24), nor PTSD impairment score indexed by the DIPA at baseline (TAU: *t* = 0.39, *p* = .70; CBT-3M: *t* = 1.09, *p* = .29) between complete cases and those lost to attrition.

In terms of acceptability, means (out of 10; *n* = 9) for caregiver ratings of CBT-3M indicated that the treatment made sense to the family (*M* = 9.36, *SD* = 1.03) and that caregivers felt: The therapy

would help ($M = 8.91$, $SD = 1.70$); the therapist wanted to help their family ($M = 9.73$, $SD = 0.90$); and they would recommend CBT-3M to a friend ($M = 9.18$, $SD = 1.25$).

Primary outcome. In all cases, apart from one (with the father), CBT-3M outcome assessments were completed with the participant's mother. Of the complete cases, on the primary endpoint of DSM-5 PTSD-YC diagnosis at post-treatment, 84.6% ($n = 11$) CBT-3M participants lost their PTSD-YC diagnosis, relative to 6.7% ($n = 1$) TAU participants; a significant difference using intent-to-treat analysis on the imputed data $OR = 0.022$ [0.002, 0.270], $p = .003$, and corroborated with per protocol analyses involving only the complete cases: $OR = 0.019$ [0.002, 0.214]; $p = .001$.

Secondary outcomes. The observed secondary outcome data are presented in Table 3. Intent-to-treat analysis on the imputed datasets for these secondary outcomes using Quade's test indicated a significant, large effect size in favor of CBT-3M at post-treatment for scores on the Preschool Feelings Checklist, $t(7.45) = 4.07$, $d = 1.34$, 95% CI [0.62, 2.05], $p = .004$. Medium-sized, though (as expected) non-significant, effect size estimates were observed for the Young Child PTSD Checklist, $t(6.17) = 1.89$, $d = 0.62$, 95% CI [-0.05, 1.28], $p = .11$, and Pediatric Emotion Distress Scale, $t(6.82) = 1.44$, $d = 0.47$, 95% CI [-0.19, 1.12], $p = .19$. A large effect was found in favor of CBT-3M for the Fear subscale of the PEDS, though again this did not reach statistical significance, $t(5.91) = 2.32$, $d = 0.76$, 95% CI [0.09, 1.42], $p = .06$.

Odds ratios were in favor of CBT-3M for remission of comorbid diagnoses (although they did not attain traditional levels of significance); major depressive disorder, $OR = 0.20$; 95% CI [0.02, 1.67], $p = .14$; oppositional defiant disorder, $OR = 0.19$, 95% CI [0.02, 2.19], $p = .18$; and specific phobia, $OR = 0.62$, 95% CI [0.04, 9.95], $p = .73$. Data were too sparse to fit logistic models for other comorbid disorders.

At three-month follow-up (for CBT-3M only due to cross-over trial design), all 8 of the assessed participants did not meet criteria for PTSD-YC.

Discussion

Building on pioneering prior work (Meiser-Stedman, McKinnon, et al., 2017; Scheeringa et al., 2012;

Smith et al., 2007), Study 2 provides proof of principle from an early-phase RCT that a trauma-based CBT package with a strong cognitive element and minimal exposure-based work, shown to be efficacious in older youth, can be successfully adapted to treat PTSD in children as young as three years within the UK healthcare system. Eighty-four per cent of treated young children lost their diagnosis (relative to ~7% in TAU), with good acceptability. This RCT is not a definitive trial but one intended to provide important information on feasibility, acceptability, and the strength of the signal of efficacy as a platform for later-stage definitive evaluations of CBT-3M. Improving access to evidence-based treatment in this younger age-group is particularly important as children in the TAU trial arm (with one exception) received no psychological intervention from the UK NHS (limiting our conclusions regarding treatment efficacy against an active intervention), which is likely due in part to the lack of UK guidance on available evidence-based interventions for this age-group (National Institute for Health & Care Excellence, 2018).

The study highlighted important feasibility issues, in particular the completion of follow-up assessments, which will be important to consider when designing a later-stage trial. Specifically, a number of families who completed the intervention stage of the trial were unavailable for the post-treatment outcome assessment, in the majority of cases because the families had moved away from the area. Closer attention to making alternative arrangements for assessment in these circumstances will be required.

General discussion

Following the presentation of developmentally sensitive criteria to characterize PTSD in young children (Scheeringa et al., 2012) culminating in the introduction of a subtype-PTSD diagnosis for preschoolers (PTSD-YC) in the DSM-5 (American Psychiatric Association, 2013), the nature of traumatic stress has now been extensively elaborated in the youngest trauma victims. Our findings reinforce the importance of using developmentally appropriate PTSD-YC criteria when evaluating posttraumatic stress in young children.

Study 1 demonstrated that the current adult-based DSM-5 diagnosis of acute stress disorder is not fit for purpose in this younger age-group, failing

Table 3 Mean (standard deviation) symptom scores at post-treatment, by group allocation for Study 2

	Young children PTSD Checklist	PEDS-total	PEDS-fear	Preschool feelings checklist
TAU	34.80 (20.86)	45.60 (14.60)	13.00 (4.42)	30.20 (19.72)
CBT-3M	16.43 (19.27)	40.50 (14.53)	8.63 (5.48)	15.86 (11.47)

Table displays observed means. CBT-3M, cognitive behavior therapy-3M (Meanings, Memories, and Management); PEDS, Pediatric Emotion Distress Scale; TAU, treatment-as-usual.

to identify a single child in the acute phase with clinically significant distress. In contrast, applying the developmentally appropriate PTSD-YC criteria immediately post-trauma identified around 9% of young children with diagnosable levels of problems – a level comparable to estimates of acute distress found in other studies, including those with older youth (Haag & Landolt, 2017; Meiser-Stedman et al., 2008; see De Young & Landolt, 2018). This suggests that developmental adjustment of traumatic stress in the DSM-5 requires extension to the acute-phase diagnosis within the first few weeks post-trauma. Our findings suggest significant enduring morbidity in young children in the absence of suitable intervention; only around 50% of those identified as at risk in the acute phase of Study 1 recovered by 3 months, while minimal recovery was reported with TAU in Study 2.

As we are now able to identify young children burdened by debilitating PTSD, it is imperative that we continue to develop and expand on suitable interventions for this age-group to provide choice for therapists and families. Here, we have provided proof-of-principle support that a trauma-based cognitive therapy (CBT-3M) can be successfully adapted for younger children (with a slightly broader range of traumas relative to Study 1) ensuring that the same intervention protocol has applicability across the young age range from 3–18 years (Meiser-Stedman, Smith, et al., 2017). A fully powered, definitive trial is now necessary to evaluate treatment efficacy and

identify mechanisms of action, as well as extending evaluation of the intervention to more complex presentations.

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Key points

- The DSM-5 PTSD in young children (PTSD-YC) diagnostic subtype may have clinical utility up to 8 years of age.
- The DSM-5 acute stress disorder diagnosis is not fit for purpose in very young children and requires revision.
- A cognitive-focused treatment for PTSD (CBT-3M) showed promising preliminary efficacy for 3- to 8-year-olds.
- A larger trial of CBT-3M is now warranted to increase treatment options for this vulnerable age-group.

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