

# Systematic Review and Meta-analysis: Group-Based Interventions for Treating Posttraumatic Stress Symptoms in Children and Adolescents

Rebecca S. Davis, DEdPsy<sup>ID</sup>, Richard Meiser-Stedman, PhD, DCLinPsy<sup>ID</sup>, Nimrah Afzal, MSc<sup>ID</sup>, John Devaney, PhD, MSW<sup>ID</sup>, Sarah L. Halligan, DPhil<sup>ID</sup>, Katie Lofthouse, BA<sup>ID</sup>, Patrick Smith, PhD<sup>ID</sup>, Paul Stallard, PhD<sup>ID</sup>, Siyan Ye, MSc<sup>ID</sup>, Rachel M. Hiller, PhD<sup>ID</sup>




**Objective:** Trauma exposure in childhood is common and can lead to a range of negative mental health outcomes, including posttraumatic stress disorder (PTSD). In many settings, resources to address this distress are scarce. Group-based interventions require minimal resources and training, can be delivered by non-mental health specialists, and target larger numbers of children and adolescents. This meta-analysis sought to establish whether such an approach is an effective method for targeting PTSD symptoms and to identify potential moderators of effectiveness.

**Method:** PubMed, PsycNET, and PTSDPubs were searched for randomized controlled trials that used a group-based PTSD intervention with children and adolescents aged 6 to 18 years. Data were extracted for PTSD symptoms and depression symptoms. A random-effects meta-analysis was conducted to obtain between-group pooled effect size estimates. This study was registered on PROSPERO (CRD42020187214).

**Results:** The initial search identified 9,650 studies, of which 42 were eligible for inclusion ( $N = 5,998$ ). Children randomized to a group-based intervention had significantly lower PTSD symptoms after treatment compared with a control group, with a medium pooled effect ( $g = -0.55$ , 95% CI  $[-0.76, -0.35]$ ). Group interventions were superior when compared with either active or passive controls, at follow-up, and for depression symptoms. There was a large amount of heterogeneity, but no evidence that this was explained by whether the intervention was delivered in a low- and middle-income or high-income country, included caregivers, or was universal or targeted.

**Conclusion:** Group PTSD interventions, particularly cognitive-behavioral therapy-based interventions, are effective at targeting posttrauma distress in children and adolescents. There was evidence of effectiveness when delivered in highly complex and resource-scarce settings and to a range of trauma-exposed groups, including groups exposed to war/conflict, natural disasters, and abuse.

**Key words:** group; PTSD; trauma; treatment

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**E**pidemiological studies have shown that trauma exposure is common in childhood, with prevalence estimates ranging from 30% to 70%.<sup>1,2</sup> Trauma exposure spans a wide range of experiences, including accidental injury (eg, motor vehicle accidents), witnessing violence, assault or maltreatment, natural disasters, and war or conflict. There is robust evidence demonstrating the detrimental effect that childhood trauma exposure can have on psychosocial outcomes across the life span.<sup>3-5</sup> One such outcome is posttraumatic stress disorder (PTSD), a trauma-specific mental health condition. Symptoms include reexperiencing (eg, flashbacks, nightmares), avoidance (avoiding thoughts, places, people, or things that might remind the person of their trauma), changes in arousal (eg, difficulty concentrating or sleeping),

and altered mood or cognition (a symptom requirement in *DSM-5*<sup>6</sup>). Meta-analytic reviews estimate that 1 in 6 trauma-exposed children, and up to 1 in 4 children exposed to interpersonal trauma, will go on to develop PTSD.<sup>7</sup> If left unaddressed, both PTSD and partial or subthreshold PTSD are associated with a range of negative outcomes, including the development of comorbid mental health difficulties,<sup>1</sup> substance abuse,<sup>8</sup> and self-harm.<sup>9</sup>

The best evidence-based treatment for PTSD is individual trauma-focused cognitive-behavioral therapy (tf-CBT).<sup>10,11</sup> These treatment programs typically last between 10 and 20 sessions, but may be longer in complex cases.<sup>12</sup> However, when considering the large proportion of children worldwide exposed to trauma and that corresponding rates of PTSD are particularly high for children in settings with

low resources,<sup>13</sup> there has been increased attention on how effective treatments can be delivered at scale. One way to do this is through group treatments, which, by definition, allow the intervention to be simultaneously delivered to a larger number of children. This mode of delivery is seen as particularly useful in the aftermath of large-scale traumas, such as natural disasters or war/conflict, and in low- and middle-income countries where resources can be particularly limited.<sup>14-16</sup> Even in high-income countries, mental health services are often not resourced to meet the needs of the large numbers of children who may require mental health support after trauma.<sup>17</sup> Besides enabling a larger number of children to access support, when compared with individual evidence-based interventions (eg, tf-CBT), group treatments often require less training for facilitators (or on-the-job training through the role of co-facilitator) and can be delivered by non-mental health professionals.<sup>18</sup>

However, the effectiveness of group interventions in reducing PTSD symptoms in children is not clear. In 2016, Gutermann *et al.*<sup>19</sup> completed a comprehensive review of treatments for PTSD in children, adolescents, and young adults, which included 66 studies of group programs. While they found a medium effect size for group interventions for reductions in pre- to post-intervention PTSD symptoms after the intervention, many studies were uncontrolled or controlled but without randomization. Given that natural recovery is common following trauma exposure,<sup>20</sup> randomized controlled trials (RCTs), particularly those that include a passive comparison group, provide necessary evidence for the specific effectiveness of the intervention. Other reviews and meta-analyses have provided initial evidence that group interventions may be effective, but also include uncontrolled or nonrandomized designs, focus solely on particular traumas,<sup>21-23</sup> or focus only on specific settings (eg, school-based programs<sup>24</sup>), limiting the generalizability of findings. In the adult literature, meta-analytic reviews show that group psychotherapy for PTSD is efficacious when compared with passive controls, but that there is no significant difference in outcomes when compared with active controls.<sup>25,26</sup>

We conducted a meta-analytic review focused exclusively on group-based PTSD-focused interventions for children and adolescents exposed to trauma. The review focused solely on RCTs, to establish the efficacy of group treatments when compared with passive and active control conditions. While our primary focus was on between-group differences in PTSD symptoms, we also explored differences in depression symptoms (as the most common comorbidity with PTSD<sup>1,27</sup>), as well as evidence of whether between-group differences were maintained at longer-term follow-ups. Alongside this, we explored several potential moderators aimed at delineating whether efficacy differed

depending on study characteristics. This included type of comparison condition (passive vs active), trauma type (interpersonal vs noninterpersonal), whether the intervention was universal or targeted (ie, included all trauma-exposed children or targeted only those with elevated PTSD symptoms), caregiver involvement, and whether the study was carried out in a low- and middle-income country or high-income country.

## METHOD

This meta-analysis was preregistered on PROSPERO (CRD42020187214) and followed PRISMA reporting guidelines.

### Search Strategy

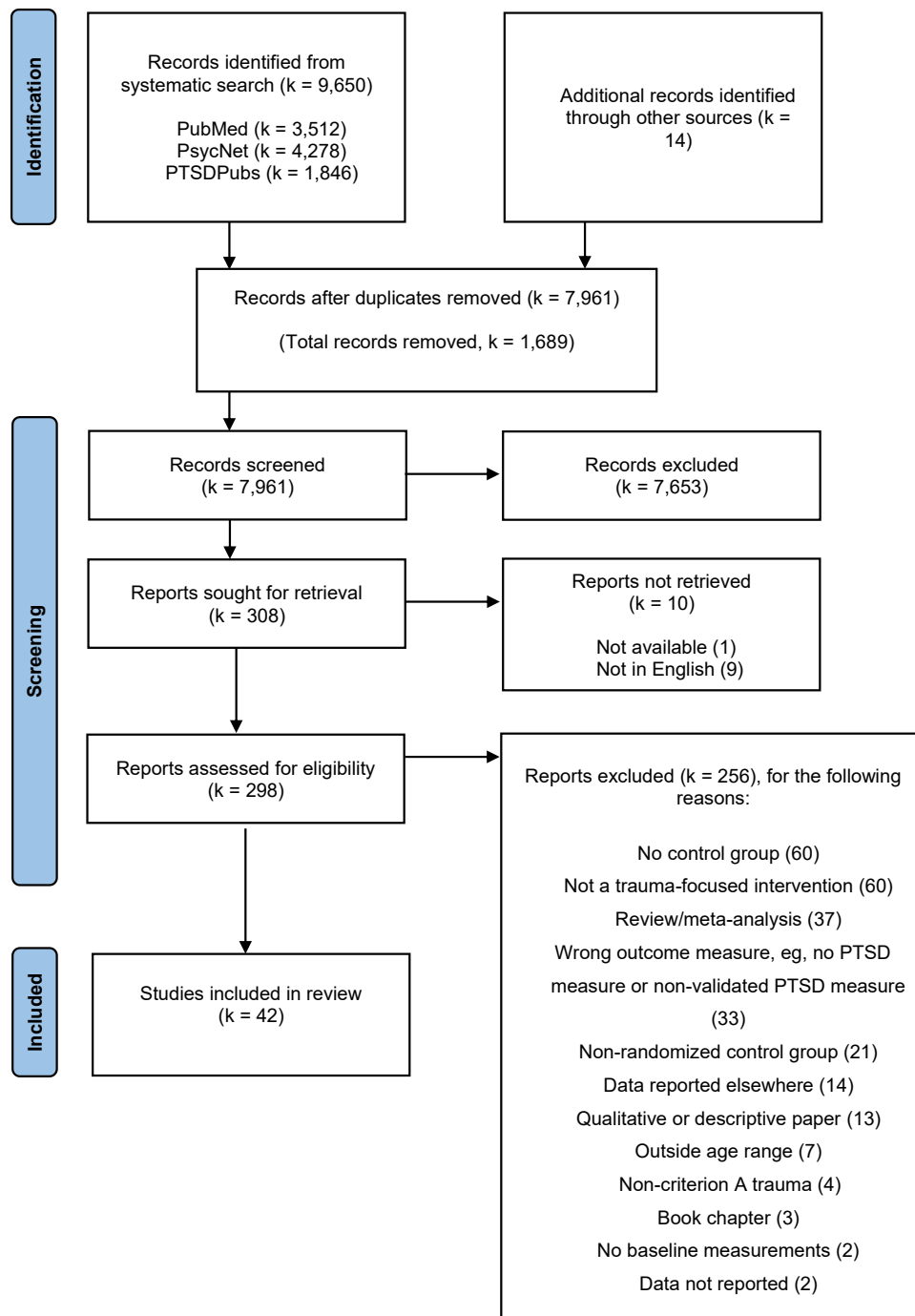
Relevant studies were identified through systematic searches of 3 electronic databases: PubMed, PsycNET and PTSDpubs. The final search was carried out on June 28, 2021. The search strategy combined free text and controlled terms relating to PTSD, group-based treatment, children, and adolescents (see Table S1, available online, for the full search terms for each database). The search was restricted to studies published in English. To ensure a comprehensive review, we also scanned reference lists of recent reviews and articles identified in the search. See Figure 1 for PRISMA diagram (and Table S2, available online, for PRISMA checklist). Initially, at the scoping stage we planned to include uncontrolled studies. However, because of the large number of studies available, a decision was made to focus the review only on groups tested via RCTs. The revised focus has more clinical utility, given natural recovery in PTSD symptoms following trauma exposure.<sup>20</sup>

### Selection Criteria

Inclusion criteria were as follows. Study populations had a mean participant age between 6 and 18 years old with the majority of the sample ( $\geq 50\%$ ) exposed to a criterion A trauma (as per *DSM-5* PTSD criteria). Studies were included if the sample included participants up to 19 years old, but mean participant age was between 6 and 18 years.

Included studies used a group-based psychological intervention that targeted a reduction in PTSD symptoms. The term group meant the intervention was delivered to  $\geq 2$  participants concurrently (excluding studies in which the group included all family members). In studies where interventions also had an individual delivery component, this had to account for  $\leq 50\%$  of the overall treatment time.

**FIGURE 1** PRISMA Flowchart Outlining the Study Selection Process



Note: PTSD = posttraumatic stress disorder. Please note color figures are available online.

Included studies had an RCT design, with any type of comparison condition (active or passive). Outcome comprised an assessment of PTSD symptoms before and after intervention, using a validated PTSD measure.

### Screening Process

Titles and abstracts were imported into Covidence (<https://www.covidence.org/>), and duplicate articles were removed (Figure 1). The first author (R.S.D.) screened all titles and

abstracts with a second reviewer (N.A.) independently screening a random 10%, with 97% agreement. Full texts were then imported, and all were reviewed independently by 2 reviewers (R.S.D. and N.A.), resulting in 84% agreement. Disagreements were discussed at a consensus meeting with 2 co-authors (S.L.H. and R.M.H.). For a complete list of all studies excluded at full-text screening, see Table S3, available online.

### Data Extraction

Two authors (R.S.D. and S.Y.) independently extracted descriptive and quantitative data using a customized data extraction template within Covidence. A third reviewer (K.L.) conducted final quality checks on all data in the final dataset. Population, intervention, comparison condition, and outcomes data were extracted. Where necessary descriptive or quantitative data could not be obtained from the article (ie, means and standard deviations), authors were contacted directly. If no reply was received after 1 month, studies were excluded from the review ( $k = 2$ ).

**Symptom Measures.** Information was extracted regarding the PTSD measure used, informant, type of measure (eg, interview, symptom checklist), and time points at which symptoms were measured. Based on what was consistently available across all studies, PTSD symptoms were extracted from child-report or combined carer/child-report symptom checklists. A small number of articles also provided carer report of child PTSD symptoms, but these data were less consistently available and were not used here. Using child report also reflects guidance on best practice when assessing internal processes and symptoms, such as PTSD.<sup>28</sup> Means and standard deviations were extracted for all available time points, along with between-group effect sizes, where reported. If follow-up data were reported for more than one time point, the last time point was used. If more than one PTSD measure was used, data from the identified primary outcome were collected. Where assessed and reported, means and standard deviations from validated child-report depression symptom measures were also extracted.

**Descriptives.** Characteristics of all included studies are reported in Table 1. Descriptives include the country where the study was conducted (categorized as high-income or low- and middle-income for moderator analysis); the setting in which the intervention occurred (eg, school, community, mental health service); and the type of intervention (eg, CBT-based, psychoeducation only, creative-based).

**Moderators.** Based on the information available in articles, we planned to explore the following moderators: trauma type, universal vs targeted intervention, low- and middle-income vs high-income country, active vs passive control, whether a caregiver was involved in the intervention, and CBT-based vs other. The last moderator was not explored, as the vast majority (90.5%) of groups were CBT-based.

Trauma type was coded based on the categorization used in the meta-analysis by Alisic *et al.*<sup>7</sup> Examples of interpersonal trauma were assault, maltreatment, and war, and examples of non-interpersonal trauma were bereavement and natural disasters. Interventions were coded as universal if they did not require all children to score above a certain threshold for PTSD severity (ie, the intervention was delivered on the basis of the trauma exposure), while targeted interventions were those delivered to children experiencing distress based on their PTSD symptom score. Caregiver involvement was coded as yes or no, with yes indicating that the caregiver had some level of involvement in the intervention (Table 1).

Comparison condition was coded as either active or passive. Passive included waitlist or no treatment conditions, and active included treatment as usual (TAU) and specific comparison interventions. If a study compared 2 different group-based trauma-focused interventions ( $k = 1$ ), the CBT-based intervention was coded as the intervention group, given the superior evidence for trauma-focused CBT interventions (Table 1). If a study included both a passive and an active comparison ( $k = 1$ ), data were extracted for the passive comparison condition only (Table 1). When coding the active comparison conditions, there were 4 studies that compared the group intervention with an individual trauma-focused intervention. As we would not expect a group treatment to outperform an individual trauma-focused intervention,<sup>19</sup> these 4 studies were grouped separately (active-individual) (discussed further in “Statistical Analysis”).

### Risk-of-Bias Assessment

Risk of bias for the primary outcome measure was assessed by the first author (R.S.D.) using the Cochrane Risk-of-Bias tool RoB 2.<sup>68</sup> A second reviewer (K.L.) independently assessed 30% of included studies (selected at random), with an agreement of 94%. Again, consensus was reached through discussion between the 2 reviewers.

### Statistical Analysis

Analyses were performed using the metafor package<sup>69</sup> in R 4.1.0.<sup>70</sup> Random-effects models were used for each meta-analysis. Hedges  $g$  statistic was derived for each study.

**TABLE 1** Characteristics of Included Studies

Study	Location	Setting	Sample size	Age, y, range (mean)	Sex, % female	Race/ethnicity (%)	Trauma type	Type of intervention	Control	Follow up period	PTSD symptom measure	Depression symptom measure
Ahmadi et al., 2020 <sup>29</sup>	US	Mental health service	11	10-15 (11)	55	NR	NR	TF-CBT (12 sessions)	RFPP (12 group sessions, 75 min; 12 individual sessions, 10 min)	12 mo <sup>a</sup>	CAPS-CA (self-report, interview)	—
Ahrens and Rexford, 2002 <sup>30</sup>	US	Youth offending	38	15-18 (16.4)	0	African American (26.3), Caucasian (60.5), Hispanic (5.3), Native American (5.3), other (2.6)	Various (including violence)	4 caregiver sessions (joint) CPT (8 sessions, 60 min)	4 caregiver sessions (joint) WL	—	PSS-SR (self-report), IES (self-report)	BDI (self-report)
Auslander et al., 2017 <sup>31</sup>	US	Outpatient mental health service	27	12-18 (14.7)	100	White (22), Black (46), other/mixed ethnicity (33)	Maltreatment	GAIN (adapted-CBITS) (10 sessions, 90 min; 2 individual sessions, 90 min)	TAU (in-home therapy, outpatient mental health services, school counseling)	6 mo	CPSS (self-report)	CDI (self-report)
Auslander et al., 2020 <sup>32</sup>	US	Community mental health service	249	12-19 (14.9)	100	African American (69.5), Hispanic (1.6), Asian (0.4), American Indian (1.6), other (non-White) (1.6), White, non-Hispanic (25.3)	Maltreatment	2 caregiver sessions. CBITS (10 sessions, 90 min; 2 individual sessions)	TAU (mental health outpatient service, in-home therapy, school counseling, and residential treatment)	6 mo	CPSS (self-report)	CDI (self-report)
Barron et al., 2013 <sup>33</sup>	Palestine	School	140	11-14 (11.08)	42.9	Palestinian (100)	War	TRT (5 sessions, 90 min)	WL	—	CRIES13 (self-report)	DSRC (self-report)
Barron et al., 2016 <sup>14</sup>	Palestine	School	154	11-15 (13.5)	59.7	NR	War	TRT (5 sessions)	WL	—	CRIES13 (self-report)	DSRC (self-report)
Barron et al., 2017 <sup>34</sup>	UK	Secure accommodation	20	14-18 (15.05)	64.7	Caucasian (100)	Domestic trauma	TRT (14 sessions, 40 min)	TAU (social education)	—	CRIES13 (self-report)	MFQ (self-report)
Barron et al., 2020 <sup>35</sup>	Brazil	NGO	30	8-13 (10.1)	46.7	Caucasian (26.7)	Community violence	TRT (5 sessions, 90 min)	WL	—	CRIES13 (self-report)	MFQ (self-report)
Basu et al., 2009 <sup>36</sup>	US	Community	10	8-12 (NR)	NR	NR	Domestic violence	Psychoeducation (10 sessions, 60 min)	WL	3 mo, 6 mo	TSCC-A-PTS (self-report)	TSCC-A-DEP (self-report)
Berger et al., 2007 <sup>37</sup>	Israel	School	142	NR	45.8	NR	Terrorism	10 caregiver sessions OTT (8 sessions, 90 min)	WL	—	UCLA PTSD RI (self-report)	—
Berger and Gelkopf, (2009) <sup>15</sup>	Sri Lanka	School	166	9-15 (NR)	47.6	NR	Natural disaster	2 caregiver sessions ERASE Stress—Sri Lanka (12 sessions, 90 min)	WL	—	UCLA PTSD RI (self-report)	BDI-brief (self-report)
Berger et al., 2012 <sup>38</sup>	Israel	School	154	11-13 (12.8)	53.9	NR	War	ERASE Stress (16 sessions, 90 min)	WL	—	UCLA PTSD RI (self-report)	—
Chemtob et al., 2002 <sup>39</sup>	Hawaii	School	248	6-12 (8.2)	61.4	Hawaiian and part-Hawaiian (30.1), White (24.9), Filipino (19.7), Japanese (9.2)	Natural disaster	1 caregiver session Psychosocial intervention (4 sessions)	Psychosocial intervention (individual)	10-12 mo	KRI (self-report)	—

(continued)

TABLE 1 Continued

Study	Location	Setting	Sample size	Age, y. range (mean)	Sex, % female	Race/ethnicity (%)	Trauma type	Type of intervention	Control	Follow up period	PTSD symptom measure	Depression symptom measure
Chen et al., 2014 <sup>40</sup>	China	School	40	NR (14.5)	68	Chinese (100)	Traumatic bereavement	TRT-adapted (6 sessions, 60 min)	No treatment	3 mo	CRIES13 (self-report)	CES-D (self-report)
Dorsey et al., 2020 <sup>41</sup>	Kenya and Tanzania	Community	640	7-13 (10.6)	50	NR	Bereavement	TF-CBT (12 sessions, 3-4 individual sessions) 12 caregiver sessions (7 individual, 5 joint)	TAU (educational support and mental health care)	6 mo <sup>a</sup> , 12 mo	CPSS (guardian and self-report)	—
Gordon et al., 2008 <sup>42</sup>	Kosovo	School	82	14-18 (16.3)	75.6	NR	War	Mind-body skills (12 sessions, 2 h)	WL	—	HTQ (self-report)	—
Jaycox et al., 2009 <sup>43</sup>	US	School	76	NR (11.5)	51.3	Hispanic/White (88), Hispanic/African American (8), non-Hispanic/African American (3), non-Hispanic/White (1)	Community violence	SSET (adapted-CBITS) (10 sessions, 45 min)	WL	6 mo <sup>b</sup>	CPSS (self-report)	CDI (self-report)
Jaycox et al., 2010 <sup>44</sup>	US	School	118	NR (11.6)	55.9	Non-Hispanic White (48), African American (46), Hispanic (5), other racial/ethnic backgrounds (2)	Natural disaster	CBITS (10 sessions, 1-3 individual sessions)	TF-CBT (individual, 12 sessions) 12 caregiver sessions (joint)	—	CPSS (self-report)	CDI (self-report)
Jordans et al., 2010 <sup>45</sup>	Nepal	School	325	11-14 (12.7)	48.6	Brahmin/Chhetri/Thakuri (45.2), Tharu (24.6), Terai caste (15.7), Dalit (7.7), other Janajati (6.8)	War	CBI (15 sessions, 60 min)	WL	—	CPSS (self-report)	DSRS (self-report)
Khamis et al., 2004 <sup>46</sup>	Palestine	School	840	6-16 (11.3)	49.6	NR	War	CBI (15 sessions, 60 min)	WL	—	IES (self-report)	—
Langley et al., 2015 <sup>47</sup>	US	School	74	NR (7.7)	50	Latino (49), Caucasian (27), African American (18), biracial (5), Asian (1)	Various (including violence)	Bounce Back (10 sessions, 50-60 min; 2-3 individual sessions, 30-50 min) 1-3 caregiver sessions	WL	6 mo <sup>b</sup>	UCLA PTSD RI (child and parent report)	CDI (child and parent report)
Layne et al., 2008 <sup>48</sup>	Bosnia	School	159	13-19 (16)	64.5	Ethnic Muslim (100)	War	TGCT (17-20 sessions, 60-90 min)	TAU (classroom skill-based psychoeducation)	4 mo	UCLA PTSD RI (self-report)	DSRS (self-report)
Lyshak-Stelzer et al., 2007 <sup>49</sup>	US	Inpatient mental health service	77	13-17 (15.1)	44.8	African American (40.1), Latino/a (35.2), White (18.3), Caribbean American (0.7), mixed ethnicity (4.9), Bangladeshi (0.7)	Various (including violence)	Trauma-focused art therapy (16 sessions)	TAU (arts and crafts activity group)	—	UCLA PTSD RI (self-report)	—
Mahmoudi-Gharaei et al., 2009 <sup>50</sup>	Iran	Community	85	11-18 (14.6)	74.1	NR	Natural disaster	CBT (4 sessions)	WL	—	PSS (self-report)	—

(continued)

**TABLE 1** Continued

Study	Location	Setting	Sample size	Age, y, range (mean)	Sex, % female	Race/ethnicity (%)	Trauma type	Type of intervention	Control	Follow up period	PTSD symptom measure	Depression symptom measure
McMullen <i>et al.</i> , 2013 <sup>51</sup>	DR Congo	NGO	50	13-17 (15.8)	0	NR	Child soldiers	TF-CBT (15 sessions, 2-4 individual sessions) 3 caregiver sessions	WL	3 mo <sup>b</sup>	UCLA PTSD RI (self-report)	—
O'Callaghan <i>et al.</i> , 2013 <sup>52</sup>	DR Congo	NGO	52	12-17 (16.02)	100	NR	Sexual abuse	TF-CBT (12 sessions, 2 h; 3 individual sessions) 3 caregiver sessions	WL	3 mo <sup>a</sup>	UCLA PTSD RI (self-report)	—
O'Callaghan <i>et al.</i> , 2015 <sup>53</sup>	DR Congo	NGO	50	14-17 (14.9)	42	NR	War	TF-CBT (9 sessions, 90 min) 2 caregiver sessions	CFS (9 group sessions, 90 min) 2 caregiver sessions	—	UCLA PTSD RI (self-report)	—
Ooi <i>et al.</i> , 2016 <sup>54</sup>	Australia	School	82	10-17 (12.6)	35.4	African (56), Asian (22), Middle Eastern (17)	War	TRT (8 sessions, 60 min)	WL	3 mo <sup>b</sup>	CRIES13 (self-report)	DSRS (self-report)
Overbeek <i>et al.</i> , 2013 <sup>55</sup>	Netherlands	Community	164	6-12 (9.2)	44.5	Dutch (43.2), Turkish/Moroccan (18.7), Antilles/Suriname (20), other countries (18.1)	Interpersonal violence	It's My Turn Now (9 sessions, 90 min) 9 caregiver sessions	You Belong (9 group sessions, 90 min) 9 caregiver sessions	6 mo	TSCC (self-report), TSCYC (parent-report)	CDI (self-report), CBCL (parent-report)
Pfeiffer <i>et al.</i> , 2018 <sup>56</sup>	Germany	Children's social care	99	13-21 (17)	7.1	Afghanistan (45.5), Syria (11.1), Gambia (10.1), Somalia (7.1) Iran (7.1), Eritrea (3), Senegal (2), Iraq (2) Ethiopia (2), Pakistan (2), Angola (2), Nigeria or Ivory Coast (2), Ghana, Guinea, Guinea-Bissau or Kurdistan (4)	War	Mein Weg (6 sessions, 90 min)	TAU (social care support)	—	CATS-S (self-report), CATS-C (carer report)	PHQ8 (self-report)
Pityaratstian <i>et al.</i> , 2015 <sup>57</sup>	Thailand	School	36	10-15 (12.3)	72.2	NR	Natural disaster	TRT-adapted (3 sessions, 2 h)	WL	1 mo	UCLA PTSD RI (self-report), Thai CRIES (self-report)	-
Qouta <i>et al.</i> , 2012 <sup>16</sup>	Palestine	School	482	10-13 (11.3)	49.4	Palestinian	War	TRT (8 sessions, 2 h)	WL	6 mo	CRIES13 (self-report)	DSRS (self-report)
Ronan and Johnston, 1999 <sup>58</sup>	New Zealand	School	113	7-13 (10.5)	54	Caucasian (European descent) (61.9), Māori (10.6), Asian (5.3), Māori/European (18.6), Asian/Māori/Pacific Islander (1.8), Asian/Pacific Islander (0.9)	Natural disaster	CBT (1 session, 60 min)	Exposure and normalizing intervention (1 session, 60 min)	4 mo <sup>b</sup>	UCLA PTSD RI (self-report)	YSR (self-report)
Runyon <i>et al.</i> , 2010 <sup>59</sup>	US	Children's social care	60	7-13 (9.9)	46.7	African American (41.7)	Physical abuse	CPC-CBT (16 sessions, 2 h) 16 caregiver sessions (~12 h joint)	Parent-only CBT and games and art group for children	3 mo <sup>a</sup>	K-SADS-PL (combined child and parent report, interview)	-

(continued)

TABLE 1 Continued

Study	Location	Setting	Sample size	Age, y, range (mean)	Sex, % female	Race/ethnicity (%)	Trauma type	Type of intervention	Control	Follow up period	PTSD symptom measure	Depression symptom measure
Salloum and Overstreet, 2008 <sup>60</sup>	US	School	56	7-12 (NR)	37.5	African American (89), Caucasian (4), Hispanic (2), African American/Native American (4)	Natural disaster	LAST intervention (10 sessions, 60 min; 1 individual session) 1 caregiver session	LAST intervention (individual) 1 caregiver session	3 wk	UCLA PTSD RI (self-report)	MFQ (self-report)
Salloum and Overstreet, 2012 <sup>61</sup>	US	School	72	6-12 (9.6)	44.3	African American (97.2)	Various (including violence)	GTI (10 sessions, 50-60 min; 1 individual session, 50-60 min) 1 caregiver session	GTI (without trauma narrative) (10 group sessions, 50-60 min; 1 individual session, 50-60 min) 1 caregiver session	3 mo, 12 mo	UCLA PTSD RI (self-report)	MFQ (self-report)
Santiago et al., 2018 <sup>62</sup>	US	School	52	NR (7.8)	36.5	African American/Black (3.8), White/Caucasian (5.9), Latino (55.8), Latino/Caucasian (23.1), Latino/Native American (5.9), missing (5.9)	Various (including violence)	Bounce Back (10 sessions, 3 individual sessions) 3 caregiver sessions	WL	6 mo <sup>b</sup>	UCLA PTSD RI (child and parent report)	CDI (child and parent report)
Stein et al., 2003 <sup>63</sup>	US	School	126	NR (11)	56.1	NR	Various (including violence)	CBITS (10 sessions, 1 individual session)	WL	6 mo <sup>b</sup>	CPSS (self-report)	CDI (self-report)
Tol et al., 2008 <sup>64</sup>	Indonesia	School	403	7-15 (9.9)	48.6	NR	War	CBI (15 sessions)	WL	6 mo	CPSS (self-report)	DSRS (self-report)
Tol et al., 2012 <sup>65</sup>	Sri Lanka	School	399	9-12 (11)	38.6	Hindu (81)	War	CBI (15 sessions)	WL	3 mo	CPSS (self-report)	DSRS (self-report)
Tol et al., 2014 <sup>66</sup>	Burundi	School	329	8-17 (12.3)	48	NR	War	CBI (15 sessions)	WL	3 mo	CPSS (self-report)	DSRS (self-report)
Trowell et al., 2002 <sup>67</sup>	UK	Mental health service	71	6-14 (10)	100	White (63), Black Caribbean (11), mixed parentage (10), Chinese (7), Mediterranean origin (6), unknown (3)	Sexual abuse	Psychoeducation (18 sessions) 13 caregiver sessions	Psychotherapy (individual) (up to 30 sessions, 50 min) Caregiver support	24 mo	Orvaschel PTSD scale (self-report, interview)	K-SADS (self-report, interview)

**Note:** A dash (—) indicates the information was not relevant to the study; BDI = Beck Depression Inventory; CAPS-CA = Clinical Administered PTSD Scale for Children and Adolescents; CATS-C = Child and Adolescent Trauma Screen—Caregiver Report; CATS-S = Child and Adolescent Trauma Screen—Self Report; CBCL = Child Behavior Checklist for Children; CBI = Classroom-Community-Culture Based Intervention; CBITS = Cognitive Behavioral Intervention for Trauma in Schools; CBT = cognitive behavioral therapy; CDI = Child Depression Inventory; CES-D = Center for Epidemiological Studies—Depression; CFS = Child Friendly Space; CPSS = Child PTSD Symptom Scale; CPT = cognitive processing therapy; CRIES13 = Child Revised Impact of Events Scale 13; DSRC = Depression Self-rating Scale for Children; ERASE Stress = Enhancing Resiliency Amongst Students Experiencing Stress; GAINS = Girls Aspiring Toward Independence; GTI = Grief and Trauma Intervention; HTQ = Harvard Trauma Questionnaire; IES = Impact of Events Scale; KRI = Kauai Recovery Inventory; K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children; LAST = Loss and Survival Team; MFQ = Mood and Feelings Questionnaire; NGO = Non-governmental organization; NR = not reported; OTT = Overshadowing the Threat of Terrorism; PHQ8 = Patient Health Questionnaire 8; PSS-SR = PTSD Symptom Scale—Self Report; RFPP = Reminder Focused Positive Psychiatry; SSET = Support for Students Exposed to Trauma; TAU = treatment as usual; TF-CBT = trauma-focused cognitive behavioral therapy; TGCT = Trauma and Grief Component Therapy for Adolescents; TRT = Teaching Recovery Techniques; TSCC = Trauma Symptom Checklist for Children; TSCC-A-DEP = Trauma Symptom Checklist for Children—Depression subscale; TSCC-A-PTS = Trauma Symptom Checklist for Children—Posttraumatic Stress subscale; TSCYC = Trauma Symptom Checklist for Young Children; UCLA PTSD RI = UCLA Post-traumatic Stress Disorder Reaction Index; WL = waitlist; YSR = Youth Self-Report.

<sup>a</sup>Follow-up assessments, but full data not reported in article.

<sup>b</sup>Not included in analysis, as waitlist control had received intervention at follow-up assessment.



Where means and standard deviations were not reported by included studies, Cohen *d* statistics were extracted and used in the analysis or were derived from other reported statistics. Estimates of heterogeneity were calculated using the *Q* statistic and the *I*<sup>2</sup> statistic; for *I*<sup>2</sup>, values >25% indicate low heterogeneity, >50% indicate moderate heterogeneity, and >75% indicate high heterogeneity.<sup>71</sup> More negative Hedges *g* statistics indicate an effect favoring the experimental condition (ie, the group-based intervention was superior to the control condition).

For clarity, the between-group differences in PTSD severity are reported by comparison condition (although the overall pooled effect is also reported). This shows the pooled effect for whether a group treatment is better than nothing (ie, passive comparison, which is particularly relevant in resource-poor contexts and when considering risk of harm) or better than another intervention (active comparison), as well as comparison against an individual trauma-focused intervention. For moderator analysis, we decided before the analysis to exclude the 4 articles that compared a group intervention with an individual trauma-focused intervention, as this reflects a noninferiority-type study. However, for transparency, the moderator analysis using the full sample is provided in Table S4, available online. There were no differences in the pattern of results.

We identified 4 manualized treatment approaches that had been tested in multiple studies: a gold standard manualized trauma-focused CBT (eg, TF-CBT, Cognitive Processing Therapy), Teaching Recovery Techniques (TRT), Cognitive Behavioral Intervention for Trauma in Schools (CBITS), and Classroom-Community-Culture Based Intervention. As a secondary analysis, we explored the pooled effectiveness of each when compared with a passive control (as was most common).

Potential publication bias for the primary outcome measure was assessed through visual inspection of the funnel plot and testing for funnel plot asymmetry. The trim-and-fill method<sup>72</sup> was used as a further estimate of publication bias. Leave-one-out models were also used as a sensitivity test.

## RESULTS

### Characteristics of Included Studies

The systematic search resulted in 7,962 studies (after duplicates were removed), of which 42 met our predefined eligibility criteria and were included in the meta-analysis (Figure 1). Full study characteristics are presented in Table 1. The 42 studies included a total of 5,998 children and adolescents. The mean age of participants was 12.4 years (range, 6-19 years), and 52.9% were female. Most

studies were carried out within schools (*k* = 25), followed by community settings (*k* = 9), mental health services (*k* = 4), social services (*k* = 3), and youth offending settings (*k* = 1). The majority of studies included participants who had been exposed to interpersonal trauma (*k* = 32; 76.2%), of which war was most commonly reported (*k* = 14). Of the 9 studies involving participants exposed to non-interpersonal trauma, natural disaster was the most frequently reported (*k* = 7). One study<sup>29</sup> did not report on trauma type. Most studies implemented a targeted (*k* = 32), rather than universal (*k* = 10), approach.

CBT-based interventions were the most commonly used treatment approach (*k* = 37); 2 studies used predominately creative approaches,<sup>39,49</sup> 2 studies used psychoeducation only,<sup>36,67</sup> and 1 study used a mind-body skills intervention.<sup>42</sup> Interventions were largely delivered by mental health professionals (*k* = 14), school staff (*k* = 11), social care professionals (*k* = 7), or adults from the local community (*k* = 4).

The majority of studies compared group treatment with a passive waitlist control group (*k* = 24), with 1 study using a nontreatment control. Of the 17 studies using an active control, 6 were TAU, 6 were a different group intervention, 4 were individual trauma-focused interventions, and 1 was a different trauma-focused group intervention.

Most studies used a child-report or combined parent/child-report PTSD symptom checklist (*k* = 39), with the remaining 3 studies using a diagnostic interview (although symptom scores were still reported). All studies had pre-intervention and postintervention measures, and 12 reported follow-up assessments. Follow-up duration ranged from 1 month to 2 years. Additionally, 26 studies (62%) investigated the impact of treatment on depression outcomes, using a validated child-report or combined parent/child-report depression screening tool.

### Risk of Bias

The majority of included studies were assessed as being overall at some risk of bias (63%), with the rest at high risk. Of the 5 risk-of-bias domains, only 4 studies were at high risk of bias regarding randomization processes, which largely related to either investigators not being blind to the forthcoming group allocation or significant baseline differences between the intervention and control groups. Eight studies were at high risk of bias due to the number of participants excluded from their analyses (eg, analyzing only participants who completed the intervention), and 9 studies were assessed as high risk due to the amount of missing data, which could be related to the outcome variable (ie, potentially linked to PTSD symptoms). Only 1 study was judged to be at high

risk of bias regarding outcome measurements. Full risk-of-bias assessments are detailed in Table S5, available online. We investigated risk of bias as a potential moderator and found no differences between studies assessed to be at high or some risk ( $Q_1 = 0.30, p = .86$ ).

### Treatment Outcomes—PTSD symptoms

The meta-analysis included 38 studies (with the 4 studies that used an individual psychological intervention as a comparator excluded). Overall, pooled effect sizes showed that children in the group condition had lower PTSD symptoms at posttreatment than children in the comparison condition, with a pooled medium effect size ( $g = -0.55, 95\% \text{ CI } [-0.76, -0.35]$ ) (Figure 2). Effect sizes ranged from medium to large when the intervention was compared with a passive control ( $g = -0.71, 95\% \text{ CI } [-0.97, -0.45]$ ) and small to medium when compared with an active control ( $g = -0.25, 95\% \text{ CI } [-0.47, -0.03]$ ). The heterogeneity for all studies was high ( $I^2 = 92\%$ ), indicating considerable variability between study outcomes.

The pooled effect for the 4 studies that compared group treatment with an individual intervention confirmed that at posttreatment, individual psychological treatment led to lower PTSD symptoms than group therapy ( $g = 0.69, 95\% \text{ CI } [0.17, 1.22]$ ) (see Figure S1, available online, for forest plot). Excluding the 4 studies that compared group treatment with individual treatment, 13 of the 38 studies reported follow-up PTSD symptom scores. At follow-up, evidence remained of an overall small effect favoring group treatment over the comparison condition ( $g = -0.28, 95\% \text{ CI } [-0.43, -0.12]$ ) (see Figure S2, available online, for forest plot). This was comparable for whether the control was passive ( $g = -0.31, 95\% \text{ CI } [-0.56, -0.06]$ ) or active ( $g = -0.27, 95\% \text{ CI } [-0.48, -0.06]$ ). There was moderate heterogeneity between studies ( $I^2 = 65\%$ ). Given the variability in follow-up duration (ranging from 1 to 12 months after treatment), we also looked at whether there was an effect of follow-up length on symptom reduction. The effect size, favoring the group treatment, was greater for studies with a follow-up of 6 months or more ( $g = -0.33, 95\% \text{ CI } [-0.51, -0.15]$ ) compared with studies with a follow-up of less than 5 months ( $g = -0.20, 95\% \text{ CI } [-0.46, -0.07]$ ). However, this is potentially driven by the large difference in sample sizes between the 2 groups ( $\geq 6$  months:  $n = 1,808$  vs  $\leq 5$  months,  $n = 797$ ).

### Moderator Analysis

The type of comparison condition (passive vs active) significantly moderated the between-group effect on symptom reduction ( $Q_1 = 4.55, p = .03$ ). As expected, the

effect size was greater for studies that used a passive control ( $g = -0.71, 95\% \text{ CI } [-0.97, -0.45]$ ) vs an active control ( $g = -0.25, 95\% \text{ CI } [-0.47, -0.03]$ ). No significant differences were found for any other moderator, including whether studies were carried out in low- and middle-income countries or high-income countries ( $Q_1 = 0.22, p = .64$ ), whether the intervention was universal or targeted ( $Q_1 = 1.18, p = .27$ ), whether the type of trauma exposure was interpersonal or noninterpersonal ( $Q_1 = 0.29, p = .59$ ), or whether caregivers were involved ( $Q_1 = 0.39, p = .53$ ) (Table 2).

We also conducted an additional subgroup analysis to further explore type of trauma exposure, by separating the interpersonal trauma group into war-related trauma and non-war-related interpersonal trauma (eg, maltreatment, family violence). No significant difference was found between the 3 trauma exposure groups (war vs maltreatment vs noninterpersonal) and treatment outcome. Thus, the overall effect size for interpersonal trauma and the lack of difference between different trauma types does not seem to be driven by the grouping of interpersonal traumas. Analyses are reported in Table S6, available online.

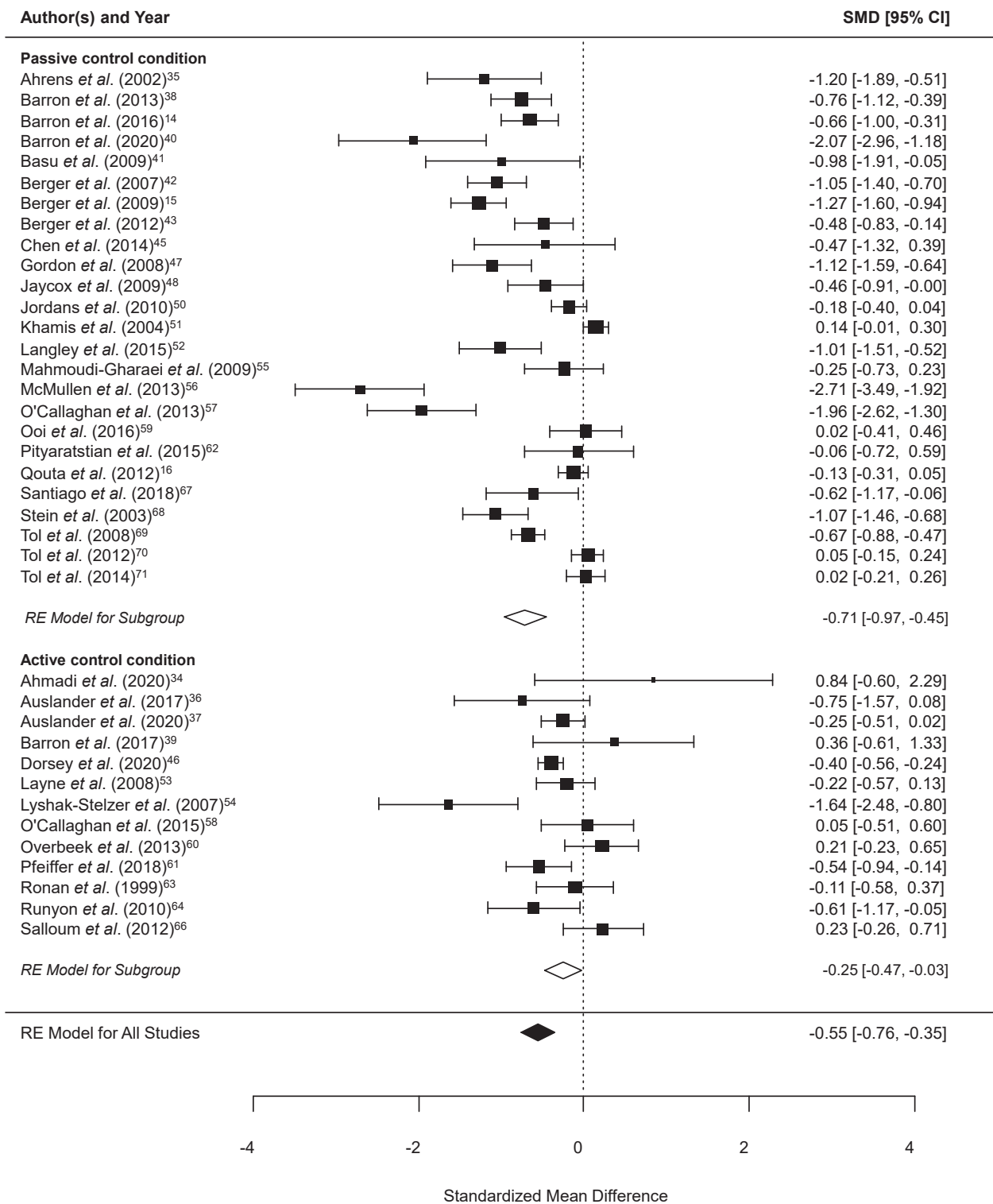
### Secondary Analysis of Treatment Manuals

When compared with a passive control group, a gold standard manualized trauma-focused CBT (eg, Trauma-Focused CBT, Cognitive Processing Therapy) ( $k = 3$ ), Teaching Recovery Techniques ( $k = 7$ ), and Cognitive Behavioral Intervention for Trauma in Schools ( $k = 2$ ) all led to significantly reduced PTSD symptoms after treatment. There was no significant difference in the pooled effect size for Classroom-Community-Culture Based Intervention ( $k = 5$ ). Data are reported in supplementary materials, along with a brief description of each intervention; see Table S7, available online.

### Treatment Outcomes—Depression symptoms

There were 26 studies that also reported on posttreatment depression symptom outcomes (with 2 studies using an individual psychological intervention as a comparison group). Pooled effect sizes of the 24 studies included in the meta-analysis showed that children in the group condition had lower depression symptoms at posttreatment than children in the comparison group, with a small effect size ( $g = -0.30, 95\% \text{ CI } [-0.48, -0.12]$ ) (see Figures S3 and S4, available online, for forest plots). Effect sizes were larger when compared with a passive ( $g = -0.35, 95\% \text{ CI } [-0.59, -0.11]$ ) vs active ( $g = -0.17, 95\% \text{ CI } [-0.45, 0.11]$ ) control. The heterogeneity for all studies was large

**FIGURE 2** Forest Plot of Effect Sizes Comparing Group Treatment With Active and Passive Control Conditions at Posttreatment



Note: RE = random effect; SMD = standardized mean difference.

**TABLE 2** Pooled Effect Sizes and Moderator Analyses for Reduction in Posttraumatic Stress Disorder (PTSD) Symptoms After Treatment

Analysis: moderator/subgroup	k	n	Hedges g	95% CI	Q (df)	I <sup>2</sup>	Q	p
All studies: posttreatment	38	5,575	-0.55	[-0.76, -0.35]	Q(37) = 282.87***	92%	—	—
All studies: follow-up	13	2,809	-0.28	[-0.43, -0.12]	Q(12) = 38.23***	65%	—	—
LMICs vs HICs							0.22	.64
LMICs	19	4,141	-0.62	[-0.95, -0.28]	Q(18) = 202.32***	96%		
HICs	19	1,434	-0.50	[-0.74, -0.26]	Q(18) = 71.53***	77%		
Universal vs targeted							1.18	.27
Universal	10	1,871	-0.78	[-1.36, -0.20]	Q(9) = 155.59***	97%		
Targeted	28	3,704	-0.48	[-0.65, -0.30]	Q(27) = 124.40***	83%		
Control condition							4.55	.03*
Active	13	1,493	-0.25	[-0.47, -0.03]	Q(12) = 31.54**	67%		
Passive	25	4,082	-0.71	[-0.97, -0.45]	Q(24) = 250.34***	93%		
Risk of bias							0.10	.75
High	14	2,122	-0.50	[-0.77, -0.22]	Q(13) = 95.13***	86%		
Some	24	3,453	-0.59	[-0.87, -0.30]	Q(23) = 183.17***	93%		
Trauma type							0.29	.59
Interpersonal	31	4,566	-0.60	[-0.83, -0.37]	Q(30) = 247.12***	93%		
Non-interpersonal	6	1,001	-0.45	[-0.85, -0.06]	Q(5) = 27.31***	82%		
Caregiver involvement							0.39	.53
Yes	15	1,691	-0.64	[-1.05, -0.24]	Q(14) = 95.33***	92%		
No	23	3,884	-0.49	[-0.72, -0.27]	Q(22) = 176.38***	90%		

Note: All analyses were run excluding the 4 studies with an individual psychotherapy control condition. HICs = high-income countries; LMICs = low- and middle-income countries.

\*p < .05; \*\*p < .01; \*\*\*p < .001.

(I<sup>2</sup> = 82%). At follow-up (k = 11), there was no pooled effect of group treatment (g = -0.11, 95% CI [-0.25, -0.02]) on depression symptoms when compared with all comparison conditions (see Figure S5, available online, for forest plot).

### Publication Bias and Sensitivity Analysis

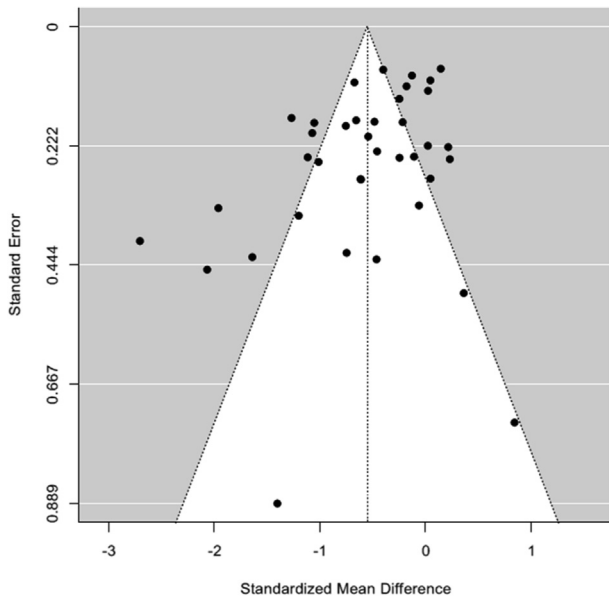
Visual inspection of the funnel plot for posttreatment PTSD outcomes (Figure 3) provided some evidence of asymmetry, although there was no evidence of a significant publication bias on further testing (p = .062). Additional leave-one-out sensitivity analysis indicated that no one study was driving the overall effect size when compared with other studies. Furthermore, trim-and-fill analysis did not impute any added studies.

## DISCUSSION

This meta-analysis sought to delineate the effectiveness of group-based treatments for PTSD symptoms in children and adolescents. Given the large proportion of children exposed to trauma before the age of 18, and that children in

low-resource contexts (whether at the family, community, or country level) are at particularly high risk of cumulative trauma exposure, group treatment provides a potential avenue for addressing trauma-related mental health on a larger scale. Our meta-analysis, focused exclusively on RCTs, found good evidence for the effectiveness of group trauma-focused interventions for improving mental health outcomes for children who have been exposed to trauma.

While we confirmed findings that individual trauma-focused interventions are superior to group interventions,<sup>10,11,73</sup> in contexts where this is not feasible or available, group programs may offer a valuable alternative for treating PTSD symptoms, with further potential gains for depression symptoms. The pooled posttreatment between-group effect of the group interventions, compared with passive controls, was similar to that found in meta-analyses of the adult literature.<sup>25,26</sup> Additionally, and in contrast to the adult literature, we found a statistically significant if small effect size when group intervention was compared with an active control. We also found that the superiority of the group intervention was maintained during follow-up. Although the effect size was small, follow-up durations ranging from 1 month to 2 years after

**FIGURE 3** Funnel Plot for Group-Based Treatment versus Control at Posttreatment

treatment were captured. Beyond PTSD symptoms, we also found small posttreatment effects for depression.

The vast majority of interventions included in this meta-analysis were CBT-based, the recommended treatment for PTSD.<sup>11,74</sup> In our subanalysis of specific manualized treatments, a manualized trauma-focused CBT delivered in a group (approximately 12 sessions, including some individual sessions), Teaching Recovery Techniques (approximately 5 sessions), and Cognitive Behavioral Intervention for Trauma in Schools (approximately 10 sessions, including some individual sessions) were all found to be effective compared with passive controls. In many cases, these interventions were being delivered in highly complex settings, in sectors including schools, mental health services, and nongovernmental organizations, and with children who had experienced multiple complex traumas (eg, former child soldiers, incarcerated youth, war exposure, sexual abuse). They were also often delivered by nonclinical professionals with limited training and using translated versions of the manual. That these interventions were effective in such contexts provides further support for the real-world scalability of group-delivered programs. Of note, at the time of the systematic search, we found no eligible studies that used eye movement desensitization and reprocessing and so are unable to draw conclusions on this particular approach in a group format.

As is common in meta-analyses of psychological treatments, there was substantial heterogeneity among studies.

Our moderator analysis largely failed to identify reasons for this, and further work is needed to understand exactly what factors help or hinder the delivery of group treatments to children exposed to trauma. We found no differences in effectiveness for children exposed to noninterpersonal (eg, natural disasters) and interpersonal (eg, war, maltreatment) traumas, which is in line with findings reported by other meta-analyses.<sup>19</sup> Similarly, there was no significant difference in effectiveness when delivered in high-income countries vs low- and middle-income countries, a moderator that has been largely unexplored in the literature to date. The finding that group-based interventions are no less effective across different countries with considerably different therapeutic resources has important clinical implications, including being readily able to implement and requiring only limited specialist mental health training and resources.

There was also no difference in effectiveness if the intervention was delivered universally (based on trauma exposure) or targeted (based on presence of symptoms). Similarly, other meta-analyses have reported that treatment effects are not moderated by percentage of children with a PTSD diagnosis before intervention<sup>73</sup> or whether children have a full PTSD diagnosis vs subthreshold PTSD.<sup>19</sup> In many contexts, screening for diagnosis or symptom severity may not be practical or possible. In such cases, where there is expected high rates of community distress, it is likely that delivery of a manualized CBT-based group intervention to the entire exposed population would support greater psychological recovery.

Lastly, we found no evidence that caregiver involvement in the intervention moderated treatment effects. This finding adds to the mixed picture from previous treatment-focused meta-analyses, in which many report improved outcomes when caregivers are involved,<sup>19,21</sup> while others report little difference in outcomes.<sup>73</sup> Here, it may be that the group context, where peer support is an inherent part, means the involvement of a caregiver is less essential. It may also be that the caregiver component is less necessary for universal interventions or where PTSD symptoms are sub-syndromal. Further research is needed to understand the mechanisms of change in these group interventions and what role caregivers may play in supporting children through interventions.

The primary limitations of this review relate to the limitations of the included studies. As reflected in the risk-of-bias assessments, the majority of studies were either at some or high risk of bias. Despite finding no impact of increased risk of bias on PTSD outcomes in our moderator analysis, it is important to recognize that the increased levels of bias across all studies may have impacted them similarly. Some studies had very small sample sizes, as shown in

Table 1. Relatedly, while there was no evidence of significant publication bias, plot inspection showed some asymmetry, which visual inspection showed may be driven by studies with smaller samples generally having greater effect sizes. Further, even with randomization, a minority of studies had significantly different levels of PTSD symptoms between groups at baseline.<sup>16,33</sup> This can make it challenging to draw conclusions from the posttreatment between-group effect. That said, this issue was rare, and a focus on pre- to post-treatment change would have been less robust, given the potential for natural recovery in trauma-exposed samples. Also, follow-up data were provided in only a third of included studies with large variance in the length of follow-up time. Overall, the field would benefit from further larger-scale RCT evaluations, particularly with longer-term follow-ups, although this type of work can be challenging in the highly complex settings where many of these studies were conducted.

It is also important to highlight that for some of our moderator analyses, the distribution of studies was skewed in the direction of one alternative (eg, trauma type and universal vs targeted intervention). It cannot be ruled out that the lack of significant difference between the 2 groups is due to sample size differences, rather than a true effect of the intervention. A further potential methodological limitation is that interrater agreement was established in only 10% of abstracts in the first step of screening. That said, this was a first-step highly conservative screen to exclude articles that clearly were not relevant (eg, articles on adults), and agreement was 97%. Lastly, consistent with the wider psychotherapy literature, we chose to categorize our control groups as either passive or active, ie, the participants received no other treatment (usually a waitlist condition), or they received TAU or another intervention. While we recognize there is some debate regarding the use of waitlist control groups and suggestion that they might inflate effect sizes,<sup>75,76</sup> we chose to include this type of control, as understanding whether an intervention is better than no treatment, particularly a low-intensity intervention, was felt to have the most clinical and translatable value. This is particularly the case within the context of poor mental health resourcing. It is also important to note that we included TAU within our active comparator group; however, descriptions of this condition in studies reflect considerable diversity in the amount or type of intervention received, and consequently it is likely that this contributed to heterogeneity across studies.

Overall, findings from this meta-analysis provide support for the use of group (particularly CBT-based) interventions for treating PTSD symptoms in trauma-

exposed children and adolescents, with potential for related reductions in depression symptoms. This has important implications for contexts in which group programs may be the most or only viable option, including communities exposed to conflict or natural disaster, as well as communities with poorly resourced services. While individual tf-CBT remains the best evidence-based treatment for PTSD in children and adolescents, our meta-analysis demonstrates that group programs are also a valuable therapeutic resource.

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Dr. Davis, Mss. Afzal and Ye, and Profs. Halligan and Stallard are with the University of Bath, United Kingdom. Prof. Halligan is also with the University of Cape Town, South Africa. Prof. Meiser-Stedman and Ms. Lofthouse are with University of East Anglia, Norwich, United Kingdom. Prof. Devaney is with the School of Social and Political Science, University of Edinburgh, United Kingdom. Dr. Smith is with the Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom. Dr. Hiller is with the Division of Psychology and Language Sciences, University College London, United Kingdom, and Anna Freud National Centre for Children & Families, United Kingdom.

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This work has been prospectively registered: [https://www.crd.york.ac.uk/prospero/display\\_record.php?RecordID=187214](https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=187214).

Prof. Meiser-Stedman served as the statistical expert for this research.

#### Author Contributions

R.S.D., R.M.H, R.M.-S., S.L.H., J.D., P.Sm., and P.St. conceived and designed the study. R.S.D., N.A., and S.Y. conducted the systematic search and article screening and extracted the data. R.S.D. and K.L. accessed and verified the underlying data reported in the manuscript. R.M.-S. analyzed the data. R.S.D. and R.M.H. wrote the first draft of the manuscript. All authors contributed to critical revisions of the manuscript. All authors had full access to all the data in the study. R.S.D. and R.M.-S. take responsibility for the integrity and accuracy of data analysis, and R.S.D. and R.M.H. were responsible for the final decision to submit for publication.

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Correspondence to Rachel M. Hiller, PhD, Research Department of Clinical, Education and Health Psychology, Division of Psychology and Language Sciences, University College London, London WC1H 0AP, UK; e-mail: [r.hiller@ucl.ac.uk](mailto:r.hiller@ucl.ac.uk)

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