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Review

Interventions for children and adolescents with posttraumatic stress disorder: A meta-analysis of comparative outcome studies

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HIGHLIGHTS

- We conducted a meta-analysis on randomized controlled trials for pediatric PTSD.
- 39 psychological and two pharmacological interventions were included.
- Psychotherapy can effectively reduce PTSD symptoms in children and adolescents.
- Trauma-focused CBT is most researched and produces the largest effect sizes.
- Lack of evidence for efficacy of psychopharmacotherapy for pediatric PTSD

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ABSTRACT

This meta-analysis aimed at determining the efficacy of psychological and psychopharmacological interventions for children and adolescents suffering from symptoms of posttraumatic stress disorder (PTSD). A search using the Medline, PsycINFO, and PILOTS databases was conducted to identify randomized controlled trials (RCTs) for pediatric PTSD. The search resulted in 41 RCTs, of which 39 were psychological interventions and two psychopharmacological interventions. Results showed that psychological interventions are effective in treating PTSD, with aggregated effect sizes of Hedge's $g = 0.83$ when compared to waitlist and $g = 0.41$ when compared to active control conditions at posttreatment. Trauma-focused cognitive behavior therapy was the most researched form of intervention and resulted in medium to large effect sizes when compared to waitlist ($g = 1.44$) and active control conditions ($g = 0.66$). Experimental conditions were also more effective than control conditions at follow-up. Interventions were further effective in reducing comorbid depression symptoms, yet the obtained effect sizes were small to medium only. The findings indicate that psychological interventions can effectively reduce PTSD symptoms in children and adolescents. There is very little evidence to support use of psychopharmacological interventions for pediatric PTSD.

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Epidemiological research indicates that a large number of children and adolescents throughout the world have been exposed to traumatic events, such as physical or sexual violence, mass conflict, serious accident, natural disaster, or chronic illness (Attanayake et al., 2009; Costello, Erkanli, Fairbank, & Angold, 2002; Perkonigg, Kessler, Storz, & Wittchen, 2000). Posttraumatic stress disorder (PTSD) is highly prevalent in traumatized children and adolescents. A recent meta-analysis on the incidence of PTSD based on 43 independent samples of trauma-exposed children and adolescent that were assessed with diagnostic interviews revealed an overall prevalence of 15% (Alisic et al., 2014). Characteristic symptoms of PTSD are intrusive memories of the traumatic event, avoidance of reminders of the traumatic event, negative alterations in cognitions and mood, and increased arousal (American Psychiatric Association, 2013). This condition occurs often in the presence of depressive symptomatology (Dixon, Howie, & Starling, 2005).

To date, different forms of interventions for pediatric PTSD exist. Previously published meta-analyses regarding psychological interventions for children and adolescents suffering from PTSD have largely focused on one specific intervention type, such as trauma-focused cognitive behavior therapy (TF-CBT) or school-based interventions, or on a particular type of traumatic exposure, such as sexual abuse (Cary & McMillen, 2012; de Arellano et al., 2014; Harvey & Taylor, 2010; Kowalik, Weller, Venter, & Drachman, 2011; Lenz & Hollenbaugh, 2015; Macdonald et al., 2012). Silverman et al. (2008) and Gillies, Taylor, Gray, O'Brien, and D'Abrew (2012) have meta-analyzed the efficacy of multiple psychological treatments for children and adolescents who have been exposed to different traumatic events. Silverman and colleagues included 21 randomized controlled trials (RCTs) in their meta-analysis and concluded that psychological interventions had positive, though modest, effects for PTSD symptoms and comorbid depression. More recently, Gillies and colleagues included 14 RCTs in their meta-analysis and concluded that CBT was most effective in treating PTSD in children and adolescents and that all included therapy forms were found to be more effective than control conditions in treating PTSD. Gillies et al., however, did not include a number of potentially relevant trials in their meta-analysis that they labeled as preventive therapy. Yet, several of the excluded publications represented RCTs with children and adolescents with clinical levels of PTSD symptoms prior to starting the intervention. Examples of the RCTs that Gillies and colleagues labeled as preventive therapy and thus did not include in their meta-analysis are Deblinger, Lippmann, and Steer (1996), Jordans et al. (2010), Kemp, Drummond, and McDermott (2010), Layne et al. (2008), and Scheeringa, Weems, Cohen, Amaya-Jackson, and Guthrie (2011). This explains the discrepancy between the number of RCTs included in the meta-analysis in Silverman et al. and Gillies et al. (21 vs 14), although the meta-analysis by Gillies et al. was published later than Silverman et al. The exclusion of potentially relevant trials in Gillies et al. might have influenced the overall effect size reported by the authors.

Research on the efficacy of psychopharmacological interventions for pediatric PTSD is rather limited. Strawn, Keeshin, DelBello, Geracioti, and Putnam (2010) conducted a systematic review of journal articles published until 2009 and found just three RCTs of selective serotonin reuptake inhibitors and one RCT of imipramine in children and adolescents with PTSD (two trials in total) and acute stress disorder (one trial only). Based on their findings, the authors concluded that there is no empirical support for the use of psychopharmacological interventions as a first-line treatment for PTSD. This finding is also concurrent with guidelines suggesting that psychopharmacological interventions for pediatric PTSD should be used cautiously (Cohen & The Work Group On Quality Issues and the AACAP Work Group on Quality Issues, 2010; National Collaborating Centre for Mental Health, 2005).

Since the publication of the meta-analyses by Silverman et al. (2008) and Gillies et al. (2012), several RCTs on the efficacy of interventions for pediatric PTSD have been published (Carrion, Kletter, Weems, Berry, & Rettger, 2013; Danielson et al., 2012; Diehle, Opmeer, Boer, Mannarino, & Lindauer, 2015; Foa, McLean, Capaldi, & Rosenfield, 2013; Ford, Steinberg, Hawke, Levine, & Zhang, 2012; Jensen et al., 2014; McMullen, O'Callaghan, Shannon, Black, & Eakin, 2013; O'Callaghan, McMullen, Shannon, & Rafferty, 2015; O'Callaghan et al., 2014; O'Callaghan, McMullen, Shannon, Rafferty, & Black, 2013; Schottelkorb, Doumas, & Garcia, 2012; Tol et al., 2014). The goal of the present study was to provide an updated quantitative, meta-analytic review of the efficacy of interventions for children and adolescents suffering from PTSD. For this purpose, we reviewed RCTs that compared the efficacy of experimental interventions to active or passive control conditions. We tested the hypothesis that psychological interventions can effectively reduce symptoms of PTSD among children and adolescents. Furthermore, we expected that psychological treatments would also reduce levels of comorbid depression. Based on the review by Strawn et al. (2010) that included two RCTs only for PTSD symptoms, we did not have any specific hypotheses regarding psychopharmacological interventions.

1. Method

The aims and methods of this meta-analysis were registered with the PROSPERO database (CRD42016032695, http://www.crd.york.ac.uk/prospero). We defined the main structured research question describing the Population, Intervention, Comparison, Outcome, and Study design (PICOS) in accordance with the recommendations by the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) group (Moher, Liberati, Tetzlaff, Altman, & Grp, 2009). The question was "In children and adolescents with PTSD (P), does psychological treatment (I), compared to control conditions (C), improve PTSD and/or depression symptoms (O) in randomized controlled trials (S)?"

1.1. Identification and selection of studies

A search for publications was conducted in early April 2015 using the databases Medline, PsycINFO, and PILOTS. As only the first 5000 hits were displayed in PILOTS and the initial search exceeded this amount, the search was limited to peer-reviewed journals only. Inclusion criteria for the meta-analysis consisted of: 1) randomized controlled trial, 2) participants must be aged 18 or younger, 3) a minimum of ten participants per intervention group, and 4) treatment targets PTSD symptoms. Additional searching was conducted by reviewing the references of systematic reviews and meta-analyses found through the aforementioned databases. No language restrictions were made.

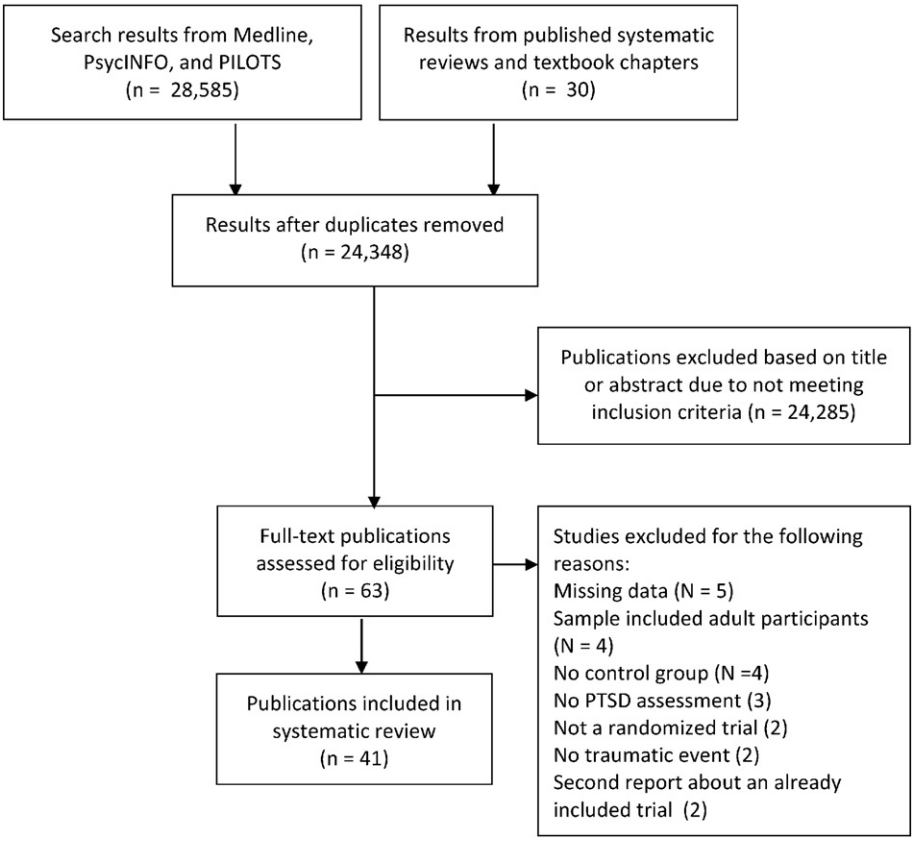


Fig. 1. Flow chart of search and inclusion process of studies.

Multi-field searches were conducted using the following terms: *Posttraumatic Stress Disorder* (*Posttraumatic stress* OR *post-traumatic stress* OR *Posttraumatic syndrome** OR *post traumatic syndrome** OR *PTSD* OR *PTSS* OR *trauma* OR *psychological distress* OR *psychotraumatology*) and *Children* (*child** OR *adolescent** OR *teen** OR *minor** OR *youth** OR *pediat** OR *boy** OR *girl**) and *Treatment* (*treatment** OR *intervention** OR *therapy* OR *psychotherapy* OR *exposure* OR *trial* OR *counselling*). Publications were then systematically excluded from the search results if they did not meet the aforementioned exclusion criteria based on title and abstract. If after fully reading the publication it remained unclear if the publication met the inclusion criteria, the publication was discussed between the first and second authors. In the case that data necessary for conducting the analysis were missing from a publication, the corresponding author was contacted and requested to provide the data. After two contact-attempts, the studies were excluded if the authors did not respond with the sufficient data to perform the meta-analysis.

The first and second authors separately coded and extracted from each study: comparison group(s), number of participants, type of outcome measure used, intervention format (individual or group), length of follow-up, age of participants, percentage of participants with a diagnosis of PTSD at preassessment, type of intervention, number of sessions, country where the trial was conducted, type of traumatic events, and outcome scores (mean and standard deviation scores). In case of disagreement between the reviewers, the discrepancies were resolved by consensus discussion between the reviewers while jointly re-evaluating the information in question. We did not assess the rate of agreement for the data extracted from each article. If separately reported, scores of depression symptoms were also coded and extracted. If posttreatment and follow-up results were published in two publications, the data were subtracted from both publications (e.g., Cohen, Deblinger, Mannarino, & Steer, 2004; Deblinger, Mannarino, Cohen, & Steer, 2006).

1.2. Quality assessment

Coding for the methodological quality of publications selected to be included in the meta-analysis was based on the quality analysis constructed by Cuijpers, van Straten, Bohlmeijer, Hollon, and Andersson (2010) and adjusted by Smit et al. (2012). The quality of the studies was coded based on the following questions: *Were PTSD symptoms assessed with a semi-structured interview*?, *Was a treatment manual used*?, *Were therapists trained either specifically for the study or in a general training*?, *Was treatment integrity checked by supervision and/or recordings and/or standardized instruments*?, *Was data analyzed with intent-to-treat analysis*?, *Was it a randomized study*?, *Was randomization done by an independent third person* (*or computer or sealed envelopes*)?, *Were blinded assessors used for interviews*?, and *Were dropouts adequately reported*? Items were scored on a four-point scale, where 3 indicates high quality (e.g., a published treatment manual was used), 2 indicates limited quality (e.g., an unpublished treatment manual was used), 1 indicates lack of required quality (e.g., no treatment manual was used), and 0 indicates unknown. The first and second authors independently rated all studies based on what was reported in the included publications.

1.3. Coding of treatment characteristics

Treatment interventions were first coded as either *active treatment* or *control group*. Next, active treatments were subdivided into *trauma-focused cognitive-behavior therapy* (*TF-CBT*; treatments focusing on the

Table 1
Overview of information of included trials.

Publication, conditions, & (number of sessions)	Number participants in analyses	Country	PTSD outcome	Follow-up in months	Type of treatment (format)	Age in years: range (Mean)	Statistical analysis	PTSD diagnosis at pretreatment (%)	Type of trauma
Ahmad, Larsson, and Sundelin-Wahlsten (2007) EMDR (8 sessions) WL	17 16	Sweden	PTSS-C	n.r.	EMDR (individual)	6–16 (10.0)	ITT	100	Multiple types
Ahrens and Rexford (2002) TF-CBT (8 sessions) WL	19 19	USA	PSS-SR	n.r.	Cognitive Processing T. (group)	15–18 (16.4)	Compl	100	Violence
Carrion et al. (2013) MDT (15 sessions) WL	38 27	USA	UPID	n.r.	Cue-centered treatment (individual, parent involvement)	8–17 (11.6)	ITT	n.r.	Multiple types
Catani et al. (2009) TF-CBT (6 sessions) Meditation (6 sessions)	16 15	Sri Lanka	UPID	6	KIDNET (individual)	8–14 (12.0)	ITT	100	Mass conflict
Celano, Hazzard, Webb, and McCall (1996) TF-CBT (8 sessions) TAU (8 sessions)	15 17	USA	CITES-R	n.r.	Recovering from abuse program (parent involvement in both conditions)	8–13 (10.5)	Compl	n.r.	Sexual assault
Chemtob et al. (2002) EMDR (3 sessions) WL	17 15	USA	CRI	n.r.	EMDR (individual)	6–12 (8.4)	Compl	100	Disaster
Cohen et al. (2004) TF-CBT (12 sessions) CCT (12 sessions)	89 91	USA	K-SADS	12	CBT CCT (parent involvement in both conditions)	8–14 (10.7)	Compl	89	Sexual assault
Cohen, Mannarino, and Knudsen (2005) TF-CBT (12 sessions) SC (12 sessions)	41 41	USA	TSCC	12	CBT (parent involvement in both conditions)	8–15 (11.4)	ITT	n.r.	Sexual assault
Cohen, Mannarino, and Iyengar (2011) TF-CBT (8 sessions) CCT (8 sessions)	64 60	USA	K-SADS	n.r.	CBT (parent involvement in both conditions)	7–14 (9.6)	ITT	25	Abuse/Neglect
Danielson et al. (2012) MDT (23 sessions) TAU (13 sessions)	15 15	USA	UPID	6	RRFT (individual, parent involvement in both conditions)	13–17 (14.8)	ITT	n.r.	Sexual assault
de Roos et al. (2011) TF-CBT (4 sessions) EMDR (4 sessions)	21 19	The Netherlands	UPID	3	CBT; EMDR (individual, parent involvement in both conditions)	4–18 (10.1)	ITT	17.3	Disaster
Deblinger et al. (1996) TF-CBT-c (12 sessions) TF-CBT-c&p (12 sessions) TF-CBT-p (12 sessions) TAU (12 sessions)	24 22 22 22	USA	K-SADS	24	CBT (child only, child&parent, parent only)	7–13 (9.8)	Compl	71	Sexual assault
Diehle et al. (2015) TF-CBT (12 sessions) EMDR (12 sessions)	23 25	The Netherlands	CAPS-CA	n.r.	CBT EMDR (individual, parent involvement in both conditions)	8–18 (12.9)	ITT	33	Multiple types
Foa et al. (2013) TF-CBT (14 sessions) SC (14 sessions)	31 30	USA	CPSS-I	12	Prolonged Exposure (individual)	13–18 (15.3)	ITT	100	Sexual assault
Ford et al. (2012) MDT (12 sessions) TAU (12 sessions)	33 26	USA	CAPS-CA	n.r.	TARGET (individual)	13–17 (14.7)	ITT	63	Multiple types
Gilboa-Schechtman et al. (2010) TF-CBT (12–15 sessions) PDP (15–18 sessions)	19 19	Israel	CPSS	17	Prolonged exposure PDP (individual)	12–18 (14.1)	ITT	100	Multiple types
Gordon, Staples, Blyta, Bytyqi, & Wilson, 2008	38 40	Kosovo	HTQ	n.r.	Mind-body skills group (group)	14–18 (16.3)	Compl	100	Mass conflict

MDT (12 sessions) WL									
Jaycox et al. (2009) CBI (10 sessions) WL	39 37	USA	CPSS	n.r.	SSET (group)	6th and 7th grade (11.5)	Compl	n.r.	Multiple types
Jensen et al. (2014) TF-CBT (15 sessions) TAU (15 sessions)	55 61	Norway	CAPS-CA	n.r.	CBT (parent involvement in both conditions)	10–18. (15.1)	ITT	66.7	Multiple types
Jordans et al. (2010) CBI (15 sessions) WL	164 161	Nepal	CPSS	n.r.	CBI, eclectic (group)	11–14. (12.7)	ITT	n.r.	Mass conflict
Kemp et al. (2010) EMDR (4 sessions) WL	12 12	Australia	CPTS-RI	n.r.	EMDR (individual)	6–12 (8.9)	Compl	n.r.	Motor vehicle accident
King et al. (2000) TF-CBT-c (20 sessions) TF-CBT-c&p (20 s.) WL	12 12 12	Australia	ADIS	3	CBT (child only, child&parent)	5–17 (11.5)	ITT	69	Sexual assault
Layne et al. (2008) CBI (18 sessions) SC (18 sessions)	66 61	Bosnia	UPID	4	CBI, eclectic (group)	13–18 (16.0)	Compl	n.r.	Mass conflict
McMullen et al. (2013) TF-CBT (15 sessions) WL	24 24	DR Congo	UPID	n.r.	CBT (group)	13–17 (15.8)	Compl	n.r.	Mass conflict
O'Callaghan et al. (2013) TF-CBT (15 sessions) WL	24 28	DR Congo	UPID	n.r.	CBT (group, parent involvement)	12–17 (16.1)	ITT	60	Mass conflict
O'Callaghan et al. (2014) MDT (8 sessions) WL	78 80	DR Congo	CRIES	n.r.	Eclectic psychosocial intervention (group, parent involvement)	7–18 (13.5)	Compl	16	Mass conflict
O'Callaghan et al. (2015) TF-CBT (9 sessions) MDT (9 sessions) (WL not used because convenience sample)	26 24	DR Congo	UPID	6	CBT eclectic psychosocial intervention (group, parent involvement in both active conditions)	8–17 (14.8)	ITT	92	Mass conflict
Peltonen, Qouta, El Sarraj, and Punamaki (2012) CBI (not reported) WL	108 64	Palestine	CPTS-RI	n.r.	CBI, eclectic (group)	10–14 (11.4)	Compl	45	Mass conflict
Qouta, Palosaari, Diab, and Punamaki (2012) CBI (8 sessions) WL	242 240	Palestine	CRIES	6	CBI, eclectic (group)	10–13 (11.3)	ITT	64	Mass conflict
Ruf et al. (2010) TF-CBT (8 sessions) WL	13 13	Germany (refugees)	UPID	6	KIDNET (individual)	7–16 (11.5)	ITT	100	Mass conflict
Schauer (2008) TF-CBT (6 sessions) Meditation	24 22	Sri Lankan	CAPS	n.r.	KIDNET (individual)	11–15 (13.1)	Compl	100	Mass conflict
Scheeringa et al. (2011) TF-CBT (12 sessions) WL	20 11	USA	PAPA	n.r.	CBT (parent involvement)	3–6 (5.3)	Compl	24	Multiple types
Schottelkorb et al. (2012) TF-CBT (17 sessions) CCPT (17 sessions)	12 14	USA (refugees)	UPID	n.r.	CBT CCPT (individual, parent involvement in both conditions)	6–13 (9.1)	Compl	58	Mass conflict
Smith et al. (2007) TF-CBT (10 sessions) WL	12 12	United Kingdom	CAPS-CA	n.r.	CBT (individual, parent involvement)	8–18 (13.8)	ITT.	100	Multiple types

(continued on next page)

Table 1 (*continued*)

Publication, conditions, & (number of sessions)	Number participants in analyses	Country	PTSD outcome	Follow-up in months	Type of treatment (format)	Age in years: range (Mean)	Statistical analysis	PTSD diagnosis at pretreatment (%)	Type of trauma
Stein et al. (2003) TF-CBT (10 sessions) WL	54 63	USA	CPSS	n.r.	CBT (group)	6th grade (11.0)	Compl	n.r.	Multiple types
Tol et al. (2008) CBI (15 sessions) WL	182 221	Indonesian	CPSS	6	CBI, eclectic (group)	7–15 (9.9)	ITT	n.r.	Mass conflict
Tol et al. (2012) CBI (15 sessions) WL	199 200	Sri-Lanka	CPSS	3	CBI, eclectic (group)	9–12 (11.0)	Compl	n.r.	Mass conflict
Tol et al. (2014) CBI (15 sessions) WL	153 176	Burundian	CPSS	3	CBI, eclectic (group)	7–15 (12.3)	ITT	n.r.	Mass conflict
Trowell et al. (2002) PDP (30 sessions) Psychoeducation (18 s.)	28 28	United Kingdom	K-SADS	24	PDP (PDP individual; Psychoeducation group)	6–14 (10.0)	Compl	n.r.	Sexual assault

Note: ADIS = Anxiety Disorders Interview Schedule; CAPS-CA = Clinician Administered PTSD Scale for Children and Adolescents; CBI = Classroom-Based Intervention; CBT = Cognitive Behavior Therapy; CCPT = Child Centered Play Therapy; CCT = Child Centered Therapy; CITES-R = Children's Impact of Traumatic Events Scales-Revised; Compl = completer analysis; CPSS = Child PTSD Symptom Scale; CPSS-I = CPSS Interview version; CPTS-RI = Child Post-Traumatic Stress - Reaction Index; CRI = Child Reaction Index; CRIES = Children's Revised Impact of Event Scale; EMDR = Eye Movement Desensitization and Reprocessing; HTQ = Harvard Trauma Questionnaire; ITT = intent-to-treat analysis; K-SADS = Schedule for Affective Disorders and Schizophrenia for School-Age Children; KIDNET = Narrative Exposure Therapy for Children; MDT = Multidisciplinary Treatment; n.r. = not reported; PAPA = The Preschool Age Psychiatric Assessment; PDP = Psychodynamic Psychotherapy; PSS-SR = PTSD Symptom Scale, Self-Report; PTSS-C = Posttraumatic Stress Symptoms Scale for Children; SC = Supportive Counselling; SSET = Support for Students Exposed to Trauma; TARGET = Trauma Affect Regulation: Guide for Education and Therapy; TAU = Treatment as Usual; TF-CBT = Trauma-focused Cognitive Behavior Therapy; TF-CBT-c = TF-CBT for child only; TF-CBT-c&p = TF-CBT for child and parent; TF-CBT-p = TF-CBT for parent only; TSCC = Trauma Symptom Checklist for Children; UPID = The University of California at Los Angeles PTSD Index; USA = United States of America; WL = Waitlist.

Table 2
Number of experimental and control conditions examined in the included studies.

Condition		PTSD		Depression	
		Post	FU	Post	FU
Experimental vs control conditions					
TF-CBT vs	ACC	7	5	6	5
	Waitlist	8	3	6	2
CBI vs	ACC	1	1	1	1
	Waitlist	6	4	6	4
EMDR vs	ACC	0	0	0	0
	Waitlist	3	0	2	0
MDT vs	ACC	2	1	2	1
	Waitlist	3	0	1	0
PDP vs	ACC	1	1	1	0
	waitlist	0	0	0	0
TF-CBT vs other experimental conditions (OEC)					
TF-CBT vs	CCT	3	1	2	1
	EMDR	2	1	1	1
	MDT	1	1	0	0
	MED	2	1	0	0
	PDP	1	1	1	1
	All OEC	9	5	3	2
Group* vs	ACC	0	0	0	0
	Waitlist	6	0	2	0

Note: * excluding Classroom-Based Interventions (CBI); ACC = Active Control Condition, included Supportive Counselling, Psychoeducation, and Treatment as Usual (TAU); EMDR = Eye Movement Desensitization and Reprocessing; FU = Follow-up; MDT = Multidisciplinary Treatment; PDP = Psychodynamic Psychotherapy; TF-CBT = Trauma-Focused Cognitive Behavior Therapy.

memory of the trauma and/or its meaning), *multidisciplinary treatment* (*MDT*; treatments including intervention techniques from different therapeutic approaches), *classroom-based intervention for students* (*CBI*), *child centered therapy* (*CCT*), *eye movement desensitization and reprocessing* (*EMDR*), *psychodynamic psychotherapy* (*PDP*), *meditation*, or *psychopharmacological treatment*. While the term TF-CBT has been used in some of the included trials as a label for one particular cognitive behavior therapy intervention. (Cohen et al., 2004), in our meta-analysis we used the term TF-CBT for all interventions that are based on cognitive behavior therapy and focus on the memory of the trauma and/or its meaning, including cognitive therapy and prolonged exposure (see Bisson, Roberts, Andrew, Cooper, & Lewis, 2013). Control conditions were subdivided into *waitlist* as well as active control conditions. Active control conditions consisted of *treatment as usual* (*TAU*), *supportive counselling* (*SC*), and *psychoeducation*. Finally, all active treatments were categorized based on whether they were delivered as individual or group treatment.

1.4. Statistical analysis

Intent-to-treat (ITT) samples were used when available (21 publications) and completer samples were utilized if ITT samples were not provided (18 publications). To calculate the effect sizes, the control group mean was subtracted from the treatment group mean at posttreatment or follow-up, respectively, and divided by the pooled standard deviation. Subsequently, to obtain the effect size Hedges's g the outcome was multiplied by a sample size correction factor $J = 1 - (3/(4df - 1))$ (Lipsey & Wilson, 2001). Subgroup analyses were conducted if a specific group of interventions consisted of at least four trials. Analyses were completed with the Metafor package (v.1.9.8) in R3.2.4 (R Core Team, 2015; Viechtbauer, 2010) using random effects model to calculate effect sizes given the heterogeneity of the studies (Field & Gillett, 2010). Effect sizes g may be conservatively interpreted with Cohen's convention of small (0.2), medium (0.5), and large (0.8) effects (Cohen, 1988). To examine homogeneity of effect sizes we calculated the Q-statistic and the I^2-statistic that is an indicator of heterogeneity in percentages, with higher percentages indicating high heterogeneity. Potential publication bias was assessed for the primary outcome measures through visual inspection of the funnel plot (for analyses including more than nine trials, see Sterne et al., 2011), by examining the relation between effect- and standard error with relatively higher effect sizes of smaller studies being an indicator for publication bias (Sterne et al., 2011). Furthermore, we calculated the likely number of missing studies using the trim-and fill procedure (Duval & Tweedie,

Table 3
Effects of psychological interventions for PTSD and depression (Hedges's g).

	Post				FU			
	k	*g*	*SE*	95% CI	*k*	*g*	*SE*	95% CI
PTSD: overall outcomes								
Exper. interv.* vs WL	20	0.83	0.15	[0.53; 1.13]	7	0.35	0.14	[0.07; 0.62]
Exper. interv.* vs ACC	11	0.41	0.11	[0.20; 0.62]	8	0.46	0.11	[0.24; 0.69]
PTSD: subgroup analyses								
E.I. excl. CBI vs WL	14	1.14	0.16	[0.82; 1.46]	3	n.a.		
E.I. excl. CBI vs ACC	10	0.44	0.12	[0.21; 0.67]	7	0.43	0.14	[0.15; 0.71]
TF-CBT vs WL	8	1.44	0.22	[1.02; 1.86]	3	n.a.		
TF-CBT vs ACC	7	0.56	0.12	[0.33; 0.80]	5	0.66	0.15	[0.38; 0.95]
TF-CBT vs OEC	9	0.19	0.10	[0.00; 0.39]	5	−0.02	0.15	[−0.33; 0.29]
CBI vs WL	6	0.23	0.12	[0.00; 0.46]	4	0.21	0.14	[−0.07; 0.49]
Depression: overall outcomes								
Exper. interv.* vs WL	15	0.30	0.08	[0.16; 0.45]	6	0.03	0.05	[−0.07; 0.14]
Exper. interv.* vs ACC	9	0.32	0.11	[0.11; 0.53]	7	0.33	0.14	[0.04; 0.61]
Depression: subgroup analyses								
E.I. excl. CBI vs WL	9	0.42	0.13	[0.16; 0.68]	2	n.a.		
E.I. excl.CBI vs ACC	8	0.37	0.12	[0.14; 0.60]	6	0.43	0.14	[0.15; 0.71]
TF-CBT vs WL	6	0.59	0.18	[0.24; 0.93]	2	n.a.		
TF-CBT vs ACC	5	0.48	0.12	[0.24; 0.71]	5	0.48	0.15	[0.16; 0.45]
TF-CBT vs OEC	4	0.22	0.12	[−0.01; 0.44]	2	n.a.		
CBI vs WL	6	0.24	0.09	[0.06; 0.42]	4	0.03	0.06	[−0.08; 0.14]

Note*: All active interventions excluding Supportive Counselling, Psychoeducation, and Treatment as Usual (TAU); ACC = Active Control Conditions, included Supportive Counselling, Psychoeducation, and TAU; CBI = Classroom-based Intervention; k = number of treatment arms; n.a. = number of trials too small ($k < 4$) to conduct analysis; OEC = Other Experimental Conditions; TF-CBT = Trauma-focused Cognitive Behavior Therapy; WL = waitlist.

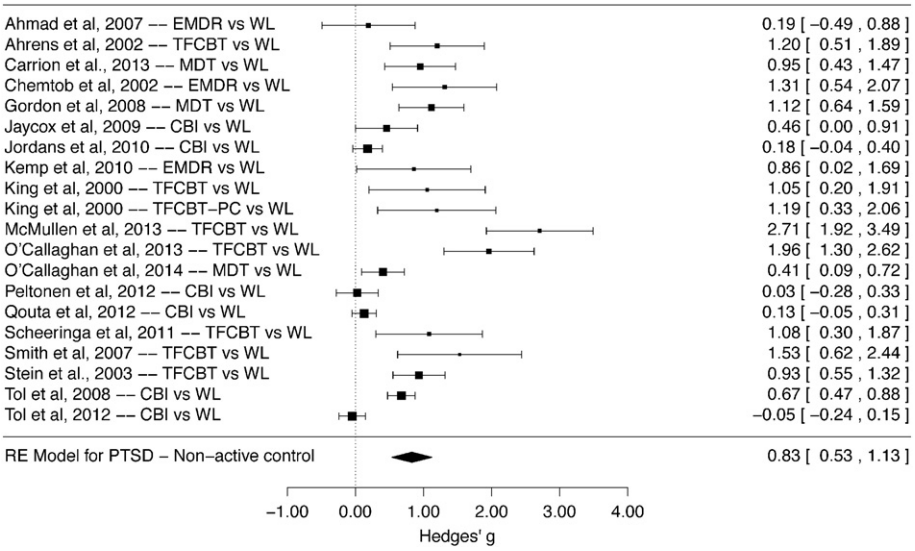


Fig. 2. Forest plot of effect sizes comparing experimental conditions to waitlist at posttreatment. Note: CBI = Classroom-Based Intervention; EMDR = Eye Movement Desensitization and Reprocessing; TFCBT = Trauma-focused Cognitive Behavior Therapy; MDT = Multidisciplinary Treatment; WL = Waitlist.

2000), which yields an estimate of the effect size after publication bias has been taken into account.

Mixed model meta-regressions were employed to examine whether the observed heterogeneity could be explained by variables of interest (Borenstein, Hedges, Higgins, & Rothstein, 2009). Seven predictors were considered: percentage of participants with PTSD diagnosis at preassessment, average age of participants, intervention format (individual vs. group), whether ITT or complete samples were used for calculation of means and standard deviations in the original publication, number of treatment sessions, whether treatment was conducted with the child alone or with the involvement of a caregiver, and assessment of methodological quality of the included publications. Borenstein et al. (2009) recommended a ratio involving at least ten studies for each moderator. Meta-regressions were conducted for each of these predictors separately and in the above listed order. Predictors were evaluated by the change in Cochran's heterogeneity Q-statistic and its associated p-value. In light of the relatively low power associated with the current set of 39 trials, we used $p = 0.10$ as the nominal significance level (Hedges & Pigott, 2001).

2. Results

2.1. Selection and characteristics of included studies

Fig. 1 describes the inclusion of studies. After examining 24,348 abstracts, 63 full text publications were reviewed. The final review resulted in 41 clinical trials. Two of the trials examined the efficacy of pharmacotherapy for treating PTSD symptoms (Cohen, Mannarino,

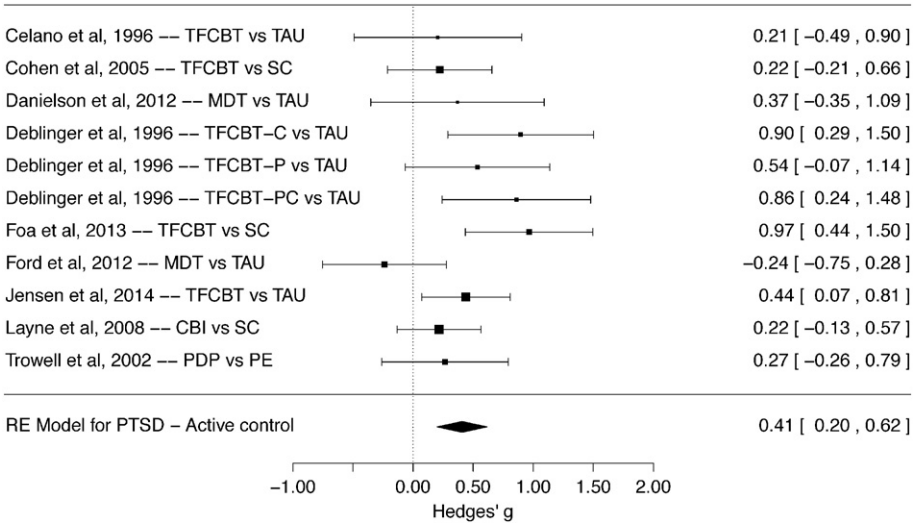


Fig. 3. Forest plot of effect sizes comparing experimental conditions to active control conditions at posttreatment. Note: CBI = Classroom-Based Intervention; EMDR = Eye Movement Desensitization and Reprocessing; PDP = Psychodynamic Psychotherapy; PE = Psychoeducation; SC = Supportive Counselling; TAU = Treatment as Usual; TFCBT = Trauma-focused Cognitive Behavior Therapy; TFCBT-C = TF-CBT for child only; TF-CBT-PC = TFCBT for child and parent; TFCBT-P = TF-CBT for parent only; MDT = Multidisciplinary Treatment; WL = Waitlist.

Perel, & Staron, 2007; Robb, Cueva, Sporn, Yang, & Vanderburg, 2010). Effect sizes could not be measured for these trials as less than four publications could be found. Accordingly, 39 trials on psychological interventions with 4184 participants in total (2713 in a treatment condition and 1471 in a waitlist condition) were examined in the meta-analysis.

Twenty-two studies contained participants with a Western nationality, while 17 contained participants with a non-Western nationality, including two studies with refugees within a Western country (see Appendix A and Table 1). All publications were in English, 38 publications were journal articles, and one was a doctoral thesis (Schauer, 2008). The mean age of participants was 12.2 years. Participants entered treatment on the basis of PTSD symptoms resulting from different traumatic events, with mass conflict being reported as the most common form of traumatic experience (see Table 1 for further information). Table 2 describes the number of experimental and control conditions being examined in the included studies. Follow-up data were reported for 20 and 16 experimental conditions regarding the efficacy of treatment on PTSD and depression symptoms, respectively. With regard to some publications, the follow-up data could not be used if waitlist participants were not followed-up without treatment (e.g., Chemtob, Nakashima, & Carlson, 2002). In one study (Ruf et al., 2010), no posttreatment data for the waitlist condition were reported, thus this study was included in the follow-up analyses only. In another study (Diehle et al., 2015), depression data were not included as less than ten participants in the experimental condition were included in the original analysis. Additionally, the waitlist condition in O'Callaghan et al. (2015)was not used as it consisted of a convenience sample.

2.2. The effect of treatment on PTSD symptomatology

A total of 19 publications examined the efficacy of 20 experimental conditions as compared to waitlist at posttreatment. This comparison resulted in a mean effect size $g = 0.83$ (see also Table 3). When compared to active control conditions, experimental conditions produced a mean effect size of $g = 0.41$ ($k = 11$). Heterogeneity was large for trials comparing experimental conditions to waitlist at posttreatment ($I^2 = 91.37$; $Q = 146.71$, $df = 19$, $p < 0.001$), indicating substantial heterogeneity in effect sizes between studies. Heterogeneity with regard to trials comparing experimental conditions to active control conditions was smaller ($I^2 = 43.79$; $Q = 17.42$, $df = 10$, $p = 0.07$). Figs. 2 and 3 show the effect sizes for all included trials that assessed the efficacy of treatment in reducing PTSD at postassessment as compared to either waitlist or active control conditions.

At follow-up, experimental conditions produced small to medium effect sizes when compared to waitlist and active control conditions ($g = 0.35$ and 0.46, respectively).

Table 3 reports the results of subgroup analyses. Given that CBI programs are usually applied to large amount of students while focusing less on individual needs than in other forms of treatment, we separately examined the efficacy of treatment while excluding CBI. This lead to a large aggregated effect size for experimental conditions when compared to waitlist ($g = 1.14$; $k = 14$) and to a medium effect when compared to active control conditions ($g = 0.44$; $k = 10$). TF-CBT interventions produced a large effect size when compared to waitlist at posttreatment ($g = 1.44$; $k = 8$) and a medium to large effect size when compared to active control conditions at post treatment ($g = 0.66$; $k = 7$). The same effect size was also found when TF-CBT was compared to active control conditions at follow-up (a comparison to waitlist at follow-up could not be made given the low number of trials). CBI interventions produced small effect sizes when compared to waitlist at posttreatment ($g = 0.23$; k = 6).

Meta-regressions showed that PTSD percentage at preassessment did not significantly explain heterogeneity neither for experimental conditions vs. waitlist ($Q = 1.09$, $p = 0.30$), nor for experimental conditions vs. active control conditions ($Q = 2.79$, $p = 0.10$). Average age explained some heterogeneity for the comparison of experimental conditions vs. waitlist ($Q = 3.11$, $p = 0.08$), which indicated that higher average age is associated with better treatment outcome when experimental conditions are compared to wait list. However, there was no indication that average age significantly accounts for heterogeneity for the comparison of experimental conditions vs. active control conditions ($Q = 0.59$, $p = 0.44$). The results further suggested that neither the format (group vs. individual), nor whether all participates were included in the original analyses (ITT vs. complete sample) nor number of treatment sessions substantially accounted for heterogeneity (all Qs < 1.33, all ps > 0.23). With regard to quality assessment, the results suggested that this variable did not significantly explain heterogeneity neither for experimental conditions vs. waitlist ($Q = 0.40$, $p = 0.53$) nor for experimental conditions vs. active control conditions ($Q = 0.24$, $p = 0.62$). finally, we examined whether caregiver involvement was associated with treatment outcome. As can be seen in Table 1, the majority of trials had included caregiver involvement in both the experimental condition as well as the active control condition. Therefore, we limited our analyses to trials that compared experimental conditions to waitlist. The results suggested that caregiver involvement did not significantly account for heterogeneity for experimental conditions vs. waitlist ($Q = 1.77$, $p = 0.18$). Note that for this last analysis we excluded the parent-only condition that was examined in Deblinger et al. (1996).

2.3. The effect of treatment on comorbid depression symptomatology

Table 3 also reports the effects of treatment for comorbid depression symptoms. As can be seen, effect sizes were small to medium only.

2.4. Quality assessment

Two raters independently rated all studies. The Intraclass Correlation Coefficient (ICC) of the total score for all studies combined was 0.89, 95% CI [0.86, 0.91], indicating very good inter-rater reliability. The results indicated a general satisfactory level of quality for most of the publications, with 33 publications (84.6%) reporting a score of two or higher. On average, six out of nine items were coded with a mean of higher than 2, which indicates good quality. The three items rated less favorably were: use of a semi-structured interview to screen study participants ($M = 1.8$), independent randomization ($M = 1.1$), and blinded assessment ($M = 1.6$).

2.5. Publication bias

For the main analyses, treatment vs. waitlist and treatment vs. active control (both at posttreatment), visual inspection of the funnel plots suggested no publication bias (see Appendix B). Trim and fill analysis similarly did not suggest publication bias with no imputed studies.

However, visual inspection indicated potential publication bias at the follow-up period. For the comparison of treatment vs. waitlist, the trim and fill procedure introduced two studies to the left side and this reduced the estimated effect from $g = 0.34$ to $g = 0.25$ (95%CI: −0.02 to 0.51, $p = 0.07$). For the comparison of treatment vs. active control, the trim and fill procedure introduced three studies to the left side and this reduced the effect size from $g = 0.46$ to $g = 0.29$ (95%CI: 0.05 to 0.53, $p = 0.02$).

With regards to TF-CBT, there was little indication of publication bias in comparison to either waitlist or active controls posttreatment. However, when comparing TF-CBT to other experimental treatments, there is some indication of publication bias but to the right side (trim and fill: 4 studies). After adjusting with the trim and fill procedure, the effect is estimated to be substantially stronger $g = 0.32$ (95%CI: 0.15 to 0.49, $p = 0.0003$; vs. $g = 0.19$ without adjustment).

3. Discussion

We assessed the efficacy of randomized controlled trials for children and adolescents with symptoms of PTSD and comorbid depression. Our systematic search resulted in 39 psychological and two psychopharmacological interventions that met the inclusion criteria. The results of the meta-analysis suggest that psychological interventions can effectively lower PTSD symptoms when compared to waitlist and active control conditions. The efficacy of interventions to reduce symptoms of comorbid depression was rather small.

The magnitude of the aggregated effect sizes resulting from comparing all experimental psychological treatments to waitlist or to other active conditions at post-treatment is somewhat lower than the effect size of 1.05 reported by Gillies et al., which was based on only six trials. On the other hand, our calculated effect sizes are higher than the small to medium effect sizes reported by Silverman et al. (2008) when experimental conditions were compared to waitlist and active control conditions combined at post-treatment. The larger sample of included trials in our review relative to previous meta-analyses enabled us to more accurately examine the efficacy of treatment at follow-up. Overall, our findings suggest that the majority of children and adolescents undergoing psychotherapy for PTSD have significantly less PTSD symptoms at post-treatment. However, the small effect sizes at follow-up suggest that experimental conditions combined did only slightly better than waitlist or active control conditions in producing long-lasting therapeutic effects. On a related note, the trim and fill procedure suggested that relevant trials regarding the efficacy of treatment at follow-up might be missing and their inclusion might somewhat reduce the efficacy of psychotherapy. It should be noted, however, that the asymmetry in the funnel plots that is tapped by the trim and fill method when considering all studies combined may well be a result of the actual heterogeneity due to the smaller studies having (actual) larger underlying effect sizes (Sterne et al., 2011).

There was a large heterogeneity between psychological interventions with effect sizes at posttreatment ranging from – 0.05 to 2.71 when experimental conditions were compared to waitlist and −0.24 to 0.97 when experimental conditions were compared to active control conditions (see Figs. 2 & 3). Several factors might explain the found heterogeneity, yet we think that the format in which the interventions were applied and the content of treatment are most important. One might expect that individual psychotherapy with the child or adolescent alone or together with his/her caregiver would on average be more efficacious than classroom based interventions that are usually applied to large groups of students at school. In an individual treatment format, the therapist can tailor psychotherapy to better meet the needs of the client than in a classroom-based intervention format. Furthermore, classroom-based interventions have been mostly developed and applied to reach broad groups of individuals who have been exposed to mass violence and who otherwise have limited access to mental health services. Consequently, such interventions need to be efficacious, capable of being scaled up to the point that it can reach large numbers of individuals, and be readily implemented in the regions in question (Tol et al., 2011). Accordingly, when we separately meta-analyzed the efficacy of classroom-based interventions in our meta-analysis, this produced small effect sizes when these interventions were compared to waitlist. Another factor that seems to have influenced the heterogeneity between treatments is content of treatment. With regard to specific forms of psychotherapy, TF-CBT was most researched and this form of treatment produced a very large effect size in reducing PTSD symptoms when compared to waitlist at posttreatment. Furthermore, TF-CBT was associated with medium effect sizes in reducing both PTSD and depression symptoms when compared to active control conditions at posttreatment. While there were not enough trials available to examine the efficacy of TF-CBT alone as compared to waitlist at follow-up, this treatment was related to medium effect sizes when compared to active control conditions at follow-up regarding both PTSD and depression symptoms. The results related to TF-CBT are in line with previous meta-analyses with children and adolescents with PTSD symptoms (de Arellano et al., 2014; Gillies et al., 2012; Harvey & Taylor, 2010) as well as with adults with PTSD (Bisson et al., 2013), including adults who had reported childhood abuse (Ehring et al., 2014). There is indication that trauma-focused interventions are underutilized in routine clinical practice (Becker, Zayfert, & Anderson, 2004; van Minnen, Hendriks, & Olff, 2010). However, our findings support the notion that trauma-focused interventions applied as sole treatment can produce large therapeutic effects. The other forms of experimental conditions were too small in number to allow any empirical conclusions about their sole efficacy in treating PTSD and depression in children and adolescents. However, the overall efficacy of psychological interventions indicates that they too may be effective in reducing PTSD symptoms among children and adolescents.

Our meta-analysis was based on trials conducted with children and adolescents who had reported exposure to different types of traumatic events. However, the majority of trials were conducted with participants who were exposed to traumatic events that are likely to have taken place over a long period of time, which sometimes in literature is labeled as type 2 trauma, whereas type 1 trauma would correspond to a relatively abbreviated exposure to a traumatic event such as a motor vehicle accident (Terr, 1991). As can be seen in Table 1, 34 out of 39 trials included participants who were exposed to mass conflict (16 samples), multiple types of trauma (ten samples), and sexual assault (eight samples). Yet, it is important to note the potential overlap in the type of trauma experienced among these three populations. For example, exposure to mass conflict is by nature exposure to multiple traumas and often also includes exposure to sexual assault. As psychotherapy proved to be effective over all trials, the overlap regarding exposure to traumatic events suggests that psychological interventions can effectively treat PTSD symptoms in children and adolescents exposed to multiple traumatic events. In our meta-analysis, some forms of treatment were more likely to have been examined among distinct samples. For example, seven out of eight trials that evaluated the efficacy of classroom-based interventions were conducted with survivors of mass conflict and the remaining trial (Jaycox et al., 2009), was conducted with participants who had reported multiple trauma types (see Table 3). Accordingly, we acknowledge that the efficacy of psychotherapy might be influenced by the nature and duration of traumatic events. Given the nature of exposure to traumatic events among the included trials and the number of included trials, we were not able to examine whether type of trauma is associated with treatment outcome and thus this notion remains to be to examined in future research.

Experimental conditions were also more effective in reducing comorbid depression symptoms than control conditions, yet the effect was rather small. Previous meta-analyses have reported mixed results on the efficacy of psychological treatments for comorbid depression. Silverman et al. (2008) reported small effect sizes when experimental conditions were compared to waitlist and active

control conditions combined at post-treatment. On the other hand, Gillies et al. (2012) reported effect sizes of 0.74 and 0.02 in favor of experimental conditions as compared to control conditions in the short and medium term, respectively. However, the number of trials included in Gillies et al. were small, with five and three in each analysis, respectively. Our findings, which are based on a larger number of trials might be seen as more accurately reflecting the efficacy of trauma therapy for comorbid depression. The rather poor outcome for the overall efficacy of overall treatments for comorbid depression might be explained by several factors. Interventions were primarily designed to address PTSD symptoms rather than depression symptoms, and it may not be surprising that interventions were less capable of reducing depression. Furthermore, not all trials measured comorbid depression and so the limited variance may have skewed the overall finding. Yet, as discussed above, when TF-CBT trials were analyzed separately, they produced medium effect sizes as compared to waitlist and active control conditions in reducing comorbid symptoms of depression. Nevertheless, the findings regarding comorbid depression symptoms indicate that psychological treatments for pediatric PTSD might need to specifically target depression symptoms to achieve a greater reduction of depression.

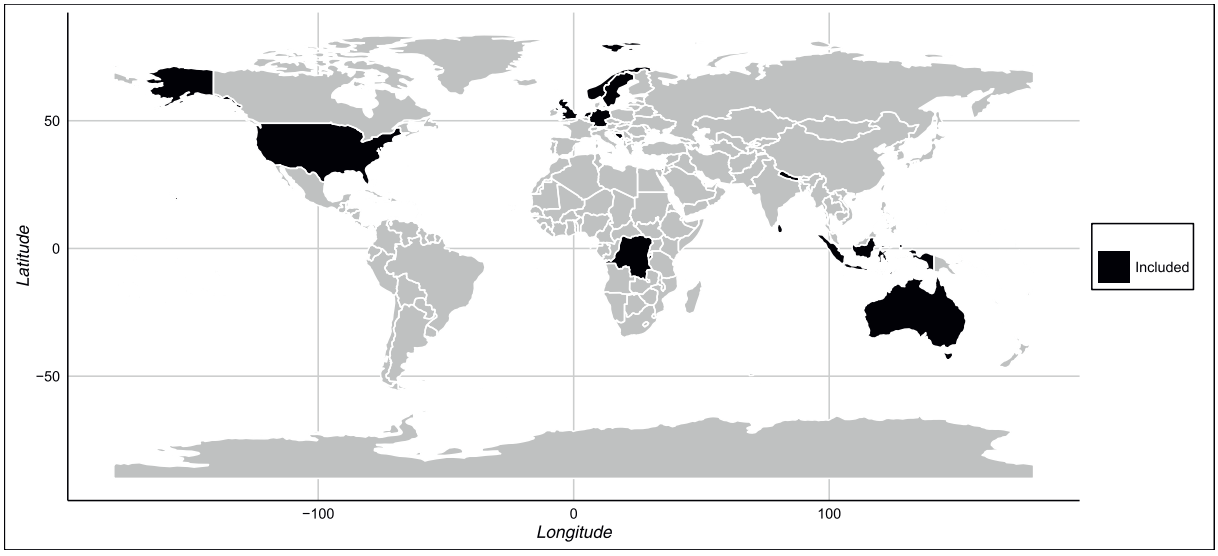
Literature has suggested that inclusion of the parent might enhance the efficacy of psychotherapy. A meta-analysis by Harvey and Taylor (2010) with 39 uncontrolled and controlled psychological trials with sexually abused children and adolescents suggested that family involvement was associated with higher reduction from pre-to post-treatment. Our analysis suggested that parent involvement was not associated with treatment outcome. One explanation for the different results might be related to the study design. Whereas our results are based on comparative studies, the findings by Harvey and Taylor resulted from uncontrolled comparisons. Perhaps more relevant is the fact that the meta-analysis by Harvey and Taylor was conducted with survivors of sexual abuse only and family involvement might be particularly important in this population, whereas our meta-analysis was based on samples with diverse histories of traumatic experiences. Finally, the lack of association between parent involvement and treatment outcome in our meta-analysis might also be a result of comparing not only diverse populations but also diverse treatments that may differ in efficacy. Deblinger et al. (1996) investigated whether caregiver involvement within one specific form of treatment (in this case TF-CBT) is associated with higher treatment outcome when compared to no caregiver involvement and more research needs to follow this example.

We were able to find only two randomized controlled trials assessing the efficacy of psychopharmacological interventions for pediatric PTSD, which indicates that research on medication for children and adolescents with PTSD is limited. As it has been reported elsewhere, this applies for both the relative efficacy of pharmacological approaches alone as well as in combination with psychological interventions (Baldwin et al., 2014; Strawn et al., 2010). Our findings are in line with guidelines suggesting that psychopharmacological interventions should be used cautiously and only after determining that the child or adolescent with PTSD may not benefit from psychotherapeutic interventions such as TF-CBT (Cohen & The Work Group On Quality Issues and the AACAP Work Group on Quality Issues, 2010; National Collaborating Centre for Mental Health, 2005).

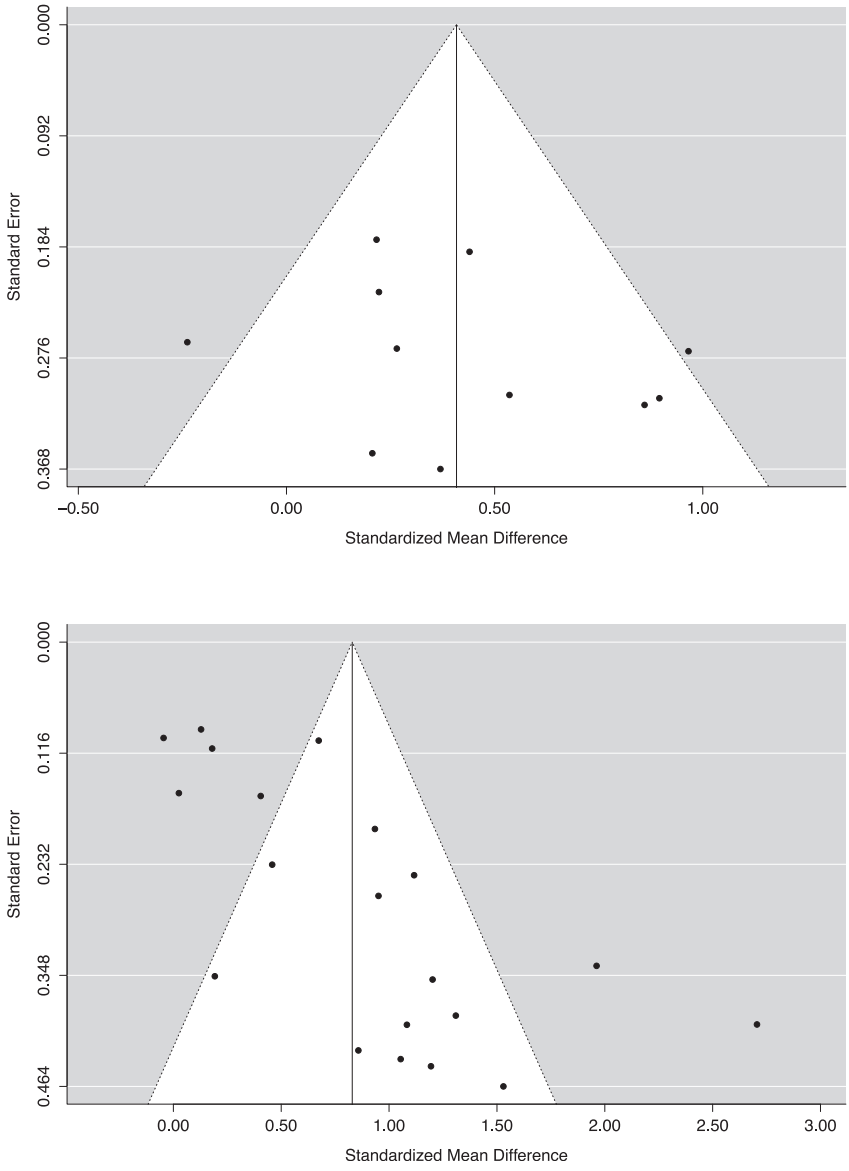
There are several limitations associated with this meta-analysis. First, there was a large heterogeneity in interventions included and several interventions were under-represented due to an insufficient number of trials per intervention type. Accordingly, there was not enough statistical power to compute relevant sub-analyses and several of our sub-analyses include a rather small number of studies. Second, 18 of the included trials reported treatment completer data and the remainder reported ITT analysis and this factor raises difficulties in interpretation of results for meta-analyses. Third, whereas the aim was to meta-analyze both psychological and pharmacological interventions, only two randomized controlled trials could be found that examined the efficacy of pharmaceutical therapy.

Findings from the current meta-analysis indicate that psychological treatments can significantly reduce levels of PTSD among children and adolescents. The treatment for which there was the best evidence of effectiveness was TF-CBT. Furthermore, there is very little evidence to support use of psychopharmacological interventions for pediatric PTSD.

Appendix A. Countries in which interventions were conducted



Appendix B. Funnel plots of trials comparing experimental to non-active control conditions (above) and trials comparing experimental conditions to waitlist (below)



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