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Title

Psychological interventions for ICD-11 Complex PTSD symptoms:
Systematic review and meta-analysis

Running Head

Psychological therapies for CPTSD

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Abstract

Background: The 11th revision to the WHO International Classification of Diseases (ICD-11) identified Complex Posttraumatic Stress Disorder (CPTSD) as a new condition. There is a pressing need to identify effective CPTSD interventions. **Methods:** We conducted a systematic review and meta-analysis of Randomised Controlled Trials (RCTs) of psychological interventions for Posttraumatic Stress Disorder (PTSD), where participants were likely to have clinically significant baseline levels of one or more CPTSD symptom clusters (affect dysregulation, negative self-concept and/or disturbed relationships). We searched MEDLINE, PsycINFO, EMBASE and PILOTS databases (January 2018), and examined study and outcome quality. **Results:** Fifty-one RCTs met inclusion criteria. Cognitive Behavioural Therapy (CBT), Exposure alone (EA), and Eye Movement Desensitization and Reprocessing (EMDR) were superior to usual care for PTSD symptoms, with effects ranging from $g = -0.90$ (CBT; $k=27$, 95% CI -1.11, -0.68; moderate quality) to $g = -1.26$ (EMDR; $k=4$, 95% CI -2.01, -0.51; low quality). CBT and EA each had moderate-large or large effects on negative self-concept, but only 1 trial of EMDR reported this outcome. CBT, EA and EMDR each had moderate or moderate-large effects on disturbed relationships. Few RCTs reported affect dysregulation data. The benefits of all interventions were smaller when compared to non-specific interventions (e.g., befriending). Multivariate meta-regression suggested childhood-onset trauma was associated with a poorer outcome. **Conclusions:** The development of effective interventions for CPTSD can build upon the success of PTSD interventions. Further research should assess the benefits of flexibility in intervention selection, sequencing and delivery, based on clinical need and patient preferences. **Keywords:** CPTSD, psychological therapies, childhood trauma, systematic review, meta-analysis, randomised controlled trials

Introduction

The 11th revision to the World Health Organization's International Classification of Diseases (ICD-11) (WHO, 2018) includes two distinct sibling conditions, Posttraumatic Stress Disorder (PTSD) (code 6B40) and Complex PTSD (CPTSD) (code 6B41), under a general parent category of 'Disorders specifically associated with stress'. PTSD is comprised of three symptom clusters including (1) re-experiencing of the trauma in the here and now, (2) avoidance of traumatic reminders, and (3) a persistent sense of current threat that is manifested by exaggerated startle and hypervigilance. ICD-11 CPTSD includes the three PTSD clusters and three additional clusters that reflect 'disturbances in self-organization' (DSO); (1) affect dysregulation, (2) negative self-concept, and (3) disturbances in relationships (Maercker et al., 2013). These disturbances are proposed to be typically associated with sustained, repeated, or multiple forms of traumatic exposure (e.g., genocide campaigns, childhood sexual abuse, child soldiering, severe domestic violence, torture, or slavery) (Karatzias et al., 2017), reflecting loss of emotional, psychological, and social resources under conditions of prolonged adversity (Cloitre et al., 2013).

The qualitative distinction between PTSD and CPTSD symptomatology has been supported in different trauma samples (see Brewin et al., 2017) including those experiencing interpersonal violence (Cloitre et al., 2013), rape, domestic violence, traumatic bereavement (Elklit, Hyland, & Shevlin, 2014), survivors of institutional abuse such as that occurring within foster care and religious organizations (Knefel et al., 2015) and refugees (Hyland et al., 2018). The distinction between PTSD and CPTSD has also been confirmed in samples of young adults (Perkonigg et al., 2014) and children (Sachser, Keller, & Goldbeck, 2016). The second-order factorial structure of CPTSD in which the disorder is comprised of both PTSD and DSO has also been supported in previous research (e.g. Karatzias et al., 2016; Hyland et al., 2017a; Hyland et al., 2017b; Shevlin et al., 2017).

To date a number of meta-analyses and systematic reviews have investigated the effectiveness of PTSD treatments in general (Barrera et al, 2013; Bisson & Andrews, 2005, 2007; Bisson et al., 2007; Bisson et al., 2013; Callahan et al 2004; DeJong & Gorey, 1996; Ehring et al, 2014; Pelekis & Dahl, 2005; Roberts et al, 2015; Sloan et al, 2013; Taylor & Harvey, 2009; Taylor & Harvey 2010; Watts et al, 2013). Overall, previous meta-analyses have supported the efficacy of trauma-focused psychological treatments, such as Cognitive Behavioural Therapy (CBT) and Eye Movement Desensitization and Reprocessing (EMDR), for the treatment of DSM-IV PTSD, a condition of three clusters of symptoms including re-experience, avoidance of the traumatic reminders and hyperarousal. CBT and EMDR target patients' memories of their traumatic events and the personal meanings of the trauma and typically include repeated in vivo and/or imaginal exposure to the trauma, reappraisal of the meaning of the trauma and its consequences, or some combination of these techniques (e.g. Bisson et al., 2013). These approaches have been identified as efficacious for a range of PTSD survivors, including rape victims, survivors of childhood abuse, refugees, combat veterans, and victims of motor vehicle accidents (Foa et al. 2009), although most existing evidence on these interventions concerns single adult traumas (e.g. Bisson et al., 2013). There is disagreement whether trauma focused treatments are optimal for more complex traumatic presentations such as CPTSD. For complex traumatic presentations, a phase-based model, originally proposed by Herman (1992), has been suggested as the preferred treatment option (Cloitre et al., 2012).

Phased interventions address disturbances in self-organization and related problems in day to day functioning (e.g., improving safety, emotion regulation and social skills) first, while explicit exploration of the trauma (e.g., exposure) is subsequently introduced (Cloitre et al., 2012b). The rationale for this sequencing is two-fold; firstly to increase emotional, psychological and social resources to improve functioning in daily life and secondly, to use these resources to enhance the effectiveness of trauma-focused work. Whilst there is some

support for this approach (e.g., Cloitre et al., 2010), it is uncertain if a stabilisation phase is necessary and it might lead to unhelpful delays in using more trauma-focused interventions (De Jongh et al., 2016). Another approach to managing complex traumatisation focuses on treating symptoms that are co-morbid with PTSD. Empirical investigations have generally demonstrated the feasibility and effectiveness of these approaches. Examples include PTSD with Substance Use Disorder (SUD) (Mills et al., 2012) where SUD and PTSD interventions are integrated and implemented relatively simultaneously and PTSD with Borderline Personality Disorder (BPD) (Harned, Korslund and Linehan, 2014) where ideally the BPD and PTSD interventions occur concurrently (but only once the patient has developed the emotional and behavioural control to tolerate the PTSD intervention). However, it is important to emphasise that CPTSD is not identical to PTSD and its co-morbidity but is rather a distinct disorder with a specific symptom profile.

Considering that ICD-11 CPTSD is a new condition, it will take a substantial amount of time before an evidence base accumulates regarding its treatment. However, there is evidence on interventions that addressed at least partially the symptoms of CPTSD, including those of DSO. The aim of this systematic review and meta-analysis was to synthesise the evidence on effectiveness of treatments for the symptoms of CPTSD and identify therapies that look most promising for treating the symptoms of CPTSD. To achieve this goal, we examined evidence from trials for PTSD where participants were also likely to have clinically significant levels of one or more CPTSD DSO symptom clusters at baseline, and where usable data on the effect of interventions on these symptoms were reported. We also aimed to explore the moderating effect of RCT quality, the developmental timing of traumatic exposure (childhood vs. adulthood), phased vs. non-phased interventions, and individual vs. group interventions on treatment outcome. Our ultimate goal was to create a list of research priorities to inspire future research in the treatment of ICD-11 CPTSD.

Method

Protocol registration

A protocol for this systematic review and meta-analysis was pre-registered (CRD42017055305) on February 2017. Changes to the protocol are listed in the supplement.

Search strategy and study selection

The search process was conducted in three main phases. First, MEDLINE, PsycINFO, EMBASE and PILOTS databases were searched for studies published from database inception to October 2017 using the following search terms: (“PTSD” or “posttrauma*” or “psychological stress*” or “combat” or “post-trauma*” or “gross stress reaction” or “stress disorder*” or “trauma*” or “psychological trauma”) AND (“randomised” or “randomized” or “randomised controlled trial” or “randomized controlled trial” or “RCT”) AND (“therapy” or “psychological therapy” or “psychological intervention” or “intervention” or “treatment”). The only limiter applied in this search was language (English only). Second, to update the search, the same databases were searched for studies published from database inception to January 2018 using similar search terms: (“PTSD” or “posttrauma*” or “psychological stress*” or “combat” or “post-trauma*” or “gross stress reaction” or “stress disorder*” or “trauma*” or “psychological trauma”) AND (“randomised” or “randomized” or “RCT”) AND (“therapy” or “intervention” or “treatment”). Limiters applied in this search were language (English only), humans, age group (adolescence, defined as between 13 and 17 years old, and adulthood, defined as 18 years and older), treatment and prevention, and randomised controlled trials. Third, the reference lists of earlier systematic reviews and meta-analyses of clinical trials for PTSD were screened for additional studies (Bisson et al., 2013; Bradley et al., 2005; Cusack et al., 2016; Ehring et al., 2014; Imel et al., 2013; Kline et al., 2018). Three independent investigators (AB, SR, PM) carried out the search. Any discrepancies between search results

were discussed and resolved with members of the research team (PHU, TK). As a final step, unpublished data were identified through contacting investigators and searching clinical trial registries (ClinicalTrials.gov and the UK Clinical Trials Gateway).

Studies were eligible for inclusion if they were randomised controlled trials (RCTs) reporting the effects of an individual or group-based psychological intervention for adults (mean age ≥ 16 years) with PTSD (ICD-10 and/or DSM-III-IV criteria), if participants experienced at least one of the additional CPTSD criteria at baseline (affect dysregulation, negative self-concept and disturbances in relationships, as defined in ICD-11), and if participants were free from developmental or intellectual disability, neurodegenerative disorders and acquired and/or traumatic brain injury. Studies where participants had comorbid substance misuse difficulties or other mental health conditions were included, but studies where participants had a primary diagnosis of substance misuse disorder were excluded. Case studies, uncontrolled trials and crossover trials were not included.

To establish whether participants had clinically significant levels of one or more of the additional CPTSD symptom clusters at baseline, any published clinical cut-offs relating to the CPTSD syndrome or individual CPTSD DSO symptoms were referred to in the first instance. If these were not available, any original validation study of the CPTSD index was referred to in order to try to identify relevant healthy norms; if the mean of the participants was more than one standard deviation (SD) away from the mean of these norms (in the direction of impairment), participants were considered to have clinically significant levels of the relevant CPTSD index. If there was no original validation study or if studies did not contain relevant healthy norms, studies that contained such norms was then searched for; if there were multiple studies, those with the largest sample sizes were prioritised. If the above clinical cut-offs or relevant norms could not be obtained, a decision about clinical significance was made on a case-by-case basis (e.g., if the participants' mean on a CPTSD DSO symptom indicated that

they were closer to being intact than impaired, they were not considered to have clinically significant levels of the relevant CPTSD symptom).

We defined a ‘psychological intervention’ as a talk-based intervention delivered by a trained therapist who adapted the treatment to patients on the basis of a therapeutic relationship (i.e., no delivery of a non-modifiable standard protocol, e.g., progressive muscle relaxation) (Benish, Imel and Wampold, 2008), and met at least two of the following four criteria: (a) a citation to an established school or approach to psychotherapy; (b) a description of the therapy that contained a reference to a psychological process (e.g., operant conditioning); (c) a reference to a treatment manual that was used to guide the delivery of the treatment; (d) the identification of active ingredients of the treatment and citations for these ingredients. Some of the face-to-face interventions we included did not meet these criteria (e.g., mindfulness, yoga), however we decided to report their effects in the interests of completeness. Online or other non-face-to-face interventions, even though they may meet these criteria, were excluded because of their different method of delivery and in an effort to reduce heterogeneity.

We further categorized psychological interventions into four different groups; (a) CBT (see definition below); (b) exposure therapy alone (i.e., psychological interventions, which were not better defined as CBT, emphasizing exposure to the trauma memory as the principal active treatment component, such as PE and imaginal exposure); (c) EMDR (i.e., psychological interventions consistent with the manual by Shapiro, 1995); (d) other psychological interventions (e.g., mindfulness). As per NICE guidelines, CBT was defined as a discrete psychological intervention where service users: (i) establish links between thoughts, feelings or actions with respect to the current or past symptoms, and/or functioning; (ii) re-evaluate their perceptions, beliefs or reasoning in relation to the target symptoms (National Collaborating Centre for Mental Health, 2014). To be categorized as CBT, the intervention also had to focus on at least one of the following: (iii) service users monitoring their own

thoughts, feelings or behaviours with respect to the symptom or recurrence of symptoms; (iv) promotion of alternative ways of coping with the target symptom (National Collaborating Centre for Mental Health, 2014). Given this broad definition of CBT, psychological interventions which involved cognitive/imagery modification with or without exposure therapy were considered to be CBT in nature.

We compared psychological intervention(s) to each other or to a control condition, which could be treatment as usual (TAU; also included 'waiting list control'), or TAU plus a non-specific therapeutic intervention (i.e. befriending, counselling).

Outcomes and data extraction

Our primary outcome was the standardised difference between groups at end of treatment in severity of (a) PTSD symptoms (as per ICD-11, DSM III-IV criteria) and (b) affect dysregulation, negative self-concept and disturbances in relationships. These were also used to calculate the associated number needed to treat (NNT) for clinically significant response, based on different estimates of response rates in the control condition.

Two reviewers (PHU, AB) extracted data relating to study characteristics, including details on participants, interventions received and outcomes assessed. Three reviewers (PM, AB, SR) also completed independent assessments of whether participants' mean baseline scores on measures of CPTSD symptoms were within the clinical range, which were then discussed and approved by two other reviewers (TK, PHU). Study authors were contacted in every case where CPTSD-relevant outcomes appeared to have been assessed but not reported. To assess outcomes, we extracted means and standard deviations (SD) where possible. If SDs were not reported, then these were derived from standard errors, confidence intervals, p-values or t-values where possible, following Cochrane Handbook procedures (Higgins and Green, 2011).

Analysis

We used Comprehensive Meta-Analysis software (version 3) for the meta-analyses. We first calculated the post-intervention standardised mean difference (Hedges' *g*) and standard error (SE) for each individual study on each outcome (PTSD, affect dysregulation, negative self-concept, disturbances in relationships). Hedges' *g* was selected as the effect size measure because it accounts for variation in sample size and sample variance (Deeks, Altman and Bradburn, 2001). A composite effect was also computed for each study by combining PTSD and any available CPTSD DSO outcome data. To do this, we computed the average Hedges' *g* and associated SE across the outcomes. The range of measures used to assess these meant it was not feasible to adjust the composite estimate for the between-outcome correlation, and had to instead assume this was zero. When the number of participants (*N*) contributing data to each domain differed, we used the smallest *N* for the composite estimate. When there was sufficient data (at least two studies), we calculated the differences between interventions and controls on PTSD, affect dysregulation, negative self-concept, and disturbances in relationships individually, using DerSimonian and Laird (1986) random-effects meta-analyses. We then pooled data from studies reporting PTSD plus (a) 1, 2 or 3 CPTSD DSO outcomes, (b) 2 or 3 CPTSD DSO outcomes, and (c) all 3 CPTSD DSO outcomes. The estimates were expressed in units of Hedges' *g* with associated 95% confidence intervals. Between group differences in clinically significant change were derived from the Hedges' *g* estimate and an assumed control event response rate (CER) using the Furukawa method (Furukawa, 1999; Furukawa and Leucht, 2011; <http://rpsychologist.com/d3/cohend/>) and presented as NNT for benefit or harm. Morina et al., (2014) report a CER of 44% for PTSD however because CPTSD is assumed to have a poorer prognosis we estimated what the NNT to benefit or harm would be if we halved this value to 22%. We also estimated what the NNT would be if the natural remission rate in the control conditions was either very high (50%) or very low (10%). Using the relative group

difference and a range of assumed CERs to compute NNT is the method recommended by the Cochrane Handbook, since this “helps users to understand the important impact that typical baseline risks have on the absolute benefit that they can expect” (Higgins and Green., 2011).

The potential impact of publication bias was assessed using funnel plots, Egger’s test and Duval and Tweedie’s Trim-and-Fill procedure (random-effects) (Duval and Tweedie, 2000; Egger et al., 1997), but only for analyses derived from at least 10 studies (Higgins and Green, 2011). Cohen’s (1988) established conventions (small = 0.2, moderate = 0.5, large = 0.8) were used to interpret individual and meta-analytical estimates of Hedges’ g. Statistical significance was inferred when p-values were below 0.05, although values between 0.01 and 0.09 were downgraded for imprecision. Heterogeneity was assessed using the I^2 statistic, and compared with thresholds specified in the Cochrane Handbook (<40% low; 30-60% moderate; 50-90% substantial; 75-100% considerable) (Higgins and Green, 2011).

Assessment of study and outcome quality

Individual study quality was assessed using the Cochrane Collaboration Risk of Bias tool (Higgins et al., 2011) and meta-analytical estimates were assessed using the GRADE approach (Guyatt et al., 2008) (see supplement). The GRADE approach considers the quality of studies contributing to each analysis, the consistency, directness and precision of the pooled estimate, and the risk of publication bias.

Cochrane risk of bias ratings were completed by two reviewers independently (PM, AB), and checked by a third (PHU). An overall individual study quality rating was also produced (see supplement for criteria). GRADE ratings were performed by one reviewer (PHU) and checked by two others (PM, TK). An overall GRADE assessment is provided alongside each outcome to inform the interpretation of these findings.

Moderator analyses

We combined all studies into a single dataset to conduct a series of pre-specified univariate moderator analyses, and one multivariate analysis, again using Comprehensive Meta-Analysis software (version 3). The outcome for each meta-regression analysis was the post-treatment group difference in CPTSD symptom severity. For this we used, in order of preference, the composite estimates of differences in (1) PTSD plus the three CPTSD DSO symptom clusters; (2) PTSD plus two CPTSD DSO symptom clusters (3) PTSD plus one CPTSD DSO symptom cluster or (4) PTSD alone.

Pre-specified univariate analyses included the relevant Cochrane Risk of Bias parameters (sequence generation, allocation concealment, detection bias, reporting bias, attrition bias), onset of trauma (childhood vs adulthood), degree to which sample met CPTSD criteria (i.e., whether data on PTSD plus three, two, one or no CPTSD DSO symptom clusters were used) and therapy format (individual vs group). There was insufficient data to support pre-specified analysis of phased vs non-phased interventions. We also examined the effect of therapy type (individual CBT, group CBT, EMDR, exposure alone, group IPT), and the effect of using a non-specific control condition (i.e., versus a usual care / waiting list control group). To ensure that all studies with 3 or more arms could be included without double-counting of participants, we split the sample size of any shared treatment or control arms in half for these comparisons, as recommended in the Cochrane Handbook (Higgins and Green, 2011), and revised the individual study effect sizes accordingly. To ensure power for the multivariate analyses, we limited this to 5 variables; study quality, therapy type, degree to which sample met CPTSD criteria, trauma onset, and use of a non-specific control condition.

Results

Study selection

The search returned 28,521 results, of which 28,310 were excluded on the basis of title or abstract (see Figure 1). Following title and abstract screening, the full texts of the remaining 211 articles were examined. One hundred and forty one full text articles were excluded. A further 19 full text articles were excluded because they described studies that did not include clinically significant levels of one or more CPTSD DSO symptom clusters at baseline. Fifty-one studies met full inclusion criteria and were included in the current study. Of these, 35 studies had a CBT arm, 11 had an exposure only arm, 9 had an EMDR arm, and 9 assessed the effect of other interventions, including interpersonal psychotherapy (IPT), mindfulness, trauma management training (TMT), dialogical exposure therapy (DET), dialectical behaviour therapy, CBT plus emotion regulation training, and stabilisation therapy. Figure 2 provides an overview of studies contributing to each analysis. A table of included study characteristics and a table of excluded studies, with reasons for exclusion, are provided in the supplement.

Insert Figure 1

Insert Figure 2

Quality assessment

The results of the Cochrane risk of bias assessment are shown in the supplement and GRADE ratings for each meta-analytical outcome are shown below and in the far right column of Tables 1-4 and Table J.1 (supplement). Just over half of the included studies used appropriate methods to generate a random sequence to allocate participants to groups, but poor reporting limited our assessment of this domain. A slightly smaller proportion had a low risk of bias for

allocation sequence concealment, but again poor reporting prevented a clear assessment of this domain. The majority of studies had a low risk of detection bias because assessors were unaware of the group that participants had been allocated to. Most also had a low risk of attrition bias with acceptable rates of missing post-intervention data (<25%). However, most had a high risk of reporting bias primarily due to a lack of a preregistered protocol. The risk of performance bias was unavoidably high across all studies due to the nature of the interventions, which precluded blinding of participants. Overall, we rated the majority of studies as high in methodological quality.

Meta-analytical outcomes

Cognitive behavioural therapy (CBT) (Table 1, and supplement)

As shown in Table 1, compared to usual care, CBT had a moderate-large effect on disturbances in relationships ($k=16$, $g = -0.66$; 95% CI = -0.84, -0.48) and large effects on affect dysregulation ($k=3$, $g = -1.42$; 95% CI = -2.20, -0.65), negative self-concept ($k=9$, $g = -0.82$; 95% CI = -1.19, -0.44) and PTSD symptoms ($k=27$, $g = -0.90$; 95% CI = -1.11, -0.68) (all moderate quality evidence), with the NNT varying from 2 (affect dysregulation assuming CER of 22%) to 6 (disturbances in relationships assuming CER of 10%). Moderate to large effects were also observed on the composite estimates of PTSD and CPTSD DSO symptoms (low to high quality evidence), with NNTs of between 3 (PTSD + 1, 2, or 3 CPTSD DSO outcomes assuming CER of 50%) and 8 (PTSD + 3 CPTSD DSO outcomes assuming CER of 10%). However few studies measured more than one type of CPTSD DSO symptom. Significant publication bias was detected whenever there were sufficient studies to assess this, however only the estimate for disturbances in relationships was reduced when trim-and-fill analysis was applied. Compared to non-specific control interventions, CBT had a small effect on disturbances in relationships ($k=3$, $g = -0.32$; 95% CI = -0.60, -0.03) and a small-moderate

effect on PTSD symptoms ($k=9$, $g = -0.37$; 95% CI = -0.66, -0.09) (moderate quality evidence), with NNTs varying between 7 (PTSD assuming 50% CER) and 15 (disturbances in relationships assuming 10% CER). Although there was no evidence it had significant effects on affect dysregulation and negative self-concept, few studies reported usable data. When we pooled effects from all 9 studies reporting data on PTSD and at least one CPTSD DSO domain, a small effect was observed ($k=9$, $g = -0.34$; 95% CI = -0.62, -0.06; low quality evidence), with NNTs of between 8 (50% CER) and 14 (10% CER), but no studies measured more than one domain.

Exposure therapy alone (Table 2, and supplement)

As shown in Table 2, compared to usual care, exposure therapy alone had a moderate effect on disturbances in relationships ($k=4$, $g = -0.59$; 95% CI = -1.12, -0.07; moderate quality evidence), a moderate-large effect on negative self-concept ($k=3$, $g = -0.73$; 95% CI = -1.03, -0.43; moderate quality evidence), and a large effect on PTSD symptoms ($k=6$, $g = -1.05$; 95% CI = -1.52, -0.58; low quality evidence), with NNTs of between 3 (PTSD - all assumed CERs) and 7 (disturbances in relationships, assuming 10% CER). No studies examined whether exposure was superior to usual care in relation to affect dysregulation. Moderate to large effects on the composite outcomes of PTSD and CPTSD DSO symptoms were observed (low to high quality evidence), with NNTs ranging from 3 (PTSD + 1, 2 or 3 CPTSD DSO outcomes, CERs of 22% and 50%) to 7 (PTSD + 2 or 3 CPTSD DSO outcomes, assuming 10% CER), however only one study provided usable data on more than one type of CPTSD DSO symptom. There was no evidence that exposure alone was superior to non-specific therapies in relation to disturbances in relationships, but only one study provided usable data. No studies reported whether exposure alone was superior to non-specific therapies in relation to either affect dysregulation or negative self-concept. Two studies found no effect of exposure alone on either

PTSD data, or the composite outcome of PTSD plus CPTSD DSO symptoms (low quality evidence). No studies provided data on more than one CPTSD DSO symptom.

Eye-Movement and Desensitisation and Reprocessing therapy (EMDR) (Table 3, and supplement)

As shown in Table 3, compared to usual care, the few available studies suggested EMDR had a moderate effect on negative self-concept ($k=1$, $g = -0.61$; 95% CI = -1.04, -0.17; low quality evidence), a moderate-large effect on disturbances in relationships ($k=4$, $g = -0.76$; 95% CI = -1.35, -0.16; moderate quality evidence), and large effects on affect dysregulation ($k=1$, $g = -1.64$; 95% CI = -2.56, -0.72; very low quality evidence) and PTSD symptoms ($k=4$, $g = -1.26$; 95% CI = -2.01, -0.51; low quality evidence), with NNTs ranging from 2 (affect dysregulation, all CERs) to 7 (disturbances in relationships, assuming CER of 10%). EMDR also had a large effect on the composite outcome of PTSD and at least one CPTSD DSO symptom ($k=4$, $g = -1.15$; 95% CI = -1.92, -0.37; low quality evidence), with NNTs of 2 (CER of 22%) or 3 (CER of 10% or 50%), but it did not have an effect on the composite outcome of PTSD and more than one CPTSD DSO symptom (very low quality evidence). There was no evidence that EMDR was superior to non-specific interventions in relation to disturbances in relationships or affect dysregulation (very low quality evidence). Although moderate-large effects on negative self-concept ($k=2$, $g = -0.78$; 95% CI = -1.56, -0.01) and PTSD symptoms ($k=3$, $g = -0.69$; 95% CI = -1.35, -0.03) (very low quality evidence) were observed, with NNTs of between 4 (negative self-concept, all CERs) and 6 (PTSD; CER of 10%), these analyses were based on only 2-3 studies. A moderate effect on the composite outcome of PTSD and at least one CPTSD DSO symptom was observed ($k=3$, $g = -0.52$; 95% CI = -0.97, -0.08; low quality evidence), with NNTs of between 5 (CER 50%) and 8 (CER 10%), but no effect was

found on the composite outcome of PTSD and more than one CPTSD DSO symptom (very low quality evidence).

Comparison of CBT, Exposure and EMDR (Table 4, and supplement)

As shown in Table 4, there was very limited evidence that EMDR had a small-moderate advantage over CBT in relation to PTSD symptoms ($k=2$, $g = 0.37$; 95% CI = 0.03, 0.71; low quality evidence), with an NNT of 7-12, but no differences between CBT, exposure alone or EMDR were observed for any other outcomes

Other comparisons (supplement)

As shown in Table J.1 (supplement), one small study (Krupnick 2008) found IPT had an advantage over usual care in reducing PTSD plus disturbances in relationships ($k=1$, $g = -1.02$; 95% CI = -1.65, -0.39; very low quality evidence), with an NNT of 3-4, and another small study (Azad marzabadi 2014) found mindfulness was more effective than usual care in relation to disturbances in relationships ($k=1$, $g = -1.60$; 95% CI = -2.43, -0.77; very low quality evidence), with an NNT of 2-3. Several other small studies compared various psychotherapeutic interventions to other interventions, or to CBT, exposure or EMDR. We found no evidence to favour any particular intervention in relation to the composite outcome of PTSD plus CPTSD DSO symptoms (very low to low quality evidence).

Moderator analyses (Figure 3, and supplement)

As shown in Table L.1 (supplement), use of a non-specific control condition rather than usual care or waiting list was associated with a smaller benefit of psychological therapy in univariate meta-regression, with a reduction in Hedges' g of 0.48, (95% CI = 0.18, 0.77). No other moderators were significant when examined individually. As shown in Table M.1

(supplement), the effect of using a non-specific control condition was larger in multivariate meta-regression, with a reduction in Hedges' g of 0.69 (95% CI = 0.39, 1.00) in this analysis. Study quality and age of trauma onset also emerged as significant moderators of therapy effects in this analysis. Low quality studies were associated with a significantly *lower* effect size, with a reduction in Hedges' g of 0.30 (95% CI = 0.00, 0.61). Studies where participants had predominantly childhood-onset trauma were associated with a reduction in Hedges' g of 0.35 (95% CI = 0.02, 0.69), when compared to trials where most participants had adult-onset trauma (Figure 3).

Discussion

We examined evidence from RCTs of psychological treatments for PTSD where participants were also likely to have clinically significant levels of one or more CPTSD DSO symptoms at baseline, and where usable data on the effect of interventions on these symptoms were reported. A total of 51 studies met inclusion criteria. Overall, results indicate that when compared to usual care, CBT, Exposure alone and EMDR perform relatively equally for symptoms of PTSD and the DSO symptoms of negative self-concept and disturbances in relationships. While the quality of this evidence was moderate for CBT, it ranged from low to moderate for Exposure alone and EMDR. Few trials reported the effectiveness of psychological therapies for symptoms of affect dysregulation. Low quality evidence suggests that EMDR has a small-moderate advantage over CBT in relation to PTSD symptoms, but there was no evidence of any differences between CBT, Exposure alone or EMDR for the other outcomes including DSO symptoms. Univariate and multivariate meta-regression confirmed that the effectiveness of psychological therapies was considerably lower when compared to non-specific therapies, which suggests that non-specific effects may account for a large proportion of therapeutic change in symptoms of CPTSD in these trials. The multivariate meta-regression

also found that treatment outcome may be moderated by the developmental time of the onset of psychological trauma, with childhood trauma being associated with smaller effects of psychological therapies on CPTSD symptoms.

The data are encouraging in that the accumulation of evidence suggests that there are specific interventions that work for several of the CPTSD symptom clusters. The data also suggest that no particular type of intervention (exposure, cognitive re-appraisal, bilateral stimulation) is necessary to resolve any one symptom cluster. A critical question is whether current treatments devised for PTSD are equally effective for those who will be diagnosed with CPTSD. Our results replicate earlier findings that individual trauma-focused treatments show large effect sizes. Although the evidence is at a very early stage, we found that some non-trauma-focused therapies, such as mindfulness and IPT, may also reduce PTSD and interpersonal disturbance, suggesting alternative options. Importantly, childhood abuse was found to moderate all outcomes across all types of treatments, suggesting those with a history of childhood trauma may experience less improvement, and that current treatments for this patient population can be improved. These results have implications for the treatment of CPTSD as those with childhood abuse are at risk for CPTSD and in this meta-analysis may represent those more likely to have the full symptom profile.

Research is needed to determine how to optimize treatment outcomes for those with childhood abuse and other populations at risk for CPTSD. This includes identifying which treatment interventions are most effective for specific symptom clusters, which are most acceptable to patients, in what order to present interventions and the optimal duration of different types of interventions. Considering current debates in the literature, it would have been useful to explore the usefulness of phased vs. non-phased interventions and individual vs. group interventions for CPTSD. Unfortunately, we did not find adequate evidence to enable further analysis of these treatment outcome moderators. There is substantial evidence

indicating that CPTSD and PTSD represent distinct patient populations with different symptoms profiles (Brewin et al., 2017), suggesting the value of developing treatments that more precisely and effectively resolve the differing effects of trauma exposure by systematically testing type, order and duration of interventions specific to each disorder and taking into account patient preferences across both disorders (Cloitre, 2015).

Our meta-analysis has a number of strengths. We minimised the risk of bias by pre-registering the review, and we minimised errors and omissions by having two or more reviewers conduct comprehensive searches, assess study quality and extract descriptive data. We considered a range of treatments from different countries and included participants with a range of backgrounds and types of psychological trauma including military, civilian and childhood trauma. Many studies have used qualified therapists and considered assessments of adherence to the protocol. However, most of the research was conducted in western countries, thus limiting the extent to which the findings may generalise to non-western countries. Furthermore, the evidence we have reviewed as part of this meta-analysis was predominantly on DSM-IV PTSD. Most studies did not present data on multiple traumatisation which typically results in CPTSD (Karatzias et al., 2016). Even when the index trauma that was targeted occurred in adulthood in included studies, it would be useful to assess lifetime traumatic history and consider the accumulative effect of multiple traumatisation. In relation to outcomes, we have only considered therapeutic gains at post-treatment. Future research should explore long-term outcomes of these interventions. Furthermore, for this meta-analysis we have used proxy measures for the CPTSD constructs. It might well be the case that a number of studies that included people with CPTSD have not been included in the study as they have not reported outcomes on relevant constructs or reported outcomes have not met clinical thresholds or our definition of 'clinical significance'. It might also be the case that the measures employed in included studies do not accurately reflect the corresponding DSO clusters, thus

introducing some measurement bias. Moreover, while the quality of the meta-analytical evidence was high or moderate for some of the outcomes (e.g., when CBT was compared with usual care or non-specific control interventions), it was low or very low for most of the outcomes. Related to this, there was substantial heterogeneity for just over half of the outcomes. Thus, there is some uncertainty in the conclusions that can be drawn. It is also worth noting that we did not downgrade the meta-analytical outcomes for indirectness, as indirect evidence of psychological interventions for CPTSD was the focus of this review. If, on the other hand, we had been interested in direct evidence of psychological interventions for CPTSD, most if not all the outcomes would have been downgraded for indirectness.

There is clearly a need for further well-designed trials of psychological therapies that incorporate appropriate methods of randomisation, blinding of assessors, long-term follow up and appropriate training of therapists and monitoring of treatment adherence. We have identified a set of research priorities to benefit people with CPTSD in the future that might directly or indirectly result from the findings of this review:

- Effectiveness of phased vs. non-phased interventions for CPTSD: Very few included studies in this meta-analysis have incorporated a phased approach to treatment and it was not possible to address this question.
- Effectiveness of trauma focused treatments vs. non – trauma focused treatments. Existing evidence is predominantly focused on trauma-focused treatments.
- Head-to-head comparisons between trauma focused treatments for CPTSD. Most studies explored the effectiveness of interventions against standard care or no treatment.
- Exploring safety of trauma focused therapies for CPTSD. It is essential that future research in this area provides information on adverse effects.
- Investigation of whether diagnosis of CPTSD moderates outcomes when compared against those who do not meet diagnosis in standard treatments. Clinical reality suggests

that many people do not meet full diagnostic criteria but still suffer from a number of debilitating symptoms that relate to that condition.

- Appropriateness and effectiveness of trauma focused treatments for CPTSD following childhood trauma. In this meta-analysis, childhood trauma was found to negatively moderate the effect of trauma focused interventions.
- Comparing pharmacotherapy vs. psychotherapy for CPTSD. In this meta-analysis we did not address the effectiveness of pharmacotherapies alone or in combination with psychotherapy.
- Considering the nature of the three DSO factors, it is worth exploring the effectiveness of attachment based interventions and relational therapies as limited evidence is currently present for these interventions.
- Exploring the effectiveness of individual vs. group interventions for CPTSD. We found no evidence addressing this question for people with CPTSD.
- Exploring the effectiveness of interventions that tackle all CPTSD symptom clusters in a single study using as a primary outcome of CPTSD based on a dedicated measure. The present review extracted proxy data from existing trials that measure the CPTSD constructs.

In conclusion, this meta-analysis is the first step in identifying effective treatments for CPTSD. Findings regarding the usefulness of trauma-focused interventions look promising but less so for CPTSD symptoms following childhood trauma. Further research is needed to explore and develop existing and new treatments for CPTSD.

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Supplementary Appendix to:

Karatzias, T., Murphy, P., Cloitre, M., Bisson, J., Roberts, N., Shevlin, M., Hyland, P., Maercker, A., Ben-Ezra, M, Coventry, P., Mason-Roberts, S., Bradley, A., Hutton, P. (2019). Psychological interventions for ICD-11 Complex PTSD symptoms: Systematic review and meta-analysis. *Psychological Medicine*.

Content of Supplementary Appendix

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A. Protocol

Title: Psychological interventions for Complex PTSD: systematic review and meta-analysis.

Reviewers: Thanos Karatzias, Mick Fleming, Susan Roberts, Aoife Bradley, Claire Fyvie, Jonathan Bisson, Neil Roberts, Philip Hyland, Marylene Cloitre, Tobias Hecker, Andreas Maercker, Paul Hutton

Review question(s)

What psychological interventions are effective for complex post traumatic stress disorder, and how effective are they? What is the safety and acceptability of psychological interventions for complex post traumatic stress disorder?

Searches

Searches of MEDLINE, PsycINFO, EMBASE and PILOTS will be conducted using the search terms listed below. Unpublished trials will be identified through contacting investigators and through searching clinical trial registries such as Clinicaltrials.gov. Language will be restricted to English. There will be no time period restrictions. #1. PTSD or posttrauma* or psychological stress* or combat or post-trauma* or gross stress reaction or stress disorder* or trauma* or psychological trauma. #2. randomised or randomized or randomised controlled trial or RCT or randomized controlled trial. #3. therapy or psychological therapy or psychological intervention or intervention or treatment).mp. [mp=ti, ab, ot, nm, hw, kf, px, rx, ui, an, eu, pm, sy, tn, dm, mf, dv, kw, fs].

Types of study to be included

Randomised controlled trials with or without rater masking will be included. Uncontrolled, non-randomised and crossover trials, qualitative studies and case studies will be excluded.

Condition or domain being studied

Complex post traumatic stress disorder (CPTSD) as described in ICD-11 proposals. According to ICD-11 individuals meet diagnostic criteria for complex PTSD if they meet existing criteria for post traumatic stress disorder (PTSD) (re-experiencing of the trauma, avoidance of reminders of the trauma, enhanced sense of threat indicated by hypervigilance and hyperarousal) and have clinically significant difficulties in affect dysregulation, a pervasive negative self-concept and experience interpersonal disturbances (Cloitre et al. 2013). Individuals meet diagnostic criteria for complex PTSD if they meet existing criteria for post traumatic stress disorder (PTSD) (re-experiencing of the trauma, avoidance of reminders of the trauma, enhanced sense of threat indicated by hypervigilance and hyperarousal) and have clinically significant difficulties in affect dysregulation, a negative self-concept and experience interpersonal disturbances (Cloitre et al. 2013).

Participants/population

We are interested in the effect of psychological interventions on adults who meet criteria for CPTSD. However, since CPTSD is a new diagnostic category, we anticipate that few studies have explicitly included this group. For this reason we will only include trials of interventions where participants meet ICD and DSM – III and IV criteria for PTSD and present with clinically significant symptoms of re-experience, avoidance hyperarousal and score within the clinically significant range on at least one of the additional CPTSD criteria, namely emotion dysregulation, negative self-concept and interpersonal disturbance. We will only include trials where the mean or median age of participants is at least 16, and we will only include trials

where participants with developmental or intellectual disability, neurodegenerative disorders and acquired or traumatic brain injury are excluded. We will include studies where participants have comorbid substance misuse difficulties, but we will exclude trials where participants have a primary diagnosis of substance misuse disorder.

Intervention(s), exposure(s)

We will include trials where participants in at least one arm receive 'bona fide' psychological interventions (defined according to criteria developed by Benish et al (2008),* delivered in group or individual format, including but not limited to CBT, interpersonal therapy, psychodynamic therapy, EMDR or psychoeducation. *The bona fide definition (Benish, Imel and Wampold, 2008) requires that treatments had to be delivered by a trained therapist who adapted the treatment to patients on the basis of a therapeutic relationship (i.e., no delivery of a non-modifiable standard protocol, e.g., progressive muscle relaxation); treatments also needed to be conducted personally and face-to-face (i.e., no online treatments or treatments conducted with, e.g., audio material). Moreover, at least two of the following four criteria had to be fulfilled with regards to their descriptions in the studies: (a) a citation to an established school or approach to psychotherapy; (b) a description of the therapy that contained a reference to a psychological process (e.g., operant conditioning); (c) a reference to a treatment manual that was used to guide the delivery of the treatment; (d) the identification of active ingredients of the treatment and citations for these ingredients.

*Benish SG, Imel ZE, Wampold BE. The relative efficacy of bona fide psychotherapies for treating posttraumatic stress disorder: A meta-analysis of direct comparisons. *Clin Psychol Rev.* 2008;28:746–58. doi:10.1016/j.cpr.2007.10.005.

Comparator(s)/control

Psychological interventions will be compared against one another and also against no additional treatment (i.e., 'treatment as usual' and 'waiting list control') and non-active interventions, such as befriending.

Context

All settings to be included.

Primary outcome(s)

The primary outcome will be twofold: 1. The between group difference, at end of treatment and 12-months post-randomisation, in severity of (a) PTSD symptoms as per ICD-11 and DSM III and IV and (b) emotion dysregulation, negative self-concept and/or interpersonal disturbance. To compute this composite outcome, we will calculate the average standardised mean difference across these outcomes taking into account the correlation between these variables where / if possible. 2. The between group difference at end of treatment and at 12-months post randomisation, in the relative and absolute risk of not achieving a clinically significant response in PTSD symptoms, defined using Jacobson criteria.

Timing and effect measures

End of treatment and 12-months post randomisation (or nearest time-point within a 3-month range).

Secondary outcome(s)

1. Safety, as measured by the between group difference, at end of treatment and at 12-months postrandomisation, in the relative risk of serious adverse events (death, suicide, attempted suicide, significant deterioration in symptoms, admission to hospital). 2. The acceptability of

the interventions, as measured by the between group difference in the relative risk of dropping out early from either the treatment or the trial (where the comparator is treatment as usual).

Timing and effect measures

End of treatment and 12-months post randomisation (or nearest time-point within a 3-month range) for safety, and end of treatment for acceptability.

Data extraction (selection and coding)

We will extract group means and associated standard deviations (and N contributing to those means) for continuous outcomes, and number of events (denominator = number randomised to arm) for dichotomous outcomes, using a spreadsheet. We will use the total number randomised if reported. For all outcomes except acceptability, we will assume those not including in the reported analyses are either missing completely at random (for continuous outcomes) or had no change from randomisation (dichotomous outcomes). Two researchers will double-extract data for all outcomes, and a third rater will be consulted in relation to any discrepancies and / or disagreements. If means and standard deviations are not reported, then we will estimate the between group difference from other statistical parameters, such as confidence intervals, standard errors, p-values, t-values or F-values, following procedures in the Cochrane Handbook, and using the Campbell Effect Size Calculator, if possible. If we need to combine data from 2 groups before entry into the meta-analysis, we will do so following the formulae specified in the Cochrane Handbook.

Risk of bias (quality) assessment

At the study level the risk of bias will be assessed using the Cochrane collection Risk of Bias Tool (Higgins et al 2011). This involves categorising studies as having a low, high or unclear risk of bias in the areas of selection and allocation of participants, intervention concealment, attrition and reporting. The results of this assessment will be used to inform interpretation of reported effect sizes and overall conclusions. The quality of overall outcomes will be assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (Guyatt et al 2011).

Strategy for data synthesis

For continuous outcomes, we will perform random-effects meta-analyses to compute an overall standardised mean difference and associated 95% confidence intervals, with Hedges's g adjustment. For dichotomous outcomes, we will also perform random-effects meta-analyses to compute an overall relative risk, an overall difference in absolute risk, and the number needed to treat for one to experience benefit / harm (computed as the inverse of the absolute risk).

Analysis of subgroups or subsets

We will examine whether the results are moderated by the degree to which the sample population meet CPTSD criteria (whether the sample score within the clinical range on 1, 2 or 3 CPTD criteria at baseline). We will also examine the potential moderating role of quality parameters including rater blinding, attrition, random sequence generation description. We will also examine whether the effectiveness of psychological treatment for CPTSD is moderated by the following: - individual vs. group format - adult onset trauma vs.. childhood onset trauma vs. both - phased / staged interventions vs. non-phased / non-staged interventions.

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Stage of review at time of this submission

<i>Stage</i>	<i>Started</i>	<i>Completed</i>
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

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B. Changes from Protocol

A subsequent change was our inclusion of some psychological interventions (e.g., mindfulness, yoga) which were not strictly ‘bona fide’ psychological interventions (Benish, Imel, & Wampold, 2008). We made this decision in the interests of completeness.

While we had planned to take into account the correlation between variables when computing the composite outcome, this was not possible due the range of measures used to assess the variables; instead we had to assume the correlation was zero.

Additional changes included abandoning our pre-specified moderator analysis of phased vs non-phased interventions due to insufficient data.

We were also unable to determine rates of clinically significant response according to our pre-specified method (Jacobsen’s criteria). We instead converted the SMDs to NNTs using the Furukawa approach, under 3 assumptions of the control event rate (10%, 50% and 22%, which is half the control event rate observed for PTSD). Secondary outcomes (safety, drop-out) and follow-up data will be reported separately.

C. Excluded Studies

The following table (**Table C.1**) details studies or reports excluded after inspection of the full-text report, or via correspondence with authors. Studies or reports excluded on basis of title or abstract alone are not detailed as these are too numerous and the vast majority were of different conditions or were otherwise unrelated to the review question.

Study reference	Reason for exclusion
Acarturk 2016	No useable CPTSD index
Acierno 2017	No relevant comparator
Akbarian 2015	No useable CPTSD index
Alghamdi 2015	Sample not suitable
Arntz 2007	Baseline CPTSD index/indices not clinically significant
Asukai 2010	No useable CPTSD index
Badura-Brack 2018	No relevant psychological intervention
Bass 2016	Sample not suitable
Beidel 2017	Not RCT
Belleau 2017	No useable CPTSD index
Betancourt 2014	Sample not suitable
Bichescu 2007	No useable CPTSD index
Blanchard 2003	Baseline CPTSD index/indices not clinically significant
Boden 2012	No useable CPTSD index
Bohus 2013	No useable CPTSD index
Bormann 2013	No useable CPTSD index
Bormann 2014	No useable CPTSD index
Bradley 2003	Sample not suitable
Bremner 2017	Baseline CPTSD index/indices not clinically significant
Brom 1989	Baseline CPTSD index/indices not clinically significant
Brunet 2013	Sample not suitable
Bryan 2016	No useable CPTSD index
Bryant 2003	No useable CPTSD index
Bryant 2008	No useable CPTSD index
Buhmann 2016	Baseline CPTSD index/indices not clinically significant
Carlson 1998	No useable CPTSD index
Castillo 2016	No useable CPTSD index
Catani 2009	Sample not suitable
Chard 2005	No useable CPTSD index
Classen 2001	Sample not suitable
Cloitre 2010	Baseline CPTSD index/indices not clinically significant
Cloitre 2012	Study has overlapping sample with another study
Coffey 2016	No useable CPTSD index
Cook 2010	No useable CPTSD index
Cooper 1989	No useable CPTSD index
Cooper 2017	No relevant comparator
Cottraux 2008	No useable CPTSD index
de Bont 2016	No useable CPTSD index
Deville 1998	No useable CPTSD index

Study reference	Reason for exclusion
Devilly 1999	No useable CPTSD index
Echeburua 1997	No useable CPTSD index
Edmond 1999	Sample not suitable
Edmond 2004	Study has overlapping sample with another study
Ertl 2011	Baseline CPTSD index/indices not clinically significant
Fecteau 1999	No useable CPTSD index
Feeny 2002	Study has overlapping sample with another study
Feske 2008	Unable to obtain relevant norms
Foa 1991	No useable CPTSD index
Foa 2004	Study has overlapping sample with another study
Foa 2013	No useable CPTSD index
Foa 2017	No useable CPTSD index
Fredman 2016	No relevant psychological intervention
Gamito 2010	No useable CPTSD index
Gersons 2000	No useable CPTSD index
Gilboa-Schechtman 2010	Sample not suitable
Glynn 1999	No useable CPTSD index
Goldstein 2018	No relevant psychological intervention
Gutner 2016	Study has overlapping sample with another study
Hien 2004	No useable CPTSD index
Hien 2009	No useable CPTSD index
Hien 2017	Baseline CPTSD index/indices not clinically significant
Hien 2017 (b)	Study has overlapping sample with another study
Hinton 2005	No useable CPTSD index
Holliday 2014	Study has overlapping sample with another study
Holliday 2015	Study has overlapping sample with another study
Ironson 2002	No useable CPTSD index
Jacob 2014	No useable CPTSD index
Jensen 1994	No useable CPTSD index
Jindani 2015	Baseline CPTSD index/indices not clinically significant
Johnson 2011	No useable CPTSD index
Johnson 2016	Not RCT
Kearney 2013	Baseline CPTSD index/indices not clinically significant
Kearney 2016	Baseline CPTSD index/indices not clinically significant
Kip 2014	Study has overlapping sample with another study
Konig 2016	Study has overlapping sample with another study
Kruse 2009	Not RCT
Lange 2003	No relevant psychological intervention
Lee 2002	No useable CPTSD index
Levi 2016	Not RCT
Liedl 2011	Retracted
Litz 2007	No relevant psychological intervention
Lovell 2011	Study has overlapping sample with another study
Macdonald 2016	No relevant psychological intervention

Study reference	Reason for exclusion
Marcus 1997	No useable CPTSD index
Markowitz 2015	Baseline CPTSD index/indices not clinically significant
Markowitz 2017	Study has overlapping sample with another study
Maxwell 2016	No useable CPTSD index
McGovern 2015	No useable CPTSD index
McLay 2017	No useable CPTSD index
McLean 2014	No useable CPTSD index
Meier 2015	No useable CPTSD index
Mills 2012	No useable CPTSD index
Monson 2012	No relevant psychological intervention
Moradi 2014	No useable CPTSD index
Morath 2014	No useable CPTSD index
Morland 2014	No relevant psychological intervention
Moser 2010	Study has overlapping sample with another study
Nacasch 2011	No useable CPTSD index
Nacasch 2015	No relevant comparator
Neuner 2004	No useable CPTSD index
Neuner 2008	No useable CPTSD index
Neuner 2010	No useable CPTSD index
Nijdam 2018	No useable CPTSD index
Nosen 2014	No useable CPTSD index
Oktedalen 2015	Baseline CPTSD index/indices not clinically significant
Pabst 2014	No useable CPTSD index
Paivio 2010	No relevant comparator
Paunovic 2001	No useable CPTSD index
Peniston 1991	No useable CPTSD index
Polusny 2015	Baseline CPTSD index/indices not clinically significant
Possemato 2016	Sample not suitable
Pruiksma 2016	Study has overlapping sample with another study
Reger 2016	No useable CPTSD index
Resick 2003	Study has overlapping sample with another study
Resick 2008	No relevant comparator
Resick 2015	No useable CPTSD index
Resick 2017	No relevant comparator
Roberts 2016	Not RCT
Rothbaum 1997	No useable CPTSD index
Rothbaum 2005	No useable CPTSD index
Rothbaum 2006	No useable CPTSD index
Rothbaum 2014	No relevant psychological intervention
Ruglass 2017	No useable CPTSD index
Sack 2016	No relevant comparator
Sannibale 2013	No useable CPTSD index
Sautter 2015	No relevant psychological intervention
Schaal 2009	Baseline CPTSD index/indices not clinically significant
Schneier 2012	No relevant psychological intervention

Study reference	Reason for exclusion
Schnurr 2003	No useable CPTSD index
Schnurr 2007	No useable CPTSD index
Schnyder 2011	No useable CPTSD index
Scott 2017	Study has overlapping sample with another study
Shea 2013	Sample not suitable
Shnaider 2017	No relevant psychological intervention
Sikkema 2007	No useable CPTSD index
Sin 2017	Not RCT
Slade 2017	Study has overlapping sample with another study
Sloan 2012	No useable CPTSD index
Spence 2011	No relevant psychological intervention
Steinert 2017	No useable CPTSD index
Study Ref	Reason for Exclusion
Tarrier 1999 (a)	No useable CPTSD index
Tarrier 1999 (b)	No useable CPTSD index
Taylor 2003	Baseline CPTSD index/indices not clinically significant
van den Berg 2016	Study has overlapping sample with another study
van der Kolk 2007	No relevant comparator
van der Kolk 2016	No relevant psychological intervention
van Emmerik 2008	No useable CPTSD index
Vaughan 1994	No useable CPTSD index
Wahbeh 2016	Baseline CPTSD index/indices not clinically significant
Wells 2015	No useable CPTSD index
Wilson 1995	No useable CPTSD index
Wilson 1997	Study has overlapping sample with another study
Wolf 2015	Not RCT
Zang 2013	No useable CPTSD index
Zang 2014	No useable CPTSD index
Zang 2017	No useable CPTSD index
Zlotnick 1997	No useable CPTSD index
Zlotnick 2009	No useable CPTSD index
Zoellner 1999	Study has overlapping sample with another study
Zoellner 2017	No relevant psychological intervention

D. Table D.1. Summary of Characteristics of the 51 Included Studies

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Ahmadi 2015	EMDR	16	Iran	Military servicemen	29.9 (7.8)	0	Unclear	5 (31.3)	Single	Non- sexual	Adulthood	Community
	REM	16					Unclear	6 (37.5)				
	Control	16						4 (25.0)				
Azad marzabadi 2014	Mindfulness	14	Iran	War victims with PTSD	Not reported	0	90mins, 8	2 (14.3)	Single	Non- sexual	Adulthood	Community
	Control	14						2 (14.3)				
Basoglu 2007	SSBT	16	Turkey	Earthquake survivors	34.0 (11)	87	60 mins, 1	1 (6.3)	Single	Non- sexual	Adulthood	Community
	RA	15						0(0)				
Beidel 2011	TMT	18	USA	Combat Veterans	58.93(N R)	0	90 mins, 29	4 (22.2)	Single	Non- sexual	Adulthood	Community
	EXP	17			59.76(N R)		90 mins, 29	1 (5.9)				
Beidel 2019	TMT	49	USA	Military veterans	37.67 (8.51)	7	90 mins, 29	14 (28)	Single	Non- sexual	Adulthood	Community
	EXP	43			33.26 (11.31)		90 mins, 29	22 (50)				

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Bryant 2013	Support/CBT	34	Australia	Adult civilian patients	41.15 (12.92)	54	90 mins, 12	13 (38.2)	Single	Non- sexual	Adulthood	Community
	Skills/CBT	36			37.86 (12.70)		90 mins, 12	3 (8.3)				
Butollo 2016	DET	74	Germany	Trauma survivors	37.99 (12.1)	66	90 mins,max.24	9 (12.2)	Multiple	Sexual and non-sexual	Adulthood	Community
	CPT	67			33.67 (10.3)		90 mins, max.24	11(14.9)				
Cloitre 2002	STAIR+MPE	31	USA	CSA survivors	34 (7.22)	100	60 -90 mins, 16	9 (29)	Single & Multiple	Sexual & Non-sexual	Childhood	Community
	MA WL	27					15 mins,12	3 (11)				
Difede 2007	CBT	15	USA	Disaster workers	45.77 (7.72)	NR	75mins ,12	8 (53.3)	Single	Non- sexual	Adulthood	Community
	TAU	16						2(12.5)				
Dorrepaal 2012	EXP	38	Netherlands	CSA survivors	40.3 (10.7)	NR	120mins, 20	7(18.4)	Multiple	Sexual and non-sexual	Childhood & Adulthood	Community
	TAU	33			37.1 (10.3)			5 (15.1)				
Duffy 2007	CT	29	Ireland	Trauma survivors	NR	NR	NR ,12	9 (31.0)	Multiple	Non- sexual	Adulthood	Community
	WL	29						3 (10.3)				
Dunn 2007	SMT	51	USA	Veterans	54.7 (6.9)	0	90 mins, 14	17(33.3)	Single	Non-sexual	Adulthood	Community

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
	PGT	50			55.0 (7.6)		90 mins, 14	6(12.0)				
Dunne 2012	TF-CBT	13	Australia	MVA survivors	32.54 (7.09)	50	60mins,10	1 (7.7)	Single	Non-sexual	Adulthood	Community
	WL	13						2(15.4)				
Ehlers 2003	CT	28	UK	MVA survivors	NR	NR	60-90mins, 12	0 (0)	Single	Non- sexual	Adulthood	Community
	SHB	28					40mins,1	3 (10.7)				
	RA	29					20mins, 1	2 (6.9)				
Ehlers 2005	CT	14	UK	PTSD patients	35.4 (10.9)	53.6	60-90mins, 4-20	0 (0)	Single	Non-sexual	Adulthood	Community
	WL	14			37.8 (11.2)			0 (0)				
Ehlers 2014	Intensive CT	30	UK	Chronic PTSD	39.7 (12.4)	58.7	18hrs over 5-7 days	1(3.3)	Multiple	Sexual and /or non-sexual	Childhood & Adulthood	Community
	Weekly CT	31			41.5 (11.7)		100mins,12	1(3.2)				
	Weekly ST	30			37.8 (9.9)		100mins ,12	3 (10)				
	WL	30			36.8 (10.5)			0 (0)				
Foa 1999	PE	25	USA	Chronic PTSD	34.9 (10.6)	100	90-120mins , 9	2 (8)	Single	Sexual or non-sexual	Childhood or Adulthood	Community
	SIT	26					90-120mins , 9	7(27)				
	PE-SIT	30					90-120mins , 9	8 (27)				
	WL	15						0 (0)				

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Foa 2005	PE	79	USA	Assault survivors	31.3 (9.8)	100	90-120mins, 9-12	27 (34.1)	Single	Sexual or non-sexual	Childhood or Adulthood	Community or University - based
	PE-CR	74					90-120mins, 9-12	30(40.5)				
	WL	26						1 (3.8)				
Forbes 2012	CPT	30	Australia	Military veteran	53.13 (13.97)	3.4	60-90 mins, 12	9(30.0)	Single	Non-sexual	Adulthood	Community
	TAU	29			53.62 (13.33)			9 (31.1)				
Ford 2011	TARGET	48	USA	Mothers with PTSD	30.7(6.9)	100	50mins, 12	12(25)	Unclear	Unclear	Adulthood	Community
	PCT	53					NR, 12	14 (26)				
	WL	45										
Galovski 2012	MCPT	53	USA	Trauma survivors	39.80 (11.74)	69	NR, 12	14 (26.4)	Single	Sexual or non-sexual	Childhood or Adulthood	Community
	SMDT	47					NR12,	7 (14.9)				
Ghafoori 2017	PE	24	USA	Trauma survivors	35.2 (12.0)	83.1	60-90 mins, 12	34 (72)	Multiple	Sexual and /or non-sexual	Adulthood	Community
	PCT	47					60-90 mins,12	16 (66)				
Harned 2014	DBT	9	USA	Women with BPS & PTSD	32.6 (12.0)	100	1 year of treatment	4(44.4)	Single	Sexual or non-sexual	Childhood or Adulthood	Community
	DBT -PE	17					1 year of treatment	7(41.2)				

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Hinton 2009	IT-CBT	12	USA	Refugees	49.92 (9.23)	60	NR, 12	0 (0)	Single	Non sexual	Adulthood	Community
	DT- CBT	12			49.08 (7.56)		NR,12	0 (0)				
Hinton 2011	CA-CBT	12	USA	Female Latino patients	47.6 (8.2)	100	60 mins, 14	0	Unclear	Unclear	Unclear	Community
	AMR	12			51.4 (5.9)		60 mins, 14	0				
Hogberg 2007	EMDR	13	Sweden	Public transportation workers	43 (8)	20.8	90mins, 5	0(0)	Single	Non sexual	Adulthood	Community
	WL	11			43 (11)			2(18.2)				
Hollified 2007	CBT	28	USA	Adults with PTSD	40.9 (13.4)		120mins,12	7 (25)	Multiple	Unclear	Childhood or Adulthood	Community
	WL	27			43.4 (13.5)			6 (22.2)				
Jung 2013	CRIM	17	Germany	CSA survivors	37.18 (10.85)	100	50 & 90mins, 2	0 (0)	Multiple	Sexual	Childhood	Community
	WL	17						0 (0)				
Keane 1989	Implosive (flooding)	11	USA	Veterans	34.7 (4.3)	0	90 minutes,14-16	1 (9.1)	Single	Non-sexual	Adulthood	Community
	WL	13			34.5 (2.1)			1(7.7)				

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Kip 2013	ART	US A	29	Veterans	41.0 (12.4)	20	60-75mins, 2-5	3 (10.3)	Single	Sexual or non-sexual	Adulthood	Community
	AC		28				60mins, 2	4 (14.3)				
Krakow 2001	CIT	88	USA	Sexual Assault survivors	40 (11.2) C 37 (12.7) NC	100	60-180mins , 3	22(25)	Multiple	Sexual	Childhood & Adulthood	Community
	WL	80			36 (9.3) C 31 (10.5) NC			0 (25) ²				
Krupnick 2008	IPT	32	USA	Trauma survivors	32 (10.2)	100	120 mins, 16	NR*	Multiple	Sexual & or non-sexual	Childhood & Adulthood	Community
	WL	16						NR*				
Kubany 2003	Immediate CTT-BW	19	USA	Battered women	36.4 (9.1)	100	90 mins,8-11	1 (5.3)	Multiple	Non-sexual	Adulthood	Community
	Delayed CTT-BW	18					90 mins, 8-11	4 (22.2)				
Kubany 2004	Immediate CTT-BW	63	USA	Battered women	42.2 (10.1)	100	90 mins,8-11	18 (28.6)	Multiple	Non-sexual	Adulthood	Community
	Delayed CTT-BW	62					90 mins, 8-11	22 (35.5)				
Lindauer 2005	BEP	12	Netherlands	Trauma survivors	37.6 (10.2)	54	45-60 mins, 16	3(25)	Multiple	Non-sexual	Adulthood	Community

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
	WL	12			40.3 (8.9)							
Marks 1998	Exposure	23	UK	Outpatients with PTSD	39 (11)	36	90 mins,10	3(13)	Single	Sexual or non-sexual	Adulthood	Community
	Cognitive	19			39 (9)		90 mins,10	1(5.3)				
	E+C	24			38 (9)		105 mins,10	5(20.8)				
	Relaxation	21			36 (10)		90 mins,10	1(4.8)				
McDonagh 2005	CBT	29	USA	CSA survivors	39.8 (9.9)	100	90-120mins, 14	12(41)	Multiple	Sexual	Childhood	Community
	PCT	22			39.6 (9.6)		90-120mins, 14	2(9)				
	WL	23			42.0 (9.8)			3(13)				
Monson 2006	CPT	30	USA	Veterans	54.0 (6.3)	10	2p/w, 12	6(20)	Single	Sexual or Non-sexual	Adulthood	Community
	WL	30						4(13)				
Mueser 2008	CBT	54	USA	Severe Mental Illness patients	44.21 (10.64)	79	NR,12-16	19	Single	Sexual or non-sexual	Childhood & Adulthood	Community
	TAU	54										
Mueser 2015	CBT	104	USA	Severe Mental Illness patients	42.96 (10.46)	72.3	NR,12- 16	37 (35.6)	Single	Sexual or non-sexual	Childhood & Adulthood	Community
	BT	97			44.52 (11.60)		NR, 3	14 (14.3)				

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Nijdam 2012	BEP	70	Netherlands	Trauma survivors	37.3 (10.6)	56.4	45-60 mins,15	25 (36)	Single	Sexual or non-sexual	Adulthood	Community
	EMDR	70			38.3 (12.2)		90 mins, NR	20 (29)				
Pacella 2012	PE	40	USA	Adults with HIV	46.37 (6.30)	36.9	90-120 mins, 10	17 (42.5)	Multiple	Sexual or non-sexual	Childhood & Adulthood	Community
	WL	24						0 (0)				
Power 2002	EMDR	39	UK	Adults with PTSD	38.6 (11.8)	41.7	90 mins,10	12 (31)	Single	Sexual or non-sexual	Adulthood	Community
	E+CR	37			43.2 (11.0)		90 mins ,10	16 (43)				
	WL	29			36.5 (11.6)			5 (17)				
Resick 2002	CPT	41	USA	Female Rape Victims	32 (9.9)	100	2 p/w 13hrs,12	11(26.8)	Multiple	Sexual & /or Non-sexual	Adulthood	Community
	PE	40					2 p/w 13hrs, 9	(27.3)				
	MA	40						(14.9)				
Scheck 1998	EMDR	30	USA	Traumatised Young Women	20.93(no SD reported)	100	90mins, 2	0 (0)	Single	Sexual	Childhood & Adulthood	Community
	AL	30					90mins, 2	1 (3.3)				
Steel 2017	CBT	30	UK	Adults with schizophrenia	42.3 (10.2)	37.7	NR ,12-16	4(13.0)	Single or Multiple	Sexual or non-sexual	Childhood & Adulthood	Community
	TAU	31						5 (16.1)				

Study Ref	Groups included	N	Country	Participants	Age, mean (SD)	% female	Duration & N sessions available	Drops outs N (%)	Trauma exposure	Type of Trauma	Trauma onset	Treatment setting
Suris 2013	CPT	72	USA	Veterans	46.1 (9.8)	84.9	Unclear , 12	25(35)	Single	Sexual	Adulthood	Community
	PCT	57					Unclear, 10-12	10(18)				
Talbot 2014	CBT-I	29	USA	Adults with PTSD	37.1 (10.4)	68.9	Unclear	2 (6.9)	Unclear	Unclear	Unclear	Community
	WL	16			37.3(11.0)			1 (6.3)				
ter Heide 2011	EMDR	10	Netherlands	Asylum seekers and refugees	40.00 (9.31)	40	90 mins , 11	5 (50)	Multiple	Non-sexual	Adulthood	Community
	Stabilisation	10			43.00 (7.93)		60 mins, 11	5(50)				
ter Heide 2016	EMDR	37	Netherlands	Refugees	43.1(10.7)	27.8	60-90mins, 9	6 (16.7)	Multiple	Non-sexual	Adulthood	Community
	Stabilisation	37			39.8(11.9)		60 mins , 12	8 (22.2)				
van den Berg 2015	PE	53	Netherlands	Severe Mental Illness patients	41.2 (10.5)	54.2	90 mins, 8	13(24.5)	Single or Multiple	Sexual &/or Non-sexual	Childhood & Adulthood	Community
	EMDR	55					90 mins, 8	11(20.0)				
	WL	47										

Abbreviations: AC, Attention Control; AL, Active Listening Control; AMR, Applied Muscle Relaxation; ART, Accelerated Resolution Therapy; BEP, Brief Eclectic Psychotherapy; BPS, Borderline Personality disorder; BT, Brief Treatment; CA-CBT, Culturally Adapted Cognitive Behaviour Therapy; CBT, Cognitive Behaviour Therapy; CBT-I, Cognitive Behavioral Therapy for Insomnia; CIT, Cognitive Imagery Treatment; CPT, Cognitive Processing Therapy; CRIM, Cognitive Restructuring and Imagery Modification; CSA, Childhood Sexual Abuse; CT, Cognitive Therapy; CTT-BW, Cognitive Trauma Therapy for Battered Women; DBT, Dialectical Behavior Therapy; DBT PE, Dialectical Behavior Therapy Prolonged Exposure; DET, Dialogical Exposure Therapy; DT –CBT, Delayed Treatment Cognitive Behaviour Therapy; E+C, Exposure and Cognitive; E+CR, Exposure plus Cognitive Restructuring; EMDR, Eye Movement Desensitization and Reprocessing Therapy; EXP, Experimental Treatment; EXP, Exposure

Therapy Only; Intensive CT, Intensive Cognitive Therapy; IPT, Interpersonal Psychotherapy; MA, Minimal Attention; MA WL, Minimal Attention Wait List; MCPT, Modified Cognitive Processing Therapy Intervention; MVA, Motor Vehicle Accident; PCT, Present Centred Therapy; PE, Prolonged exposure; PE-CR, Prolonged Exposure plus Cognitive Restructuring; PE-SIT, Prolonged Exposure + Stress Inoculation Training; PGT, Psychoeducational Group Therapy; PTSD, Post-traumatic Stress Disorder; RA, Repeated Assessments; REM, Rapid Eye Movement; SHB, Self-help booklet; SIT, Stress inoculation training; SMDT, Symptom –Monitoring Delayed Treatment; SMT, Self-Management Therapy; SSBT, Single Session of Behavioural Treatment; STAIRS + MPE, Skills Training in Affective and Interpersonal Regulation with modified Prolonged Exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; TFCBT, Trauma-Focused Cognitive-Behavioural Therapy; TMT, Trauma Management Therapy; Weekly CT, Weekly Cognitive Therapy; Weekly ST, Weekly Supportive Therapy ;WL, Waitlist.

E. Table E.1. Participants' baseline scores on the CPTSD symptom clusters and corresponding norms

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
Ahmadi 2015	EMDR	Emotional control subscale of the Mississippi Scale for PTSD, -5.3 (4.4) [these are the mean (SD) change scores]	-	-	-	Interpersonal relation subscale of the Mississippi Scale for PTSD, -4.7 (5.2)	-	Only change scores were reported (no baseline scores).	Include – although exclude in sensitivity analysis.
	REM	-6.4 (3.9) [these are the mean (SD) change scores]	-	-	-1.3 (2.7)				
	Control	0.7 (2.5) [these are the mean (SD) change scores]	-	-	-0.08 (2.3)				
Azad marzabadi 2014	Mindfulness	-	-	-	-	Social life subscale of the WHOQOL-26, 5.5 (1.65)	-	Baseline scores indicate that the participants were on average at least dissatisfied in their social life.	Include
	Control	-	-	-	-	5.21 (0.97)			

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
Beidel 2019	TMT	-	-	-	-	Duration of Daily Social Interaction (outside of family interactions at home) (mins per day), 49.7 (54.3)	-	On average, a non-clinical group aged 16–36 years engage in 63.49 h of structured activity per week, and activity levels below 30 h are indicative of poor social functioning (Hodgekins et al., 2015).	Include
	EXP	-	-	-	52.7 (61.9)	-			
Bryant 2013	Support/CBT	-	-	PTCI-self, 4.08 (1.29)	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	-	-	-	Include
	Skills/CBT	-	-	4.41 (1.18)	-	-	-		
Butollo 2016	DET	-	-	PTCI-self, 3.71 (1.2) [these are the mean (SD) across both groups]	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	IIP-C, 1.34 (0.59)	1.28 (0.52) (non-clinical) (Brahler et al., 1999)	-	Include NSC data but not DR data.
	CPT	-	-			1.38 (0.57)			
Cloitre 2002	STAIR+MPE	NMR, 85 (15.6)	-	-	-	IIP, 1.88 (0.57)	-	-	

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	MA WL	84 (17.9)	101.6 (15.43) (non-clinical) (Cantanzaro & Mearns, 1990)	-		1.70 (0.46) (the weighted mean across these groups is 1.79)	1.28 (0.52) (non-clinical) (Brahler et al., 1999)		Include AD data but not DR data.
Difede 2007	CBT	-	-	-	-	SAS-SR, 2 (0.4)	1.59 (0.33) (non-clinical) (Weissman et al., 1978)	-	Include
	TAU	-	-	-	-	2.28 (0.44)			
Dorrepaal 2012	EXP	-	-	-	-	-	-	As all participants in this study had to meet diagnostic criteria for complex PTSD as assessed by the SIDES, this study is relevant.	Include
	TAU	-	-	-	-	-			
Duffy 2007	CT	-	-	-	-		-		Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	WL	-		-		SDS-social subscale, 7.7 (2.4) [these are the mean (SD) across both groups]		A score of 7 or above on this subscale indicates a marked impairment. Moreover, it has been suggested that clinicians should pay special attention to patients who score 5 or greater on this subscale (Rush et al., 2000).	
Dunn 2007	SMT	SCQD, 86.14 (12.95)	101.2 (15.46) (non-clinical)	-	-	-	-	-	Include
	PGT	79.74 (17.77)	(Mezo & Heiby, 2004)	-		-			
Dunne 2012	TF-CBT	-	-	-	-	SF-36 social functioning subscale, 43.46 (18.12)	85.66 (19.83) (among male norms aged 25-44); 88.54	-	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	WL	-		-		45.42 (13.97)	(18.09) (among male norms aged 35-55); numerous other norms are available as well (Ware et al., 1993).		
Ehlers 2003	CT	-	-	-	-	SDS, 5.9 (2.4)	-	A score of 4 to 6 on this scale indicates a moderate impairment. Moreover, it has been suggested that clinicians should pay special attention to patients who score 5 or greater on this subscale (Rush et al., 2000).	Include
	SHB	-		-	6.3 (2)				
	RA	-		-	6.1 (1.9)				
Ehlers 2005	CT	-	-	-	-	SDS, 7.6 (1.9)	-		Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	WL	-		-		6.7 (1.9)		A score of 7 or above on this scale indicates a marked impairment. Moreover, it has been suggested that clinicians should pay special attention to patients who score 5 or greater on this subscale (Rush et al., 2000).	
Ehlers 2014	Intensive CT	-	-	-	-	SDS, 20.48 (5.55)	-	Each of the baseline mean SDS scores need to be divided by 3 so they are comparable to those of Ehlers, 2003 and 2005 above (e.g., $21.39/3 = 7.13$).	Include
	Weekly CT	-	-	-	21.39 (5.11)				
	Weekly ST	-	-	-	19.65 (6.97)				
	WL	-	-	-	17.28 (7.74)				
Foa 1999	PE	-	-	-	-	SAS (interview version), 3.73 (0.83)	-	Normative data for the interview	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	SIT	-		-		3.79 (1.23)		version of the SAS were not available. This version of the SAS is a 7-point scale. Assuming a 0-6 scoring method, scores of 3 or greater indicate that participants are closer to being impaired than intact.	
	PE-SIT	-		-		4 (1.11)			
	WL	-		-		3.93 (1.16)			
Foa 2005	PE	-	-	-	-	SAS social subscale (interview version), 4 (0.9)	-	Normative data for the interview version of the SAS social	Include
	PE-CR	-		-		3.9 (1)			

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	WL	-		-		3.9 (1.2)		subscale were not available. This version of the SAS social subscale is a 7-point scale. Assuming a 0-6 scoring method, scores of 3 or greater indicate that participants are closer to being impaired than intact.	
Forbes 2012	CPT	-	-	-	-		-		Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	TAU	-		-		Social subscale of the WHO-QOL Bref, 8.1 (2.8) [this is the mean (SD) across both groups]		Normative data for this subscale were not available. If a participant were to answer "neither satisfied or dissatisfied" on 2 of the items and "dissatisfied" on the other item they would receive a score of 8. Therefore, a score of 8.1 indicates that participants are closer to being impaired than intact.	
Ford 2011	WL	NMR, 96.9 (20)	101.6 (15.43) (non-clinical) (Cantanzaro & Mearns, 1990)	PTCI-self, 67.1 (28.3) [A mean of 67.1 is equivalent to a mean of 3.2 when scored the same way as the normative data]	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	RSQ secure attachment subscale, 13.5 (3.3)	15.57 (SD = 3.01) (non-clinical) (Bäckström & Holmes, 2001)	-	Include NSC data but not AD or DR data.

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	TARGET	106.1 (18.1)		51.3 (23.5) [A mean of 51.3 is equivalent to a mean of 2.44 when scored the same way as the normative data]		13.7 (3.8)			
	PCT	103.1 (20.2)		53.7 (25.4) [A mean of 53.7 is equivalent to a mean of 2.56 when scored the same way as the normative data]		14 (3.5)			
Galovski 2012	MCPT	-	-	TRGI guilt cognitions subscale, 1.57 (0.11) [this is the least square mean (SE)]	1 (0.5) (among participants with a history of potentially traumatic CSA/CPA	SF-36 social functioning subscale, 42.87 (4.06) [this is the least square mean (SE)]	85.66 (19.83) (among male norms aged 25-44); 88.54 (18.09) (among male norms aged 35-55); numerous other norms are available as well (Ware et al., 1993).	-	Include both NSC and DR data
	SMDT	-		1.62 (0.12) [this is the least square mean (SE)]	without any axis-I disorder; these are more severe than healthy individuals) (Rausch et al., 2016)	37.45 (4.29) [this is the least square mean (SE)]			
Ghafoori 2017	PE	-	-	-	-	SDS social subscale, 7 (2.6)	-	A score of 7 or above on this	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	PCT	-		-		7.3 (2.5)		subscale indicates a marked impairment. Moreover, it has been suggested that clinicians should pay special attention to patients who score 5 or greater on this subscale (Rush et al., 2000).	
Harned 2014	DBT	-	-	TRGI guilt cognitions subscale, 2.4 (0.9)	1 (0.5) (among participants with a history of potentially traumatic CSA/CPA without any axis-I disorder; these are more severe than healthy individuals) (Rausch et al., 2016)	-	-	-	Include
	DBT -PE	-		2.4 (0.8)		-			
Hinton 2009	IT-CBT	ERS, 0.9 (0.6)	-	-	-	-	-		Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	DT-CBT	0.8 (0.5)		-		-		Normative data for this scale were not available. This scale is rated on a 0-4 Likert-type scale, rating the ability to distance from affects, ranging from "not at all" to "very much so." These scores appear to indicate that participants are only edging towards somewhat being able to distance from affects.	
Hinton 2011	CA-CBT	ERS, 0.7 (0.5)	-	-	-	-	-		Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	AMR	0.9 (0.4)		-		-		As above with Hinton, 2009, these scores appear to indicate that participants are only edging towards somewhat being able to distance from affects.	
Hogberg 2007	EMDR	-	-	-	-	SDI, 4.5 (2.3)	1.53 (1.13)	- (among subjects who had experienced traumatic events but who had never developed PTSD) (Nardo et al., 2011)	Include
	WL	-	-	-	-	5.9 (4.5)			
Hollified 2007	CBT	-	-	-	-	SDS global rating scale, 4.09 (0.81)	-	Normative data for this scale	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	WL	-		-		4 (1.02)		were not available. Participants' scores on this scale appear to be impaired as possible scores on this scale appear to range from 0 to 5, with higher scores indicating greater impairment.	
Jung 2013	CRIM	-	-	RSES, 22.1 (7.8)	49.2 (8.2) (non-clinical) (Roth et al., 2008)	-	-	This version of the RSES appears to range from 1-60.	Include
	WL	-		20.6 (5.7)		-			
Keane 1989	Implosive (flooding)	-	-	-	-	Social subscale of the Social Adjustment Measures, 4 (1.9)	-	Normative data for this scale were not available. The	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
Krakow 2001	CIT	-	-	-	-	SDS social life/leisure activities index (no baseline scores were reported)	-	Inferential statistics including effect sizes showing changes in the SDS social life/leisure activities index in the groups were reported (no baseline scores).	Include – although exclude in sensitivity analysis.
	WL	-	-	-					
Krupnick 2008	IPT	-	-	-	-	IIP	-	Patients with a score of 3 or higher on any item of the IIP (indicating significant interpersonal distress) qualified for participation in the study.	Include
	WL	-	-	-					
Kubany 2003	Immediate CTT-BW	-	-	RSES, 13.6 (5.2)	22.62 (5.80) (non-clinical)	-	-	It is also worth noting that an	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	Delayed CTT-BW	-		12.7 (6.7)	(Sinclair et al., 2010)			inclusion criterion in this study was a score on the TRGI global guilt scale reflecting at least moderate abuse-related guilt.	
Kubany 2004	Immediate CTT-BW	-	-	RSES, 14.8 (5.4)	22.62 (5.80) (non-clinical)	-	-	It is also worth noting that an inclusion criterion in this study was a score on the TRGI global guilt scale reflecting at least moderate abuse-related guilt.	Include
	Delayed CTT-BW	-		14.5 (4.5)	(Sinclair et al., 2010)	-			
Lindauer 2005	BEP	-	-	-	-	Relationships Questionnaire,	-	At least 50% of the sample had	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
Monson 2006	CPT	ACS	-	TRGI guilt cognitions subscale	-	SAS-SR, 2.48 (0.39)	1.59 (0.33) (non-clinical) (Weissman et al., 1978)	-	Include (exclude AD and NSC data in sensitivity analysis, as baseline AD and NC data were not available)
	WL					2.68 (0.54)			
Mueser 2008	CBT	-	-	PTCI-self, 3.89 (1.11)	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	-	-	-	Include
	TAU	-		3.64 (1.14)		-			
Mueser 2015	CBT	-	-	PTCI-self, 4.10 (1.36)	Median (SD) among people with no trauma: 1.08 (0.76)	CAPS social functioning subscale, 2.35 (0.79)	-	Using the "1, 2" rule (i.e., a frequency score of 1 and an	Include NSC data but not DR data.

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	BT	-		4.15 (1.31)	(Foa et al., 1999)	2.36 (0.81)		intensity score of 2) for the CAPS social functioning subscale to determine symptom severity, scores above 3 meet the clinical threshold (Weathers et al., 1999)	
Nijdam 2012	BEP	-	-	-	-	Relating to others subscale of the PTGI, 14.38 (7.92) [this is the mean (SD) across both groups]	23.04 (no SD reported) (non-clinical) (Tedeschi & Calhoun, 1996)	-	-
	EMDR	-		-					
Pacella 2012	PE	-	-	PTCI-self, 3.23 (1.19)	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	-	-	-	Include
	WL	-		3.04 (1.38)		-			
Power 2002	EMDR	-	-	-	-	SDS, 21.3 (5.4)	-	Each of the baseline mean	Include
	E+CR	-		-		22.8 (6.3)			

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
Steel 2017	CBT	-	-	PTCI-self, 4.46 (1.13) [this is the mean (SD) across both groups]	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	-	-	-	Include
	TAU	-				-			
Suris 2013	CPT	-	-	PTCI-self, 4.80 (1.12)	Median (SD) among people with no trauma: 1.08 (0.76) (Foa et al., 1999)	-	-	-	Include
	PCT	-		4.82 (1.25)		-			
Talbot 2014	CBT-I	-	-	-	-	WSAS, mean of >24 for both groups (as depicted in a graph)	-	Baseline scores above 20 on the WSAS suggest moderately severe or worse psychopathology (Mundt et al., 2002).	Include
	WL	-		-					
ter Heide 2011	EMDR	-	-	-	-	Social subscale of the WHO-QOL Bref, 2.4 (0.86)	-	Normative data for this subscale were not available. A	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	Stabilisation	-		-		3.07 (0.49)		weighted mean of less than 3 represents being between dissatisfied (2) and neither satisfied nor dissatisfied (3; which is in the middle) on the different items of this subscale. Therefore, participants are closer to being impaired than intact.	
ter Heide 2016	EMDR	-	-	-	-	Social subscale of the WHO-QOL Bref, 2.71 (0.80)	-	Normative data for this subscale were not available. A	Include

Study Ref	Groups included	Name of AD assessment, baseline mean (SD)	Normative AD data for interpretation, mean (SD)	Name of NSC assessment, baseline mean (SD)	Normative NSC data for interpretation, mean (SD)	Name of DR assessment, baseline mean (SD)	Normative DR data for interpretation, mean (SD)	Other information for interpretation	Decision
	Stabilisation	-		-		2.55 (0.98)		weighted mean of less than 3 represents being between dissatisfied (2) and neither satisfied nor dissatisfied (3; which is in the middle) on the different items of this subscale. Therefore, participants are closer to being impaired than intact.	
van den Berg 2015	PE	-	-	PTCI-self, 4.52 (1.22)	Median (SD) among people with no trauma:	-	-	-	Include
	EMDR	-		4.4 (1.12)		-			
	WL	-		4.26 (0.96)	1.08 (0.76) (Foa et al., 1999)	-			

Abbreviations: AC, Attention Control; ACF, Affect Control Scale; AL, Active Listening Control; AMR, Applied Muscle Relaxation; ART, Accelerated Resolution Therapy; BEP, Brief Eclectic Psychotherapy; BPS, Borderline Personality disorder; BT, Brief Treatment; CA-CBT, Culturally Adapted Cognitive Behaviour Therapy; CAPS, Clinician-Administered PTSD Scale; CBT, Cognitive Behaviour Therapy; CBT-I, Cognitive Behavioral Therapy for Insomnia; CIT, Cognitive Imagery Treatment; CPT, Cognitive Processing Therapy; CRIM, Cognitive Restructuring and Imagery Modification; CSA, Childhood Sexual Abuse; CT, Cognitive Therapy; CTT-BW, Cognitive Trauma Therapy for Battered Women; DBT, Dialectical Behavior Therapy; DBT PE, Dialectical Behavior Therapy Prolonged Exposure; DET, Dialogical Exposure Therapy; DT –CBT, Delayed Treatment Cognitive Behaviour Therapy; E+C, Exposure and Cognitive; E+CR, Exposure plus Cognitive Restructuring; EMDR, Eye Movement Desensitization and Reprocessing Therapy; ERS, Emotion Regulation Scale; EXP, Experimental Treatment; EXP, Exposure Therapy Only; Intensive CT, Intensive Cognitive Therapy; IIP, Inventory of Interpersonal Problems; IIP-C, Inventory of Interpersonal Problems – Circumplex Version; IPT, Interpersonal Psychotherapy; MA, Minimal Attention; MA WL,

Minimal Attention Wait List; MCPT, Modified Cognitive Processing Therapy Intervention; MVA, Motor Vehicle Accident; NMR, General Expectancy for Negative Mood Regulation Scale; PCT, Present Centred Therapy; PE, Prolonged exposure; PE-CR, Prolonged Exposure plus Cognitive Restructuring; PE-SIT, Prolonged Exposure + Stress Inoculation Training; PGT, Psychoeducational Group Therapy; PTCI, Posttraumatic Cognitions Inventory; PTGI, Post-Traumatic Growth Inventory; PTSD, Post-traumatic Stress Disorder; RA, Repeated Assessments; REM, Rapid Eye Movement; RSES, Rosenberg Self-Esteem Scale; SAS, Social Adjustment Scale; SAS-SR, Social Adjustment Scale-Self-Report; SCQD, Self-Control Questionnaire for Depression; SDI, Social Disability Index; SDS, Sheehan Disability Scale; SF-36, Short Form-36 Health Survey; SHB, Self-help booklet; SIDES, Structured Interview for Disorders of Extreme Stress; SIT, Stress inoculation training; SMDT, Symptom –Monitoring Delayed Treatment; SMT, Self- Management Therapy; SSBT, Single Session of Behavioural Treatment; STAIRS + MPE, Skills Training in Affective and Interpersonal Regulation with modified Prolonged Exposure; TARGET, Trauma Affect Regulation: Guide for Education and Therapy; TAU, Treatment as usual; TFCBT, Trauma-Focused Cognitive-Behavioural Therapy; TMT, Trauma Management Therapy; TRGI, Trauma Related Guilt Inventory; TSCS, Tennessee Self-Concept Scale; TSI, Traumatic Stress Institute Beliefs Scale; Weekly CT, Weekly Cognitive Therapy; Weekly ST, Weekly Supportive Therapy ;WL, Waitlist; WHOQOL-26, World Health Organization Quality of Life Questionnaire; WHO-QOL Bref, The short form of the World Health Organization Quality of Life scale; WSAS, Work and Social Adjustment Scale.

References for comparator samples or scoring guidelines referred to in Table E.1 above

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F. Risk of Bias Criteria

Selection Bias: random sequence generation

A judgement of unclear risk of bias was made where randomisation was referred to but described in insufficient detail to determine independent random sequence generation. There was judged to be low risk of bias where this procedure was explicitly reported.

Selection Bias: allocation concealment

A judgement of unclear risk of bias was made where randomisation was referred to but described in insufficient detail to determine allocation concealment. There was judged to be low risk of bias where this procedure was explicitly reported.

Performance Bias: blinding of participants and personnel

Blinding of participants and personnel was not possible due to the nature of the interventions, as is the case with trials of psychosocial interventions in general. This resulted in a judgement of high risk of performance bias across studies.

Detection Bias: blinding of assessments

Detection bias was judged to be high where non-blinding of assessors was stated or where no information was given, and low if blinding was explicitly reported.

Attrition Bias: incomplete outcome data

A judgement of high risk of attrition bias was made where data for $\geq 25\%$ of those randomised was missing (Xia et al., 2009) or if attrition was not reported (or clearly reported) and a completer analysis was carried out. If attrition was low ($<25\%$) and completer analysis was used risk of attrition bias was rated as low.

Reporting Bias: selective outcome reporting

If outcomes are pre-specified and reported a low risk of reporting bias rating was given. However, if no protocol is reported a high risk of reporting bias rating was given. If subgroup analysis is reported but not pre-specified a high risk of reporting bias rating was given.

Overall Quality

An overall quality rating for each study was also produced. Performance bias was not taken into consideration when producing this rating, as blinding of participants was not possible due to the nature of the interventions. All of the other criteria above were considered (i.e., selection bias: random sequence generation and allocation concealment, detection bias, attrition bias, and reporting bias). A high overall quality rating was given if a study received a low risk of bias rating for detection bias, at least another low risk of bias rating, and ≤ 2 high risk of bias ratings. A low overall quality rating was given if a study did not meet these criteria.

G. Table F.1. Risk of Bias in Included Studies – Summary

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting	Overall Quality
Ahmadi 2015	Unclear	Unclear	High risk	High risk	High risk	High risk	Low quality
Azad marzabadi 2014	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality
Basoglu 2007	Low risk	Unclear	High risk	Low risk	Low risk	High risk	High quality
Beidel 2011	Unclear	Unclear	High risk	High risk	High risk	High risk	Low quality
Beidel 2019	Unclear	Unclear	High risk	High risk	High risk	High risk	Low quality
Bryant 2013	Low risk	Low risk	High risk	Low risk	High risk	High risk	High quality
Butollo 2016	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality
Cloitre 2002	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
Difede 2007	Unclear	Unclear	High risk	High risk	High risk	High risk	Low quality
Dorrepaal 2012	Unclear	Low risk	High risk	Low risk	Low risk	High risk	High quality
Duffy 2007	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality
Dunn 2007	Low risk	High risk	High risk	Low risk	High risk	High risk	High quality
Dunne 2012	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality
Ehlers 2003	Low risk	Low risk	High risk	Low risk	Low risk	High risk	High quality
Ehlers 2005	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
Ehlers 2014	Low risk	Low risk	High risk	Low risk	Low risk	High risk	High quality
Foa 1999	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
Foa 2005	Unclear	Unclear	High risk	Low risk	High risk	High risk	Low quality
Forbes 2012	Low risk	Low risk	High risk	Low risk	Low risk	High risk	High quality
Ford 2011	Low risk	Low risk	High risk	High risk	High risk	High risk	Low quality
Galovski 2012	Low risk	Unclear	High risk	Low risk	High risk	High risk	High quality
Ghafoori 2017	Low risk	Unclear	High risk	High risk	High risk	High risk	Low quality
Harned 2014	Low risk	Unclear	High risk	Low risk	High risk	High risk	High quality
Hinton 2009	Low risk	Unclear	High risk	Low risk	Low risk	High risk	High quality
Hinton 2011	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality
Hogberg 2007	Unclear	Low risk	High risk	High risk	Low risk	High risk	Low quality
Hollified 2007	Low risk	Low risk	High risk	High risk	High risk	High risk	Low quality
Jung 2013	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality
Keane 1989	Unclear	Unclear	High risk	High risk	Low risk	High risk	Low quality

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting	Overall Quality
Kip 2013	Low risk	Unclear	High risk	High risk	Low risk	Low risk	Low quality
Krakow 2001	Low risk	Unclear	High risk	Low risk	Low risk	High risk	High quality
Krupnick 2008	Unclear	Unclear	High risk	High risk	High risk	High risk	Low quality
Kubany 2003	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
Kubany 2004	Unclear	Unclear	High risk	Low risk	High risk	High risk	Low quality
Lindauer 2005	Low risk	Unclear	High risk	Low risk	High risk	High risk	High quality
Marks 1998	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
McDonagh 2005	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
Monson 2006	Unclear	Unclear	High risk	Low risk	Low risk	High risk	High quality
Mueser 2008	Low risk	Low risk	High risk	Low risk	High risk	High risk	High quality
Mueser 2015	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High quality
Nijdam 2012	Low risk	Low risk	High risk	Low risk	High risk	Low risk	High quality
Pacella 2012	Low risk	Unclear	High risk	Low risk	Low risk	High risk	High quality
Power 2002	Low risk	Low risk	High risk	Low risk	High risk	High risk	High quality
Resick 2002	Unclear	Unclear	High risk	High risk	High risk	High risk	Low quality
Scheck 1998	Low risk	Low risk	High risk	Low risk	High risk	High risk	High quality
Steel 2017	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High quality
Suris 2013	Low risk	Low risk	High risk	Low risk	High risk	High risk	High quality
Talbot 2014	Low risk	Low risk	High risk	Low risk	Low risk	High risk	Low quality
ter Heide 2011	Low risk	Unclear	High risk	High risk	High risk	High risk	High quality
ter Heide 2016	Low risk	Unclear	High risk	Low risk	Low risk	Low risk	High quality
van den Berg 2015	Low risk	Low risk	High risk	Low risk	Low risk	Low risk	High quality

H. Table H.1. Risk of Bias in Included Studies – Detailed

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
Ahmadi 2015	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	<i>“The drop-out rate from the study was also high comprising over 31% of the initial participants.”</i> No follow-up data – beyond post-intervention data.	Protocol not available.
	Unclear	Unclear	High risk	High risk	High risk	High risk
Azad marzabadi 2014	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	<i>“Two participants dropped out in each group as the study continued (due to reasons like being discharged from the hospital or stopping participation in the study).”</i>	Protocol not available.
	Unclear	Unclear	High risk	High risk	Low risk	High risk
Basoglu 2007	<i>“A computer-generated sequence of random numbers that ensured equal cell sizes and did not lead to allocation of more than two consecutive cases to the same experimental</i>	Not reported.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>“The assessors were blind as to the participants’ experimental condition at the week 4 and week 8 assessments.”</i>	Only four non-completer cases, and ITT was used.	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	<i>condition was used in the randomization.”</i>					
	Low risk	Unclear	High risk	Low risk	Low risk	High risk
Beidel 2011	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported (for the relevant assessments).	5 of the 35 participant did not complete the intervention and then another 5 did not complete the relevant post-intervention assessments. ITT was used. 10/35 = 29%. No follow-up data – beyond post-intervention data.	Protocol not available.
	Unclear	Unclear	High risk	High risk	High risk	High risk
Beidel 2019	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	<i>“Participants were randomized to either TMT or EXP prior to initiating treatment. However, clinicians and participants were blinded to group assignment until VRET and the mid-treatment assessment were completed.”</i>	Not reported.	<i>“The overall dropout rate was 39%, consistent with other clinical trials examining treatment for combat-related PTSD (Reger et al., 2016; Resick et al., 2015). The dropout rate was 28% for TMT and 50% for EXP, which was not significantly different ($\chi^2 = 2.14, df = 91, p < 0.14$).”</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	Unclear	Unclear	High risk	High risk	High risk	High risk
Bryant 2013	<i>“Randomization was conducted by a process of minimization stratified on gender, trauma type and Clinician Administered PTSD Scale-2 (CAPS-2; Blake et al. 1995) total score. Participants were randomly assigned according to a random numbers system administered by an individual who was independent of the study and who worked at a site that was distant from the treatment centre.”</i>	<i>Distance randomisation – “Participants were randomly assigned according to a random numbers system administered by an individual who was independent of the study and who worked at a site that was distant from the treatment centre.”</i>	<i>Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.</i>	<i>“Post-treatment and 6-month follow-up assessments were conducted by independent clinicians who were unaware of the treatment condition of participants. Blindness was maintained by ensuring that clinicians who conducted assessments did not have access to (a) participant notes or (b) condition allocation of participants.”</i>	<i>“Of the participants, 51 (73%) completed treatment and 32 (46%) completed the 6-month follow-up assessment.”</i>	<i>Protocol not available.</i>
	Low risk	Low risk	High risk	Low risk	High risk	High risk
Butollo 2016	<i>Randomisation was referred to, but there was no more relevant information.</i>	<i>Randomisation was referred to, but there was no more relevant information.</i>	<i>Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.</i>	<i>“The IES-R [36] , a self-report instrument that measures the intensity of PTSD symptoms, was our primary outcome measure. It was administered by the therapist before each session as a process</i>	<i>“Drop-out rates at the posttreatment assessment were 12.2% for DET (4.1% of those allocated to DET did not start treatment, 8.1% dropped out of treatment) and</i>	<i>Protocol not available.</i>

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
				<i>measure, as well as before and after treatment and at the follow-up."</i>	<i>14.9% for CPT (6.0% declined treatment after allocation, 9.0% dropped out of treatment). At the 6-month follow-up, study drop-out rates were markedly higher, increasing the overall study dropout to 47.3% in the DET and 37.3% in the CPT condition."</i>	
	Unclear	Unclear	High risk	High risk	Low risk	High risk
Cloitre 2002	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Clinician raters of the CAPS (PTSD measure) were blind to treatment condition at pre- and posttreatment. No reference to any blinding (e.g., re scoring) the NMR and IIP.	<i>"Of the 58 women who entered treatment, 12 dropped out: 9 from the active treatment (29%) and 3 from the wait list (11%)." This is <25% overall.</i>	Protocol not available.
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
Difede 2007	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	<i>"Our dropout rate of 40% was higher than the typical exposure therapy study for PTSD, where dropouts are</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
					<i>reported in the 20% to 30% percent range (Bradley et al., 2005). " Also, >30% dropped out of the allocated intervention.</i>	
	Unclear	Unclear	High risk	High risk	High risk	High risk
Dorrepaal 2012	<i>"The randomization was performed independently on a 1:1 basis, stratified per site, by a methodologist not involved in the study. Condition assignments were e-mailed to the group leader, who then informed the patient without informing the researchers or assessors." No more relevant information.</i>	<i>"The randomization was performed independently on a 1:1 basis, stratified per site, by a methodologist not involved in the study. Condition assignments were e-mailed to the group leader, who then informed the patient without informing the researchers or assessors."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"The interviews were conducted by trained independent assessors, who were blind to the treatment condition and were audiotaped for use in supervision."</i>	Attrition was 16%.	Protocol not available.
	Unclear	Low risk	High risk	Low risk	Low risk	High risk
Duffy 2007	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	21% dropped out.	Protocol not available.
	Unclear	Unclear	High risk	High risk	Low risk	High risk

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
Dunn 2007	<i>"The study statistician (J. Soucek [J.So.] provided randomization numbers and group assignments from a list generated by the PLAN procedure in SAS, version 6.11. We randomized in blocks of two, in the order of participants' enrollment, to facilitate equal participant numbers in each group."</i>	The list of random numbers provided could suggest that investigators could possibly foresee assignments.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Interviewers were blind to participants' therapy group assignments throughout the study."</i>	30% of those allocated to the interventions did not complete them, and 41% of those allocated to the interventions were lost to follow-up at 12 months.	Protocol not available.
	Low risk	High risk	High risk	Low risk	High risk	High risk
Dunne 2012	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	<i>"Participants in this study were also not blinded to condition."</i>	<i>"Although the use of the same assessor for the diagnostic interview for all participants at all 3 time points is a methodological strength, this also meant the assessor was not blinded to the treatment condition representing a potential bias in postassessment and follow-up assessment."</i>	<i>"A further strength of the study was the use of the intent-to-treat sample for data analyses, despite the relatively low attrition in this study (9% at 6-mo follow-up)."</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	Unclear	Unclear	High risk	High risk	Low risk	High risk
Ehlers 2003	Reference to using the random permuted blocks within strata algorithm.	Investigators enrolling participants could not possibly foresee assignments as the allocation list was kept locked in a central office and the patient's allocation was only revealed three weeks later – following the self-monitoring assessment.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Independent assessors, blind to treatment condition, administered the CAPS. No reference to how the SDS (which is a self-report measure) was scored.	Attrition was < 25%.	Protocol not available.
	Low risk	Low risk	High risk	Low risk	Low risk	High risk
Ehlers 2005	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Independent assessors, blind to treatment condition, administered the CAPS. No reference to how the SDS (which is a self-report measure) was scored.	No patient dropped out.	Protocol not available.
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
Ehlers 2014	<i>“The participants were then randomly allocated to one of the four trial conditions by an independent researcher who was not involved in assessing patients using the minimization</i>	<i>“The participants were then randomly allocated to one of the four trial conditions by an independent researcher who was not involved in assessing patients using the minimization procedure (15) to stratify for sex and</i>	<i>“Participants were not blind to the nature of the treatment, but care was taken to create similarly positive expectations in each treatment group by informing them that several psychological treatments were effective in PTSD and it</i>	<i>“The assessments of treatment outcome were conducted by independent evaluators without knowledge of the patient's treatment condition. Patients were asked not to reveal their group</i>	Attrition was < 25%.	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	<i>procedure (15) to stratify for sex and severity of PTSD symptoms. The assessors determining the suitability of a patient for inclusion were not informed about the stratification variables and algorithm."</i>	<i>severity of PTSD symptoms. The assessors determining the suitability of a patient for inclusion were not informed about the stratification variables and algorithm."</i>	<i>was unknown which worked best, and by giving a detailed rationale for the treatment condition to which the patient was allocated."</i>	<i>assignment to the evaluators."</i>		
	Low risk	Low risk	High risk	Low risk	Low risk	High risk
Foa 1999	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Assessors were unaware of treatment assignment.	17.7 dropped out altogether; although drop-out were not spread evenly throughout the groups – 8% dropped out of the PE group, 27% of the SIT group, 27% of the PE-SIT group, 0% of the WL group. ITT was used.	Protocol not available.
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
Foa 2005	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Independent evaluations were conducted at pretreatment and posttreatment and 3-, 6-, and 12-month posttreatment. All</i>	<i>"The overall dropout rate was 32.4% and was lower for WL (3.8%) than PE/CR (40.5%)... and PE (34.2%)"</i> These	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
				<i>evaluations were conducted by trained doctoral or master's level CTSA clinicians who were blind to study condition."</i>	were not available for post-intervention assessment.	
	Unclear	Unclear	High risk	Low risk	High risk	High risk
Forbes 2012	A random number ordered list was used.	After full assessment by an independent clinical assessor, participants were randomised by the project manager at an independent research centre.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Assessors were blind to allocation and treatment.	20% did not complete the post-intervention assessment and 31% did not complete the 3 month follow-up (which is a short-term follow-up).	Protocol not available.
	Low risk	Low risk	High risk	Low risk	Low risk	High risk
Ford 2011	<i>"One hundred forty six women (ages 18–45; M=30.7, SD=6.9) completed the screening and baseline assessment and then were randomized (by a study assessor using numbers concealed in sealed envelopes previously prepared by a different study staff member using the Excel random number generator) to WL (N=45), TARGET</i>	<i>"One hundred forty six women (ages 18–45; M=30.7, SD=6.9) completed the screening and baseline assessment and then were randomized (by a study assessor using numbers concealed in sealed envelopes previously prepared by a different study staff member using the Excel random number generator) to WL (N=45), TARGET</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"All interviewers were blind to the experimental condition in baseline interviews, but due to technical difficulties they were not blind to experimental condition at posttherapy or follow-up interviews."</i>	32% of those allocated to treatment did not complete the post-intervention assessment.	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	<i>(N=48), or PCT (N=53)."</i>	<i>(N=48), or PCT (N=53)."</i>				
	Low risk	Low risk	High risk	High risk	High risk	High risk
Galovski 2012	<i>"If eligible, participants were randomly assigned in a 1:1 ratio using computer generated simple randomization to MCPT or to SMDT following the pre-treatment assessment."</i>	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Finally, because it is technically possible to remain PTSD positive with a score of 20 on the PDS and reporting bias can exist in the therapy situation (e.g., patient wants to please therapist), a blind rater conducted the CAPS to ensure that the participant no longer met criteria for PTSD."</i> The other relevant measures were self-report, and no reference to any blind scoring of these.	27% of those randomised did not complete an assessment at the time of the completion of the CBT intervention.	Protocol not available.
	Low risk	Unclear	High risk	Low risk	High risk	High risk
Ghafoori 2017	A pre-determined, computer-generated, randomised list was used.	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Outcome assessors were not blind to participant assignments.	More than half of the sample terminated prematurely before completion of the treatment, and follow-up assessment time points were included.	Protocol not available.
	Low risk	Unclear	High risk	High risk	High risk	High risk

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
Harned 2014	<i>"A minimization randomization procedure was used."</i>	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"All assessments were conducted by independent clinical assessors who were blind to treatment condition."</i>	<i>"Completion rates for the one year of treatment did not differ between conditions (DBT=55.6%, DBT + DBT PE=58.8%)."</i>	Protocol not available.
	Low risk	Unclear	High risk	Low risk	High risk	High risk
Hinton 2009	Coin was tossed.	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Outcome assessor was blind to treatment condition.	<i>"All 24 randomized patients completed the study, and there were no missing data."</i>	Protocol not available.
	Low risk	Unclear	High risk	Low risk	Low risk	High risk
Hinton 2011	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	All assessments were self-report, although it does not clarify whether or not these were scored blind.	<i>"There was no missing data."</i>	Protocol not available.
	Unclear	Unclear	High risk	High risk	Low risk	High risk
Hogberg 2007	No more relevant information other than what is in the next column.	<i>"The randomization was done by picking a sealed ballot in the presence of a research nurse who coordinated the study and followed the participants through all phases."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	<i>"Three subjects dropped out after randomization but before treatment/WL. One of them had a strong aversive reaction to the SPECT examination and decided to interrupt"</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
					<i>the examination. Two other subjects left the study because of difficulty with finding time for the study." 5/24 = 21%.</i>	
	Unclear	Low risk	High risk	High risk	Low risk	High risk
Hollified 2007	<i>"Before enrolling participants, 90 study ID numbers were prerandomized to study group (acupuncture, CBT or WLC) by the research coordinator (RC) using a computerized random numbers procedure without restrictions."</i>	<i>"When a participant was enrolled, the RC opened the assignment program to reveal the participant's group assignment. This allocation procedure was concealed from clinicians."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"The research coordinator collected, entered, and helped analyze the data. Although he was aware of participant group allocation at the time he collected data, he did not assist participants in completing the self-rated assessments. It is possible, yet we think quite unlikely, that he could have systematically influenced participant reports."</i>	<i>"Eighty-four participants were randomized, 73 began the protocol, and 61 (73% of those randomized and 84% of those who began the protocol (acupuncture 79% vs. CBT 84% vs. WLC 88%) completed treatment or wait-list assessments. End treatment and 3-month follow-up assessments were obtained for 60 and 58 participants, respectively." 24/84 = 29%.</i>	Protocol not available.
	Low risk	Low risk	High risk	High risk	High risk	High risk
Jung 2013	Randomisation was referred to, but there	Randomisation was referred to, but there	Blinding of participants is generally not possible	The PDS and RSES (the relevant	<i>"34 participants were randomly</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	was no more relevant information.	was no more relevant information.	due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	measures) were self-report, but there is no reference to these being blindly scored.	<i>assigned to either the CRIM group (n = 17) or WL group (n = 17). Two patients in each condition decided against treatment after randomization and were defined as nonstarters. Further, 2 patients (1 in each condition) were excluded from the study due to protocol violations, specifically, because they had received further psychological treatment while participating in the study. No patient dropped out of treatment.</i> 6/34 = 18%.	
	Unclear	Unclear	High risk	High risk	Low risk	High risk
Keane 1989	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>“Post-test assessments for the Wait-list Control were conducted either by the therapist who would then treat the patient or, in the case of patients to be</i>	No reference to any missing data at post-assessment.	<i>“The original design of this study involved random assignment of subjects to the implosive therapy group, a stress management group wherein subjects were taught behavioral skills to</i>

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
				<i>treated elsewhere, by an unsystematically assigned therapist from the four involved in the study.</i>		<i>re-duce anxiety but exposure to traumatic memories was limited, and the waiting list control. Only 5 subjects completed the stress management condition, and thus, these data are not included in the present manuscript.</i>
	Unclear	Unclear	High risk	High risk	Low risk	High risk
Kip 2013	<i>“Eligible service members/veterans were randomly assigned to the ART or AC regimen in a 1:1 ratio using a random number generator and variable blocking scheme (blocks of 4, 6, and 8).”</i>	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>“Random assignment was unblinded; hence, the potential existed for over-reporting of reductions in pain with the ART intervention.”</i>	Attrition was <25%.	<i>“The trial was registered with ClinicalTrials.gov (NCT01559688).”</i> The relevant PTSD measure was reported as the primary outcome in this protocol.
	Low risk	Unclear	High risk	High risk	Low risk	Low risk
Krakow 2001	<i>“To mask treatment assignment, patients mailed back a postcard after intake to complete entry into the protocol. The postcard’s time and date were logged into a computer and entered into a previously generated list of numbers that</i>	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>“To limit external bias, blinding occurred at 3 points of data collection: (1) at intake, group assignment had not been established; (2) at 3-month follow-up, questionnaires were completed through the mail; and (3) at 6-month follow-up,</i>	<i>“Of the 168 randomized participants, 96 completed 3-month follow-ups by mail, and 99 completed the 6-month follow-ups in person. In total, 114 individuals completed at least 1 follow-up, and 77</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	<i>randomly assigned participants to treatment and control groups. All numbers and group assignments were generated at the start of the protocol."</i>			<i>interviewers were unaware of group status."</i>	<i>participants completed both follow-ups."</i>	
	Low risk	Unclear	High risk	Low risk	Low risk	High risk
Krupnick 2008	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	<i>"At termination, we obtained assessments for only 20 (out of 32) treatment and 7 (out of 16) control participants. These figures increased to 26 treatment and 10 control participants for the 4-month follow-up interview."</i> Therefore, attrition at termination was >25%.	Protocol not available.
	Unclear	Unclear	High risk	High risk	High risk	High risk
Kubany 2003	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	The assessors (of the CAPS; the PTSD measure) were blind to participants' condition assignments. The RSES was also used, but this is a self-report measure and there is	<i>"Eighteen of 19 women assigned to the Immediate CTT-BW condition completed CTT-BW. Fourteen of 18 women assigned to the Delayed CTT-</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
				no reference to this being blindly scored.	<i>BW condition completed CTT-BW. Overall, 86% of the 37 women who started CTT-BW (n = 32) completed treatment." It appears these participants also completed the assessment at the time of the completion of Immediate CTT-BW condition; therefore there was <25% attrition. Re follow-ups, "three-month follow-up data was obtained for 78% of the women who completed Immediate CTT-BW (n = 14) and for 79% of the women who completed Delayed CTT- BW (n = 11)."</i>	
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
Kubany 2004	Randomisation was referred to, but there	Randomisation was referred to, but there	Blinding of participants is generally not possible due to the nature of	The assessors (of the CAPS; the PTSD measure) were blind to	Posttreatment assessment data were only available	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	was no more relevant information.	was no more relevant information.	psychological trials. Nothing in this trial to suggest otherwise.	participants' condition assignments. The RSES was also used, but this is a self-report measure and there is no reference to this being blindly scored.	for 84 of 125 randomised participants; there attrition was >25%.	
	Unclear	Unclear	High risk	Low risk	High risk	High risk
Lindauer 2005	<i>"A colleague who had done no assessments used a computer program to randomly assign 12 patients to each condition in a block design."</i>	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Each patient was assessed by a researcher (R.J.L.L. or E.P.M.M.), who were blind to all patients' condition."</i>	<i>"In the per-protocol analysis (patients who completed the treatment), the sample sizes were 7 (58%) for the treatment group and 11 (92%) for the waitlist group". Attrition = 25%.</i>	Protocol not available.
	Low risk	Unclear	High risk	Low risk	High risk	High risk
Marks 1998	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Assessors were kept unaware of the treatment condition."</i>	<i>"Ten subjects (11%) dropped out but they did not differ significantly by group."</i>	Protocol not available.
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
McDonagh 2005	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"A separate group of female clinicians, who were blind to treatment condition and who had no other role in the study"</i>	<i>"The dropout rate for the study was 23%, with a rate of 41% (12 of 29) for CBT, 9% (2 of 22) for PCT, and 13% (3 of 23) for WL."</i>	Protocol not available. Moreover, the following suggests a deviation from the protocol: <i>"When it became clear that the dropout rate was greater for CBT, we changed the</i>

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
				<i>conducted the four CAPS interviews."</i>		<i>random assignment process to increase the chance of assignment to CBT."</i>
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
Monson 2006	Randomisation was referred to, but there was no more relevant information.	<i>"The study biostatistician provided the participants' condition assignment to the study coordinator."</i> This does not necessarily suggest allocation concealment.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"The independent clinician assessors were blinded to condition assignment and participants were instructed to not disclose their condition assignment to them."</i>	<i>"The overall drop-out rate was 16.6% (20% from CPT, 13% from the wait-list condition)."</i>	Protocol not available.
	Unclear	Unclear	High risk	Low risk	Low risk	High risk
Mueser 2008	<i>"Randomization was conducted at a central location in the research center by a computer based randomization program with assignments not known in advance by either clinical or research staff..."</i>	<i>"Randomization was conducted at a central location in the research center by a computer based randomization program with assignments not known in advance by either clinical or research staff..."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Assessments were conducted by blinded interviewers at baseline, following the 4-6 months treatment period for the CBT program, and 3- and 6-months later."</i>	Only 59/108 were analysed at post-treatment.	Protocol not available.
	Low risk	Low risk	High risk	Low risk	High risk	High risk
Mueser 2015	<i>"Participants were randomised to the CBT or brief groups via a computer program operated by an off-site data manager, with no</i>	<i>"Participants were randomised to the CBT or brief groups via a computer program operated by an off-site data manager, with no study personnel aware</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"All interviewers were masked to treatment assignment."</i>	20% of randomised participants were not analysed at post-treatment.	<i>"All study procedures were approved by the Rutgers and Dartmouth Institutional Review Boards (trial registration: clinicaltrials.gov</i>

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	<i>study personnel aware of assignments in advance."</i>	<i>of assignments in advance."</i>				<i>identifier: NCT00494650)."</i>
	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Nijdam 2012	<i>"Random assignment was done on a 1:1 basis by a computer program, with a weighted maximum of subscribing four times the same treatment in a row."</i>	<i>"To ensure masking of assessors, one psychologist who had no other engagement in the study, had access to the computer program, kept a log file of all random assignments and assigned the patients to the therapists."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Assessments were conducted by trained, independent, masked assessors who were master's level clinical psychologists or master's level psychology students supervised by an experienced clinical psychologist."</i>	32% of randomised participants were lost to the first post-assessment.	<i>"Trial registration: Dutch Trial Register, number NTR46 and ISRCTN64872147."</i>
	Low risk	Low risk	High risk	Low risk	High risk	Low risk
Pacella 2012	<i>"The principal investigator (DLD) generated the allocation sequence using blocked randomization (4:3 ratio of experimental:control participants)."</i>	No more relevant information other than what is in the previous column.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"The graduate student conducting the assessments remained blind to group membership."</i>	<i>"At the post-intervention assessment, 23 participants were retained in the PE group (32% drop-out rate) and 24 participants were retained in the control group (0% drop-out rate)." It also says: "Unequal numbers of participants were assigned to each group, as it was anticipated that the PE group</i>	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
					would have a higher dropout rate.”	
	Low risk	Unclear	High risk	Low risk	Low risk	High risk
Power 2002	“Randomization was by means of a predetermined schedule unbeknown to the assessors, therapists or patients.”	“Following completion of the entire initial assessment, for those patients who met entry criteria, the blind assessor then opened a sealed envelope that informed as to which group patients were to be allocated.”	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	“Assessments pre- and post-treatment were conducted by two independent assessors respectively, who were blind to treatment conditions.”	“A total of 105 patients met entry criteria and were randomized to groups as follows: 39 to EMDR, 37 to ECCR and 29 to WL. Drop-out rates between these three groups were as follows, 12 (31%) from EMDR, 16 (43%) from E+CR and five (17%) from WL.”	Protocol not available.
	Low risk	Low risk	High risk	Low risk	High risk	High risk
Resick 2002	Randomisation was referred to, but there was no more relevant information.	Randomisation was referred to, but there was no more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Not reported.	Attrition was > 25%.	Protocol not available.
	Unclear	Unclear	High risk	High risk	High risk	High risk
Scheck 1998	“Envelopes filled with papers labeled either EMDR or AL were shuffled and numbered 1 through 100.”	“During each interview, envelopes were opened consecutively to identify which therapy was to be assigned to the participant.”	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	“During the post-test assessment, a trained volunteer who was blind to group assignment administered the	29% dropped out.	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
				<i>standardized instruments</i> ".		
	Low risk	Low risk	High risk	Low risk	High risk	High risk
Steel 2017	<i>"Block randomization was conducted independently of the research team through the OpenCDMS database specifically developed for the study."</i>	<i>"Block randomization was conducted independently of the research team through the OpenCDMS database specifically developed for the study."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Robust procedures were adopted to minimize the risk of interviewers being able to identify the group allocation of participants..."</i>	50/61 were analysed at post-treatment.	<i>"The trial was given ethical approval by Berkshire Research Ethics Committee (SC/09/H0505/85) and was registered as ISTCRN 67096137."</i>
	Low risk	Low risk	High risk	Low risk	Low risk	Low risk
Suris 2013	<i>"For the purpose of randomization, participants were assigned sequential PIN numbers as they entered the study. Blocks of random numbers were generated for each therapist, and were allocated to either CPT or PCT using a conditional statement."</i>	<i>"The random number sequence was maintained on an Excel spreadsheet, and as subjects' PINs were entered into the spreadsheet, the preassigned condition was revealed."</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Assessors were blind to treatment condition.	<i>"Excluding data from this therapist reduced the final sample to 86 participants from the original 129."</i>	This study has a high risk of reporting bias as lots of participants were removed from the analysis due to low treatment fidelity of a certain clinician.
	Low risk	Low risk	High risk	Low risk	High risk	High risk
Talbot 2014	<i>"Blind assignment was determined by a computer generated random allocation schedule operated by</i>	<i>"Group allocation was provided to the study coordinator in opaque, sealed envelopes that were opened by the study coordinator with</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	<i>"Clinical interviewers and the polysomnography technician were blind to participants' treatment conditions</i>	Only 16% in total were lost to follow-up.	Protocol not available.

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
	<i>the study statistician.</i> ”	<i>the participant following the completion of baseline measures.</i> ”		<i>during both pretreatment and posttreatment administration and scoring.</i> ”		
	Low risk	Low risk	High risk	Low risk	Low risk	High risk
ter Heide 2011	Coin was tossed.	No more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	The relevant measures were self-report and there is no reference to these being blindly scored. Re the clinician administered measure – “ <i>blindness was maintained only in 70% of SCID interviews, thus threatening the reliability of clinician rated outcomes.</i> ”	10/20 (50%) dropped out.	Protocol not available.
	Low risk	Unclear	High risk	High risk	High risk	High risk
ter Heide 2016	Coin was tossed.	No more relevant information.	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	“ <i>Interviews were administered by trained Master’s students in psychology who were kept masked to treatment condition by having limited access to participant data and by asking participants not to reveal treatment content.</i> ”	Attrition was <25%.	“ <i>Trial registration: NARCIS (Dutch National Academic Research and Collaborations Information System) OND1324839; ISRCTN20310201.</i> ”
	Low risk	Unclear	High risk	Low risk	Low risk	Low risk

Study	Selection Bias: random sequence generation	Selection Bias: allocation concealment	Performance Bias: blinding of participants and personnel	Detection Bias: blinding of assessments	Attrition Bias: incomplete outcome data	Reporting Bias: selective outcome reporting
van den Berg 2015	<i>“An independent randomization bureau randomized the treatment condition using stratified randomization blocks per therapist with equal strata sizes.”</i>	<i>“An independent randomization bureau randomized the treatment condition using stratified randomization blocks per therapist with equal strata sizes.”</i>	Blinding of participants is generally not possible due to the nature of psychological trials. Nothing in this trial to suggest otherwise.	Assessors were blind to treatment allocation.	Attrition was <25%.	<i>“The trial design was approved by the medical ethics committee of the VU University Medical Center and was registered at isrctn.com (ISRCTN79584912).”</i>
	Low risk	Low risk	High risk	Low risk	Low risk	Low risk

I. GRADE Assessment Criteria

We applied the following criteria for downgrading to each outcome.

Risk of Bias

If >50% of studies had a low overall quality rating, the quality of the outcome was downgraded by 1. If >75% of studies had a low overall quality rating, the quality of the outcome was downgraded by 2.

Imprecision

We downgraded an outcome for imprecision by 1 point if “a recommendation or clinical course of action would differ if the upper versus the lower boundary of the CI represented the truth” and/or the number of events and sample size meant the optimal information size was not reached (Guyatt et al., 2011). We downgraded by 2 points if an analysis was based on only 1-2 studies.

Inconsistency

We downgraded an outcome for inconsistency by 1 point if the I^2 statistic was $\geq 40\%$ in the context of an unclear direction of effect or $\geq 75\%$ in the context of a clear direction of effect. We downgraded by 2 points if the I^2 statistic was $\geq 75\%$ in the context of an unclear direction of effect.

Publication Bias

We downgraded an outcome for publication bias by 1 point when, for outcomes with at least 10 studies (Higgins & Green, 2011), the funnel-plots showed asymmetry and this was not better explained by selective reporting bias or some other factor. However, if the ‘trim and fill’ method indicated that any publication bias was not likely to affect the overall magnitude of the effect size, we did not downgrade.

Indirectness

Indirectness was assessed by considering the relevance of the outcome data to the construct of interest for each outcome, together with that of the study population, nature of the intervention under investigation and the control condition.

J. Table J.1. Other Comparisons

Studies	Outcome	Comparison (A vs B)	k included studies	Group A N	Group B N	Hedges' g (95% CI), p-value	Heterogeneity, I ² , p-value	Quality (GRADE)
<i>Versus TAU/WL</i>								
Krupnick 2008	PTSD + DR	IPT vs WL	1	32	16	-1.02 (-1.65, -0.39), 0.002	-	Very low -2 RoB -2 imprecision
Azad marzabadi 2014	DR	Mindfulness vs TAU	1	14	14	-1.60 (-2.43, -0.77), <0.001	-	Very low -2 RoB -2 imprecision
<i>Head-to-head comparisons</i>								
Beidel 2011	PTSD, DR & AD	TMT vs exposure	1	14	16	-0.09 (-0.79, 0.61), 0.801	-	Very low -2 RoB -2 imprecision
Beidel 2019	PTSD & DR	TMT vs exposure	1	43	49	-0.05 (-0.46, 0.36), 0.815	-	Very low -2 RoB -2 imprecision
Butollo 2016	PTSD & NSC	DET vs CBT	1	66	72	0.27 (-0.07, 0.60), 0.118	-	-Very low -2 RoB -2 imprecision
Bryant 2013	PTSD & NSC	CBT + ERT vs CBT + SC	1	36	34	-0.04 (-0.51, 0.43), 0.866	-	Low -2 imprecision

Studies	Outcome	Comparison (A vs B)	k included studies	Group A N	Group B N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Quality (GRADE)
Harned 2014	PTSD & NSC	DBT + Exposure vs DBT	1	12	6	0.51 (-0.43, 1.45), 0.291	-	Low -2 imprecision
ter Heide 2011, ter Heide 2016	PTSD & DR	EMDR vs STBT	2	36	34	-0.16 (-0.61, 0.29), 0.486	0%, 0.360	Low -2 imprecision

Abbreviations: AD=affect dysregulation; CBT=cognitive behavioural therapy; DBT=dialectical behaviour therapy; DET=dialogical exposure therapy; DR=disturbances in relationships; EMDR=eye-movement and desensitisation and reprocessing therapy; ERT=emotion regulation training; IPT=interpersonal psychotherapy; NSC=negative self-concept; PTSD=posttraumatic stress disorder; SC=supportive counselling; STBT=stabilisation treatment; TAU=treatment as usual; TMT=trauma management therapy; WL=waiting list.

K. Table K.1. Clinically Significant Response (number needed to treat per control group event rate)

Treatment	Comparator	Outcome	g (95% CI), p-value	10% CER*	22% CER*	50% CER*
CBT	vs TAU/WL	DR	-0.66 (-0.84, -0.48), <0.001	6B (4B, 9B)	4B (3B, 6B)	4B (3B, 5B)
CBT	vs control	DR	-0.32 (-0.60, -0.03), 0.029	15B (7B, 186B)	9B (5B, 111B)	8B (4B, 84B)
CBT	vs TAU/WL	AD	-1.42 (-2.20, -0.65), <0.001	2B (1B, 6B)	2B (1B, 4B)	2B (2B, 4B)
CBT	vs control	AD	-0.82 (-2.91, 1.26), 0.440	5B (1B, 3H)	3B (1B, 2H)	3B (2B, 3H)
CBT	vs TAU/WL	NSC	-0.82 (-1.19, -0.44), <0.001	5B (3B, 10B)	3B (2B, 7B)	3B (3B, 6B)
CBT	vs control	NSC	-0.24 (-0.69, 0.21), 0.295	20B (6B, 24H)	13B (4B, 15H)	11B (4B, 12H)
CBT	vs TAU/WL	PTSD	-0.90 (-1.11, -0.68), <0.001	4B (3B, 6B)	3B (2B, 4B)	3B (3B, 4B)
CBT	vs control	PTSD	-0.37 (-0.66, -0.09), 0.011	12B (6B, 60B)	8B (4B, 36B)	7B (4B, 28B)
CBT	vs TAU/WL	PTSD + 1, 2 or 3	-0.81 (-1.00, -0.62), <0.001	5B (3B, 6B)	3B (3B, 5B)	3B (3B, 4B)
CBT	vs TAU/WL	PTSD + 2 or 3	-0.78 (-1.31, -0.24), 0.005	5B (2B, 20B)	4B (2B, 13B)	4B (2B, 11B)
CBT	vs TAU/WL	PTSD + 3	-0.53 (-0.96, -0.09), 0.017	8B (4B, 60B)	5B (3B, 36B)	5B (3B, 28B)
CBT	vs control	PTSD + 1, 2 or 3	-0.34 (-0.62, -0.06), 0.019	14B (6B, 91B)	9B (5B, 55B)	8B (4B, 42B)
CBT	vs control	PTSD + 2 or 3	-			
CBT	vs control	PTSD + 3	-			
Exposure	vs TAU/WL	DR	-0.59 (-1.12, -0.07), 0.028	7B (3B, 78B)	5B (2B, 47B)	5B (3B, 36B)
Exposure	vs control	DR	-0.12 (-0.60, 0.37), 0.642	44B (7B, 12H)	27B (5B, 8H)	21B (4B, 7H)
Exposure	vs TAU/WL	AD	-			
Exposure	vs control	AD	-			
Exposure	vs TAU/WL	NSC	-0.73 (-1.03, -0.43), <0.001	5B (3B, 10B)	4B (3B, 7B)	4B (3B, 6B)
Exposure	vs control	NSC	-			
Exposure	vs TAU/WL	PTSD	-1.05 (-1.52, -0.58), <0.001	3B (2B, 7B)	3B (2B, 5B)	3B (2B, 5B)
Exposure	vs control	PTSD	-0.08 (-0.47, 0.30), 0.675	68B (9B, 16H)	41B (6B, 10H)	31B (6B, 8H)
Exposure	vs TAU/WL	PTSD + 1, 2 or 3	-0.86 (-1.25, -0.47), <0.001	4B (3B, 9B)	3B (2B, 6B)	3B (3B, 6B)
Exposure	vs TAU/WL	PTSD + 2 or 3	-0.56 (-0.99, -0.14), 0.009	7B (4B, 37B)	5B (3B, 23B)	5B (3B, 18B)
Exposure	vs TAU/WL	PTSD + 3	-			

Treatment	Comparator	Outcome	g (95% CI), p-value	10% CER*	22% CER*	50% CER*
Exposure	vs control	PTSD + 1, 2 or 3	-0.19 (-0.57, 0.20), 0.336	27B (7B, 25H)	17B (5B, 16H)	13B (5B, 13H)
Exposure	vs control	PTSD + 2 or 3	-			
Exposure	vs control	PTSD + 3	-			
EMDR	vs TAU/WL	DR	-0.76 (-1.35, -0.16), 0.012	5B (2B, 32B)	4B (2B, 20B)	4B (2B, 16B)
EMDR	vs control	DR	-0.35 (-1.01, 0.31), 0.312	13B (3B, 15H),	9B (3B, 10H)	7B (3B, 8H)
EMDR	vs TAU/WL	AD	-1.64 (-2.56, -0.72), 0.000	2B (1B, 5B)	2B (1B, 4B)	2B (2B, 4B)
EMDR	vs control	AD	0.25 (-0.57, 1.08), 0.548	20H (5B, 3H)	12H (5B, 2H)	10H (5B, 3H)
EMDR	vs TAU/WL	NSC	-0.61 (-1.04, -0.17), 0.006	7B (3B, 30B)	5B (3B, 19B)	4B (3B, 15B)
EMDR	vs control	NSC	-0.78 (-1.56, -0.01), 0.049	4B (2B, 566B)	4B (2B, 336B)	4B (2B, 251B)
EMDR	vs TAU/WL	PTSD	-1.26 (-2.01, -0.51), 0.001	3B (2B, 8B)	2B (1B, 6B)	3B (2B, 5B)
EMDR	vs control	PTSD	-0.69 (-1.35, -0.03), 0.041	6B (2B, 186B)	4B (2B, 111B)	4B (2B, 84B)
EMDR	vs TAU/WL	PTSD + 1, 2 or 3	-1.15 (-1.92, -0.37), 0.004	3B (2B, 12B)	2B (2B, 8B)	3B (2B, 7B)
EMDR	vs TAU/WL	PTSD + 2 or 3	-1.36 (-3.13, 0.42), 0.134	2B (1B, 11H)	2B (1B, 7H)	2 (2B, 6H)
EMDR	vs TAU/WL	PTSD + 3	-			
EMDR	vs control	PTSD + 1, 2 or 3	-0.52 (-0.97, -0.08), 0.020	8B (4B, 68B)	6B (3B, 41B)	5B (3B, 31B)
EMDR	vs control	PTSD + 2 or 3	-0.44 (-1.31, 0.43), 0.321	10B (2B, 10H)	7B (2B, 7H)	6B (2B, 6H)
EMDR	vs control	PTSD + 3	-			
CBT (T)	vs exposure (C)	DR	0.07 (-0.26, 0.39), 0.689	78C (19T, 12C)	47C (12T, 8C)	36C (10T, 7C)
CBT (T)	vs exposure (C)	AD	-			
CBT (T)	vs exposure (C)	NSC	-0.31 (-0.67, 0.04), 0.082	15T (6T, 139C)	10T (4T, 83C)	8T (4T, 63C)
CBT (T)	vs exposure (C)	PTSD	-0.03 (-0.23, 0.17), 0.784	186T (22T, 30C)	111T (14T, 19C)	84T (11T, 15C)
CBT (T)	vs exposure (C)	PTSD + 1, 2, or 3	-0.04 (-0.27, 0.19), 0.719	139T (18T, 27C)	83T (11T, 17C)	63T (9T, 13C)
CBT (T)	vs exposure (C)	PTSD + 2 or 3	-			
CBT (T)	vs exposure (C)	PTSD + 3	-			
CBT (T)	EMDR (C)	DR	0.28 (-0.29, 0.34), 0.338	17C (16T, 14C)	11C (11T, 9C)	9C (9T, 8C)

Treatment	Comparator	Outcome	g (95% CI), p-value	10% CER*	22% CER*	50% CER*
CBT (T)	EMDR (C)	AD	-			
CBT (T)	EMDR (C)	NSC	-			
CBT (T)	EMDR (C)	PTSD	0.37 (0.03, 0.71), 0.031	12C (186C, 5C)	8C (111C, 4C)	7C (84C, 4C)
CBT (T)	EMDR (C)	PTSD + 1, 2, or 3	0.31 (-0.07, 0.68), 0.111	15C (78T, 6C)	10C (47T, 4C)	8C (36T, 4C)
CBT (T)	EMDR (C)	PTSD + 2 or 3	-			
CBT (T)	EMDR (C)	PTSD + 3	-			
EMDR (T)	Exposure (C)	DR	-0.10 (-0.51, 0.31), 0.640	54T (8T, 15C)	33T (6T, 10C)	25T (5T, 8C)
EMDR (T)	Exposure (C)	AD	-			
EMDR (T)	Exposure (C)	NSC	0.16 (-0.25, 0.57), 0.444	32C (20T, 7C)	20C (12T, 47C)	16C (10T, 5C)
EMDR (T)	Exposure (C)	PTSD	0.10 (-0.28, 0.49), 0.604	54C (17T, 9C)	33C (11T, 6C)	25C (9T, 5C)
EMDR (T)	Exposure (C)	PTSD + 1, 2, or 3	0.06 (-0.35, 0.46), 0.789	91C (35T, 9C)	55C (9T, 6C)	42C (7T, 6C)
EMDR (T)	Exposure (C)	PTSD + 2 or 3	0.06 (-0.35, 0.46), 0.789	91C (35T, 9C)	55C (9T, 6C)	42C (7T, 6C)
EMDR (T)	Exposure (C)	PTSD + 3	-			
IPT	vs TAU/WL	PTSD + DR	-1.02 (-1.65, -0.39), 0.002	3B (2B, 12B)	3B (2B, 8B)	3B (2B, 7B)
Mindfulness	vs TAU/WL	DR	-1.60 (-2.43, -0.77), <0.001	2B (1B, 5B)	2B (1B, 4B)	2B (2B, 4B)
TMT (T)	Exposure (C)	PTSD + DR + AD	-0.09 (-0.79, 0.61), 0.801	60T (5T, 7C)	36T (3T, 5C)	28T (4T, 4C)
TMT (T)	Exposure (C)	PTSD + DR	-0.05 (-0.46, 0.36), 0.815	110T (9T, 13C)	66T (6T, 8C)	50T (6T, 7C)
DET (T)	CBT (C)	PTSD + NSC	0.27 (-0.07, 0.60), 0.118	18C (78T, 7C)	11C (47T, 5C)	9C (36T, 4C)
CBT + ERT (T)	CBT + SC (C)	PTSD + NSC	-0.04 (-0.51, 0.43), 0.866	139T (8T, 10C)	83T (6T, 7C)	63T (5T, 6C)
DBT + Exp (T)	CBT (C)	PTSD + NSC	0.51 (-0.43, 1.45), 0.291	8C (10T, 2C)	7C (7T, 2C)	5C (6T, 2C)
EMDR (T)	STBT (C)	PTSD + DR	-0.16 (-0.61, 0.29), 0.486	32T (7T, 16C)	20T (5T, 11C)	16T (4T, 9C)

Abbreviations: AD=affect dysregulation; CBT=cognitive behavioural therapy; CPTSD=complex posttraumatic stress disorder; CER=control event rate; DBT=dialectical behaviour therapy; DET=dialogical exposure therapy; DR=disturbances in relationships; DSO=disturbances in self-organisation; EMDR=eye-movement and desensitisation and reprocessing therapy; ERT=emotion regulation training; IPT=interpersonal psychotherapy; NSC=negative self-concept; PTSD=posttraumatic stress disorder; PTSD + 1, 2 or 3=PTSD + 1, 2 or 3 CPTSD (DSO) outcomes; PTSD + 2 or 3=PTSD + 2 or 3 CPTSD (DSO) outcomes; PTSD + 3=PTSD + all 3 CPTSD (DSO) outcomes;

SC=supportive counselling; STBT=stabilisation treatment; TAU=treatment as usual; TMT=trauma management therapy; WL=waiting list. *Note: B = benefit; H = harm; T = favours T; C = favours C

L. Table L.1. Meta-regression Moderators (univariate)

Moderator (univariate)	Coefficients (95% CI)	R² or ΔR²	p-value	Effects per group	Quality
Random sequence generation (low vs unclear or high risk of bias, k=52)	Unclear risk of bias -0.14 (-0.43, +0.16)	2%	0.358	Low (k=26) -0.64 (-0.84, -0.45) Unclear (k=26) -0.78 (-0.99, -0.56) High (k=0)	Low -1 missing information -1 imprecise
Allocation concealment (low vs unclear or high risk of bias, k=52)	Unclear risk of bias -0.24 (-0.53, +0.06)	5%	0.112	Low (k=20) -0.57 (-0.79, -0.35) Unclear (k=32) -0.80 (-0.99, -0.61) High (k=0)	Low -1 missing information -1 imprecise
Detection bias (low vs unclear or high risk of bias, k=52)	High risk of bias -0.04 (-0.35, +0.28)	1%	0.820	Low (k=35) -0.69 (-0.87, -0.52) Unclear (k=0) High (k=17) -0.72 (-0.99, -0.47)	Moderate -1 imprecise
Selective reporting bias (low vs unclear or high risk of bias, k=52)	High risk of bias -0.35 (-0.81, +0.11)	7%	0.131	Low (k=5) -0.39 (-0.82, 0.04) Unclear (k=0) High (k=47) -0.74 (-0.89, -0.59)	Moderate -1 imprecise

Moderator (univariate)	Coefficients (95% CI)	R ² or ΔR ²	p-value	Effects per group	Quality
Attrition bias (low vs unclear or high risk of bias, k=52)	High risk of bias +0.10 (-0.20, +0.39)	1%	0.524	Low (k=31) -0.65 (-0.87, -0.42) Unclear (k=0) High (k=21) -0.74 (-0.93, -0.55)	Moderate -1 imprecise
Quality (high quality vs low quality, k=52)	Low quality +0.05 (-0.26, +0.35)	0%	0.754	Low quality (k=20) -0.67 (-0.91, -0.44) High quality (k=32) -0.72 (-0.91, -0.54)	Moderate -1 imprecise
CPTSD symptoms (PTSD alone vs various CPTSD, k=52)	PTSD + ER -0.57 (-1.44, +0.32) PTSD + NC + ID + ER -0.03 (-1.01, +0.50) PTSD + ID -0.20 (-0.92, 0.53) PTSD + NC -0.11 (-0.85, 0.63) PTSD + NC + ID -0.26 (-1.11, +0.59)	PTSD + AD 1% PTSD + NSC + DR + AD 2% PTSD + DR 3% PTSD + NSC 3% PTSD + NSC + DR 7% Overall 7%	PTSD + AD 0.215 PTSD + NSC + DR + AD 0.955 PTSD + DR 0.593 PTSD + NSC 0.778 PTSD + NSC + DR 0.548 Overall 0.741	PTSD (k=3) -0.53 (-1.25, 0.18) PTSD + AD (k=4) -1.09 (-1.66, -0.53) PTSD + NSC + DR + AD (k=2) -0.55 (-1.27, 0.17) PTSD + DR (k=24) -0.72 (-0.94, -0.50) PTSD + NSC (k=15) -0.63 (-0.90, -0.36) PTSD + NSC + DR (k=4) -0.78 (-1.29, -0.27)	Moderate -1 imprecise
Comparator (TAU/WL vs control, k=52)	Control +0.48 (+0.18, +0.77)	28%	0.001	TAU/WL (k=38) -0.83 (-0.99, -0.67) Control (k=14) -0.35 (-0.60, -0.10)	Moderate -1 imprecise

Moderator (univariate)	Coefficients (95% CI)	R ² or ΔR ²	p-value	Effects per group	Quality
Treatments (individual CBT vs others, k=52)	EMDR -0.08 (-0.53, +0.38) Exposure +0.04 (-0.53, +0.38) Group CBT +0.42 (-0.15, +0.99) Group IPT -0.29 (-1.34, +0.75)	EMDR 1% Exposure 0% Group CBT 7% Group IPT 2% Overall 10%	EMDR 0.736 Exposure 0.834 Group CBT 0.150 Group IPT 0.581 Overall 0.608	CBT (k=33) -0.73 (-0.91, -0.54) EMDR (k=7) -0.80 (-1.23, -0.38) Exposure (k=8) -0.68 (-1.06, -0.31) Group CBT (k=3) -0.30 (-0.86, 0.25) Group IPT (k=1) -1.02 (-2.07, 0.04)	Moderate -1 imprecise
Therapy format (individual vs group, k=52)	Group only or in addition +0.27 (-0.25, +0.78)	4%	0.309	Individual (k=48) -0.73 (-0.88, -0.58) Group only or in addition (k=4) -0.46 (-0.95, 0.03)	Moderate -1 imprecise
Trauma onset (Adult vs child, k=48)	Child +0.18 (-0.16, +0.52)	2%	0.308	Adult (k=37) -0.76 (-0.93, -0.59) Child (k=11) -0.58 (-0.88, -0.29)	Moderate -1 imprecise

Abbreviations: AD=affect dysregulation; CBT=cognitive behavioural therapy; DR=disturbances in relationships; EMDR=eye-movement and desensitisation and reprocessing therapy; k= number of included comparisons; NSC=negative self-concept; PTSD=posttraumatic stress disorder; CPTSD=complex posttraumatic stress disorder; TAU=treatment as usual; WL=waiting list.

M. Table M.1. Meta-regression Moderators (multivariate)

Moderator (k=48, multivariate)	Coefficients (95% CI)	ΔR^2	p-value	Narrative summary	Quality
Quality (high vs low)	Low +0.30 (+0.00, +0.61)	Low 1%	Low 0.048	The effect for low quality studies is 0.30 lower than high quality studies	Moderate -1 imprecise
CPTSD symptoms (PTSD alone vs various CPTSD)	PTSD + AD -0.13 (-1.06, +0.80) PTSD + NSC + DR + AD +0.39 (-0.62, +1.40) PTSD + DR +0.28 (-0.43, +1.00) PTSD + NSC +0.06 (-0.63, +0.75) PTSD + NSC + DR +0.25 (-0.52, +1.02)	PTSD + AD -1% PTSD + NSC + DR + ER 1% PTSD + DR 0% PTSD + NSC 0% PTSD + NSC + DR 2% Overall 2%	PTSD + AD 0.783 PTSD + NSC + DR + ER 0.447 PTSD + DR 0.437 PTSD + NSC 0.860 PTSD + NSC + DR 0.518 Overall 0.504	No association between number or type of CPTSD symptoms reported and effect size was observed (direction of effect favoured smaller effects with more CPTSD symptoms).	Moderate -1 imprecise
Comparator (TAU/WL vs control)	Control +0.69 (+0.38, +1.00)	Control 34%	Control <0.0001	Use of a control condition is associated with a moderate to large reduction in effect size.	High

Moderator (k=48, multivariate)	Coefficients (95% CI)	ΔR^2	p-value	Narrative summary	Quality
Treatments (individual CBT vs others)	EMDR -0.25 (-0.69, +0.18) Exposure +0.07 (-0.30, +0.44) Group CBT +0.23 (-0.36, 0.82) Group IPT -0.70 (-1.66, 0.25)	EMDR 3% Exposure 0% Group CBT 7% Group IPT 1% Overall 11%	EMDR 0.254 Exposure 0.697 Group CBT 0.441 Group IPT 0.147 Overall 0.282	No association between overall effect size and type of intervention was observed.	Moderate -1 imprecise
Trauma onset (adult vs child)	Child +0.35 (+0.02, +0.69)	Child 5%	Child 0.038	Inclusion of participants with predominantly childhood-onset trauma is associated with a small-moderate reduction in effect size, compared to trials where participants have mainly adult-onset trauma	Low -1 imprecise -1 ecological bias

Abbreviations: AD=affect dysregulation; CBT=cognitive behavioural therapy; DR=disturbances in relationships; EMDR=eye-movement and desensitisation and reprocessing therapy; k= number of included comparisons; NSC=negative self-concept; PTSD=posttraumatic stress disorder; CPTSD=complex posttraumatic stress disorder; TAU=treatment as usual; WL=waiting list.

N. Forest Plots – Cognitive/imagery modification with or without exposure vs TAU/WL or non-specific control

Fig. N.1. Disturbances in relationships (DR): Cognitive/imagery modification with or without exposure vs TAU/WL

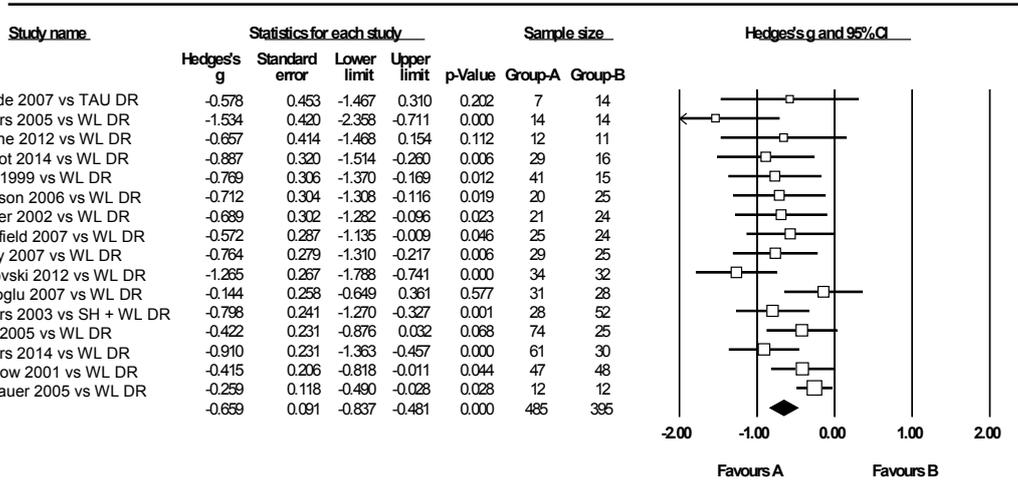


Fig. N.2. Disturbances in relationships (DR): Cognitive/imagery modification with or without exposure vs non-specific control

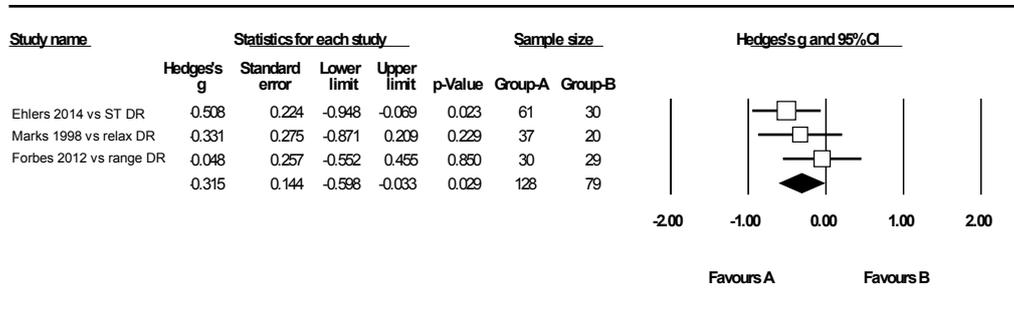


Fig. N.3. Affect dysregulation (AD): Cognitive/imagery modification with or without exposure vs TAU/WL

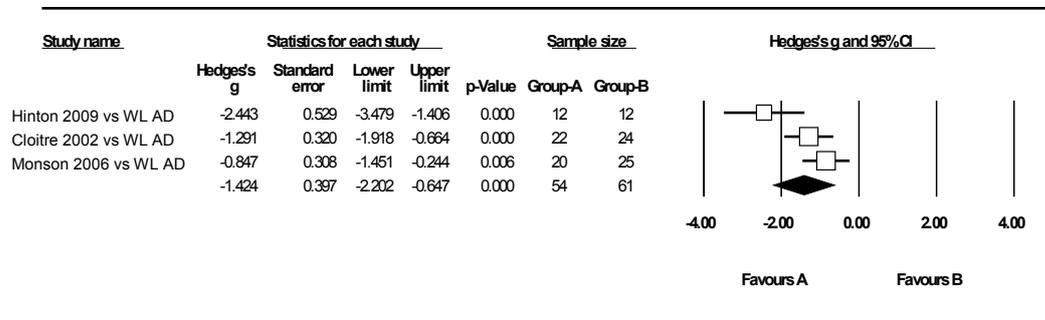


Fig. N.4. Affect dysregulation (AD): Cognitive/imagery modification with or without exposure vs non-specific control

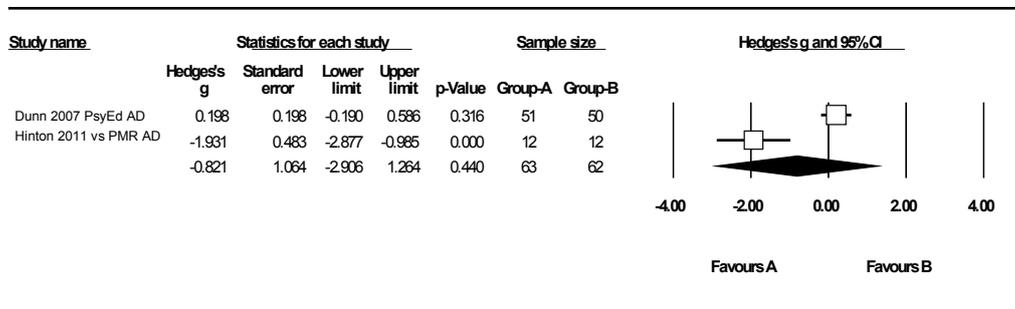


Fig. N.5. Negative self-concept (NSC): Cognitive/imagery modification with or without exposure vs TAU/WL

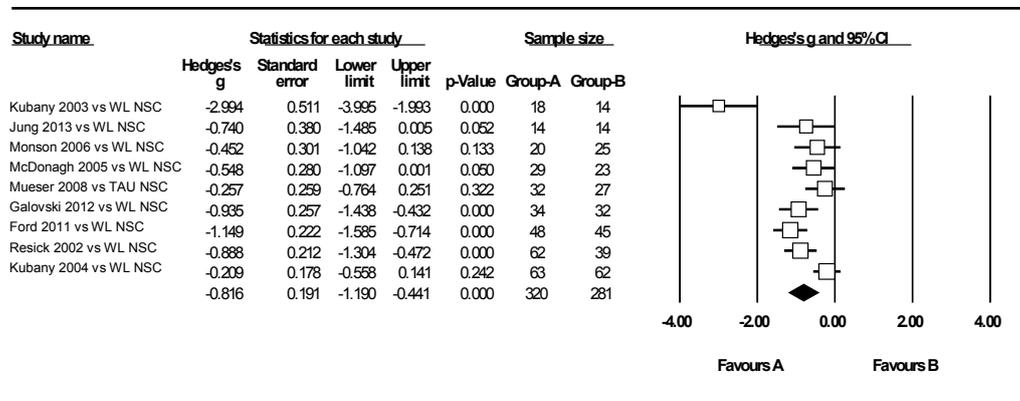


Fig. N.6. Negative self-concept (NSC): Cognitive/imagery modification with or without exposure vs non-specific control

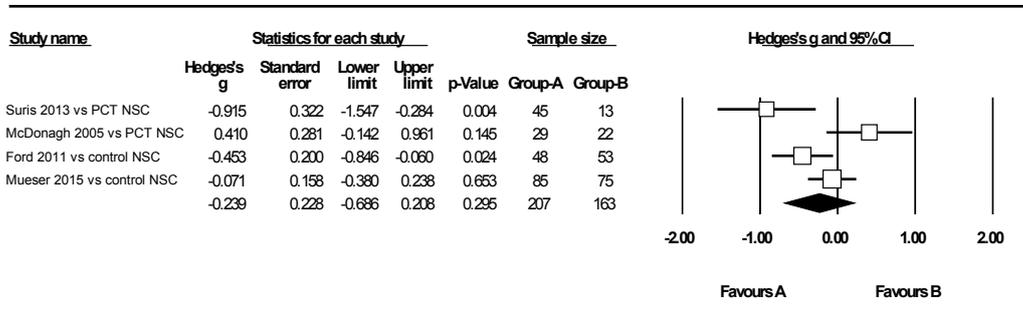


Fig. N.7. PTSD: Cognitive/imagery modification with or without exposure vs TAU/WL

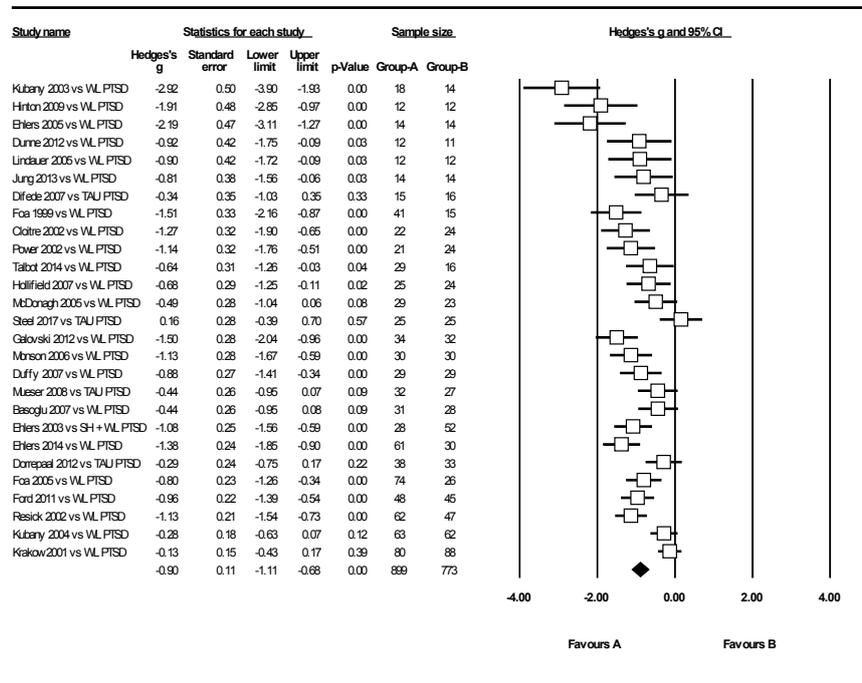


Fig. N.8. PTSD: Cognitive/imagery modification with or without exposure vs non-specific control

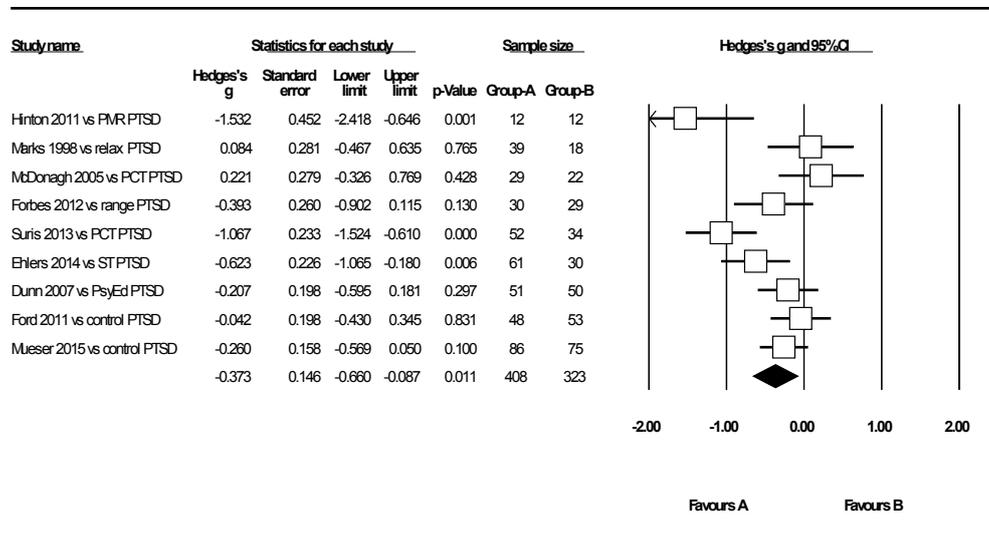


Fig. N.9. PTSD plus 1, 2 or 3 CPTSD outcomes: Cognitive/imagery modification with or without exposure vs TAU/WL

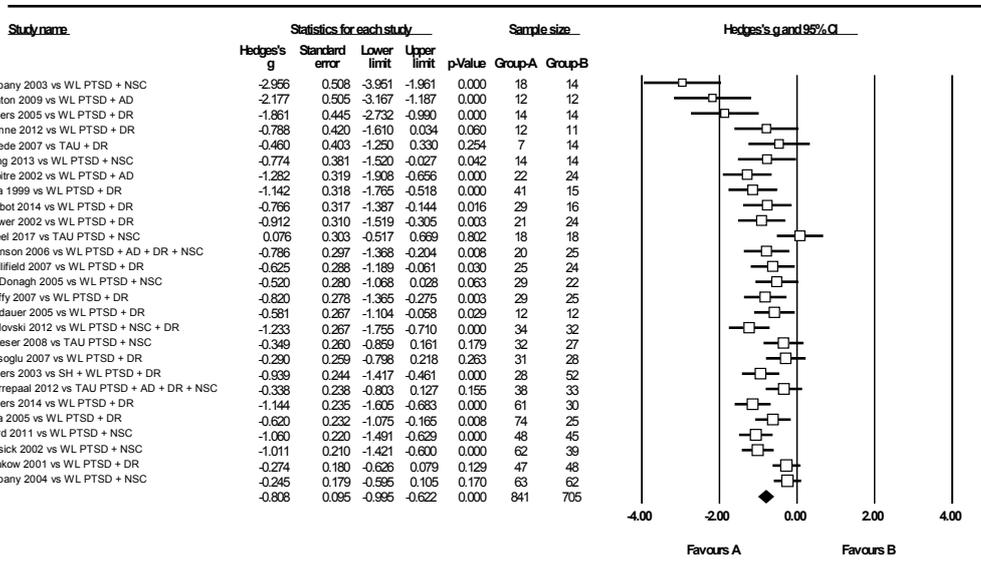


Fig. N.10. PTSD plus 2 or 3 CPTSD outcomes: Cognitive/imagery modification with or without exposure vs TAU/WL

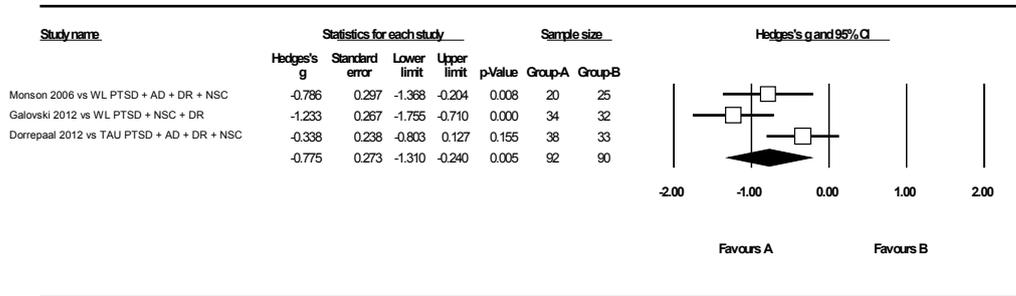


Fig. N.11. PTSD plus all 3 CPTSD outcomes: Cognitive/imagery modification with or without exposure vs TAU/WL

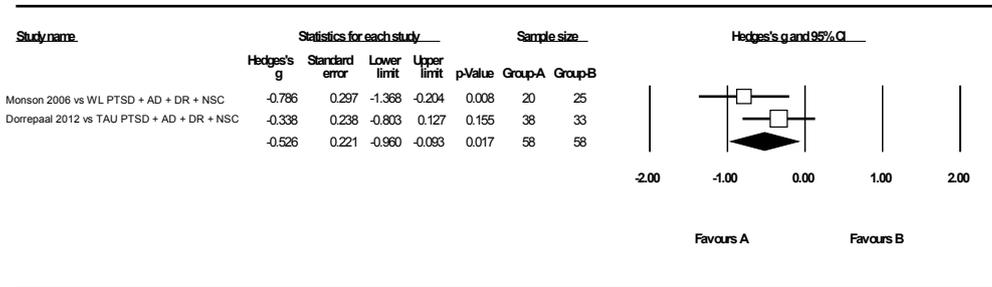
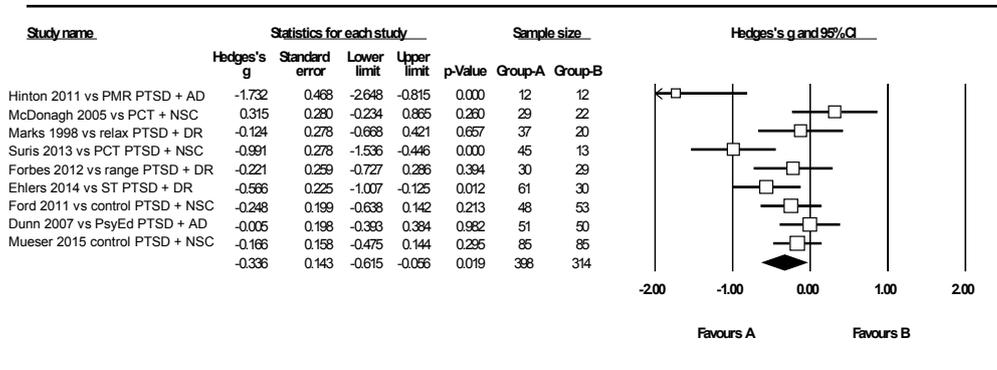


Fig. N.12. PTSD plus 1, 2 or 3 CPTSD outcomes: Cognitive/imagery modification with or without exposure vs non-specific control



O. Forest Plots – Exposure only vs TAU/WL or non-specific control

Fig. O.1. Disturbances in relationships (DR): Exposure only vs TAU/WL

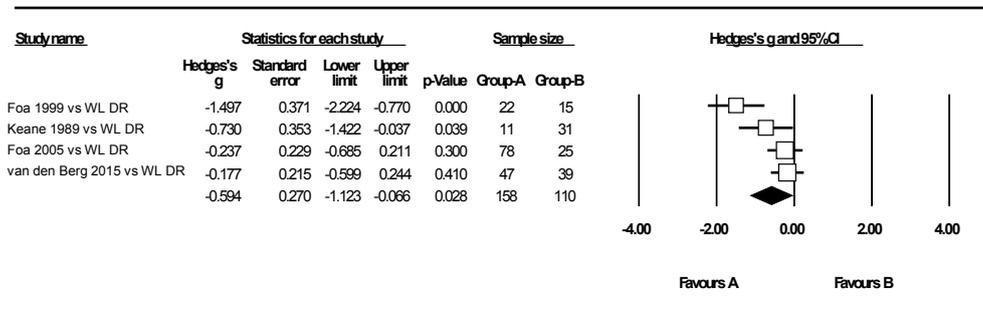


Fig. O.2. Disturbances in relationships (DR): Exposure only vs non-specific control

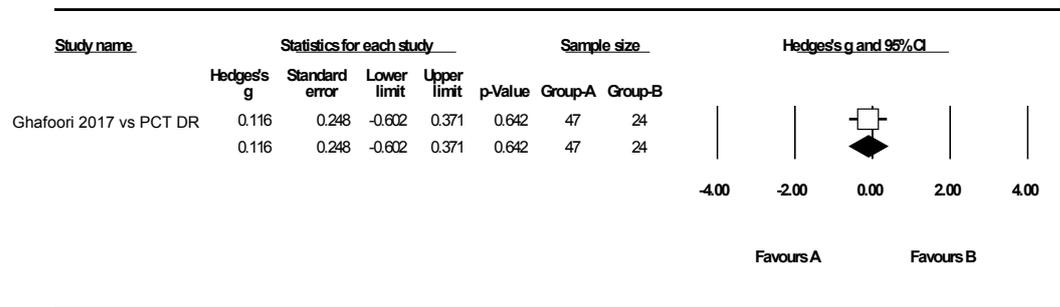


Fig. O.3. Negative self-concept (NSC): Exposure only vs TAU/WL

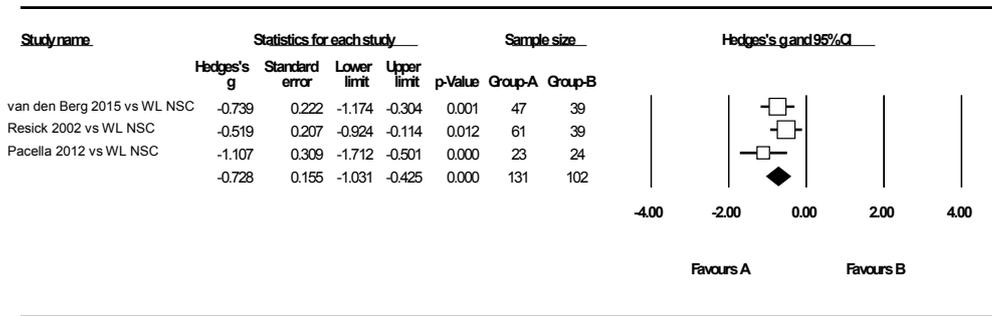


Fig. O.4. PTSD: Exposure only vs TAU/WL

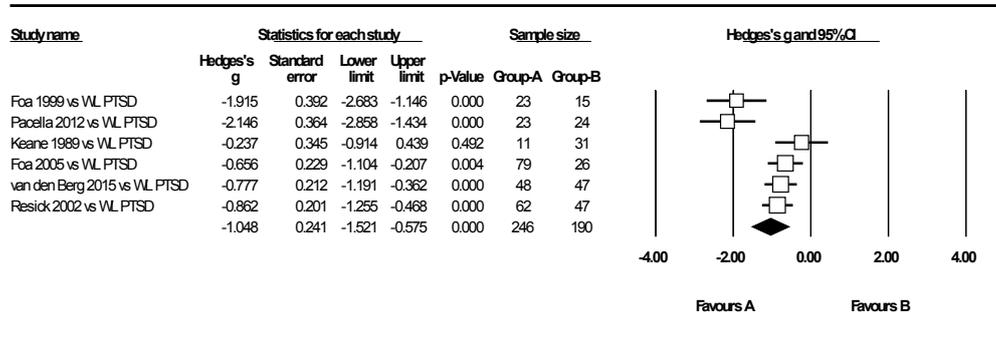


Fig. O.5. PTSD: Exposure only vs non-specific control

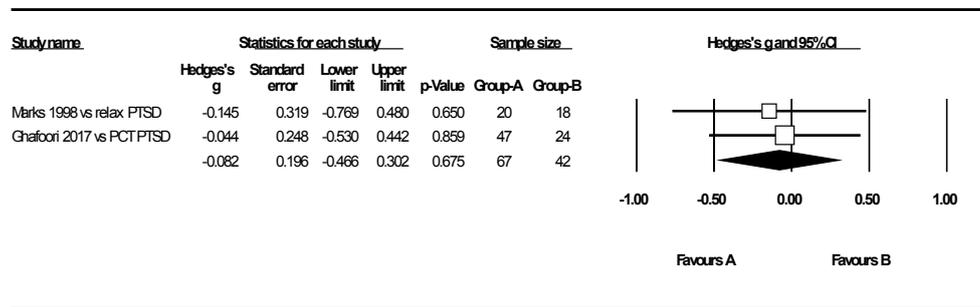


Fig. O.6. PTSD plus 1, 2 or 3 CPTSD outcomes: Exposure only vs TAU/WL

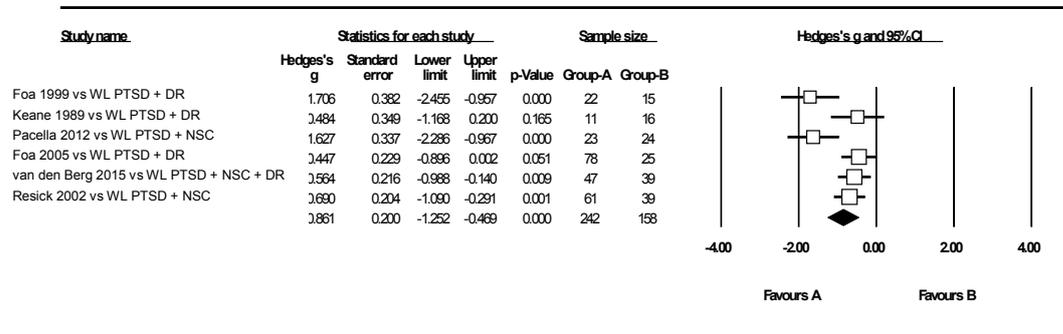


Fig. O.7. PTSD plus 2 or 3 CPTSD outcomes: Exposure only vs TAU/WL

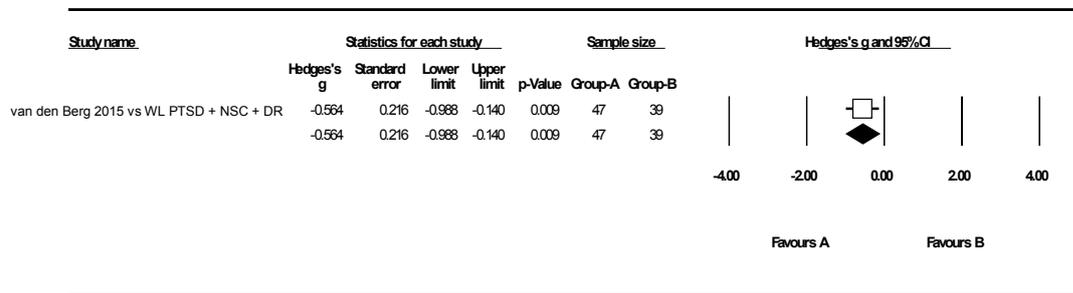
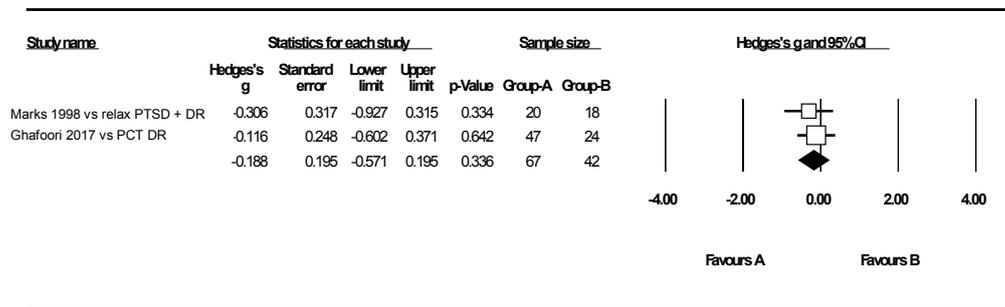


Fig. O.8. PTSD plus 1, 2 or 3 CPTSD outcomes: Exposure only vs non-specific control



P. Forest Plots – EMDR vs TAU/WL or non-specific control

Fig. P.1. Disturbances in relationships (DR): EMDR vs TAU/WL

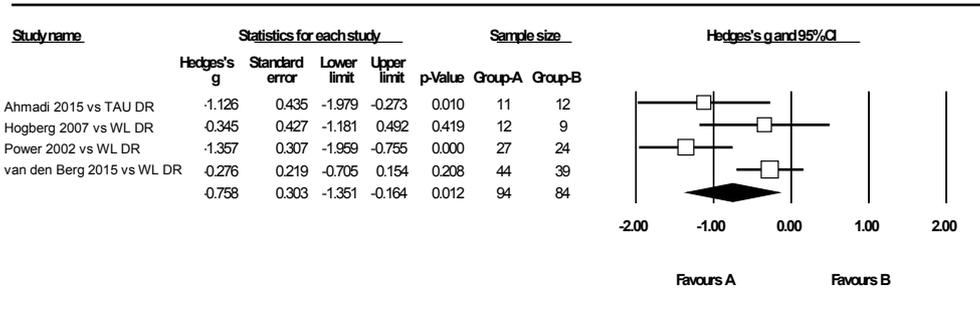


Fig. P.2. Disturbances in relationships (DR): EMDR vs non-specific control

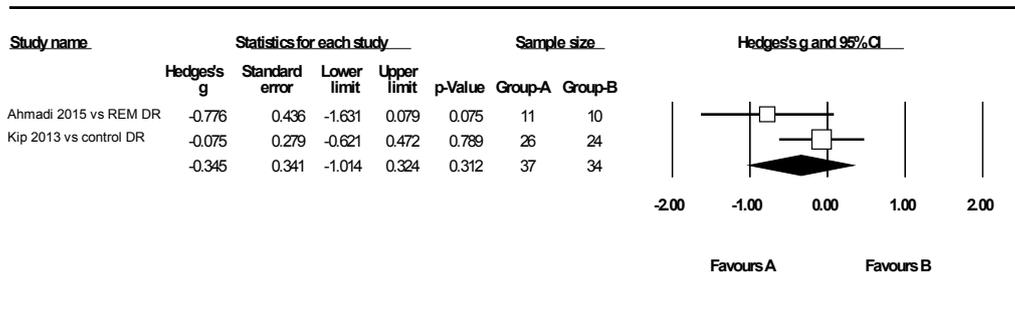


Fig. P.3. Affect dysregulation (AD): EMDR vs TAU/WL

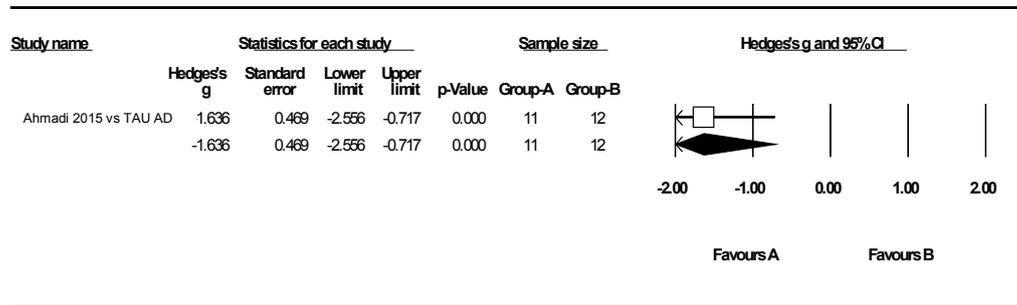


Fig. P.4. Affect dysregulation (AD): EMDR vs non-specific control

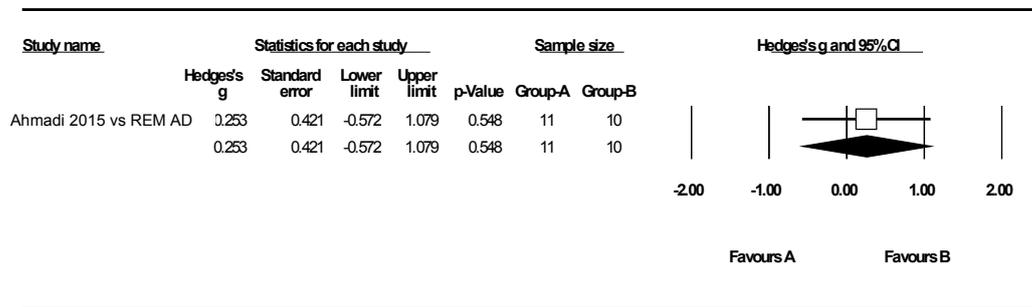


Fig. P.5. Negative self-concept (NSC): EMDR vs TAU/WL

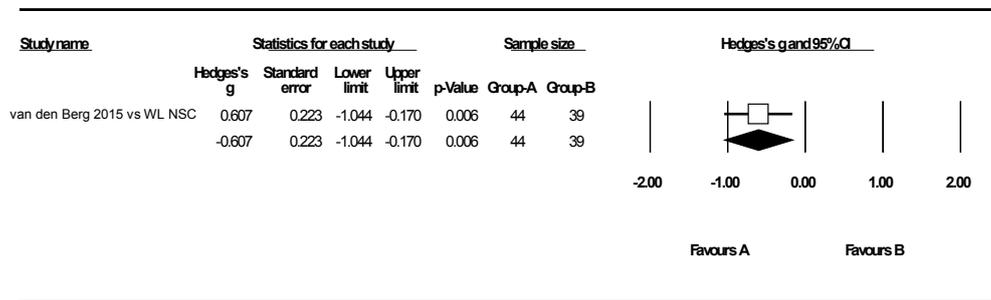


Fig. P.6. Negative self-concept (NSC): EMDR vs non-specific control

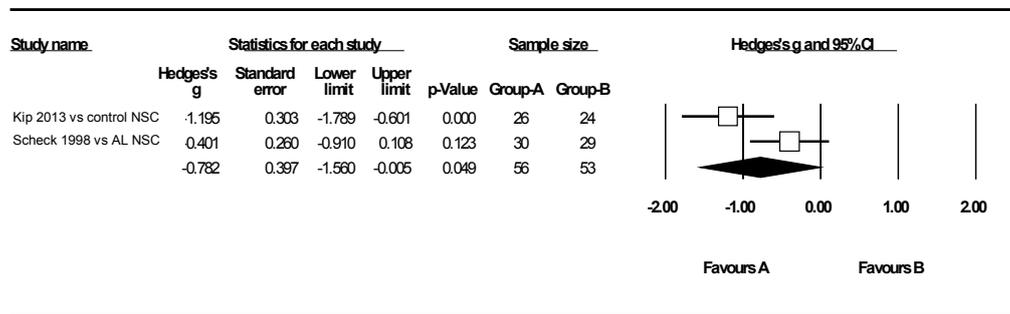


Fig. P.7. PTSD: EMDR vs TAU/WL

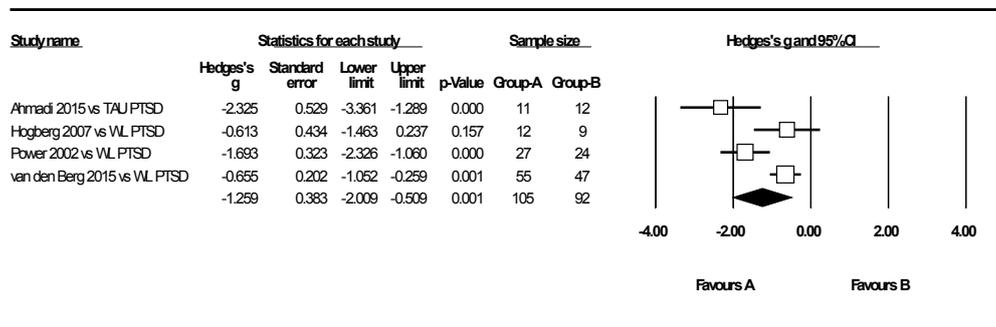


Fig. P.8. PTSD: EMDR vs non-specific control

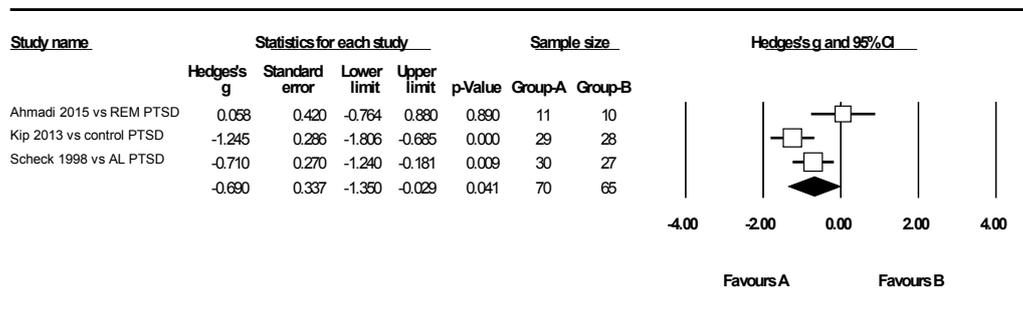


Fig. P.9. PTSD plus 1, 2 or 3 CPTSD outcomes: EMDR vs TAU/WL

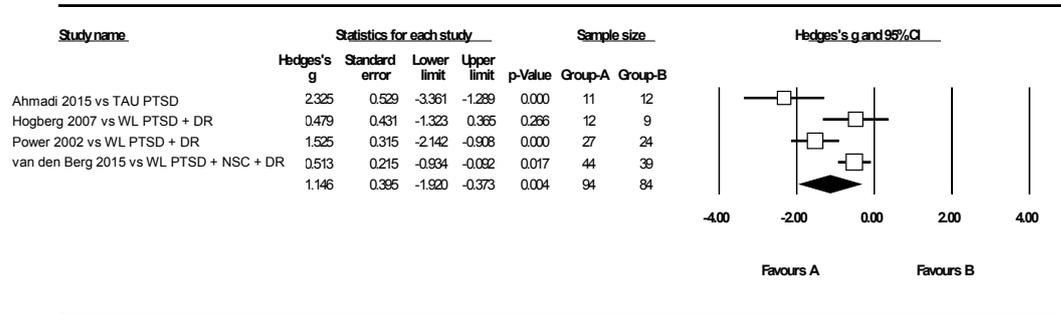


Fig. P.10. PTSD plus 2 or 3 CPTSD outcomes: EMDR vs TAU/WL

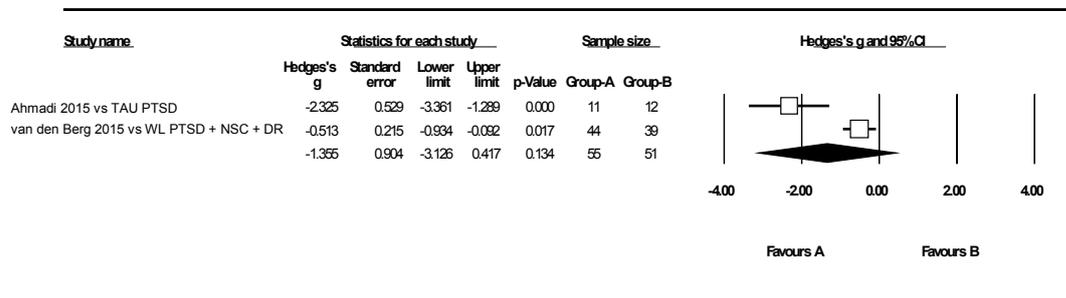


Fig. P.11. PTSD plus 1, 2 or 3 CPTSD outcomes: EMDR vs non-specific control

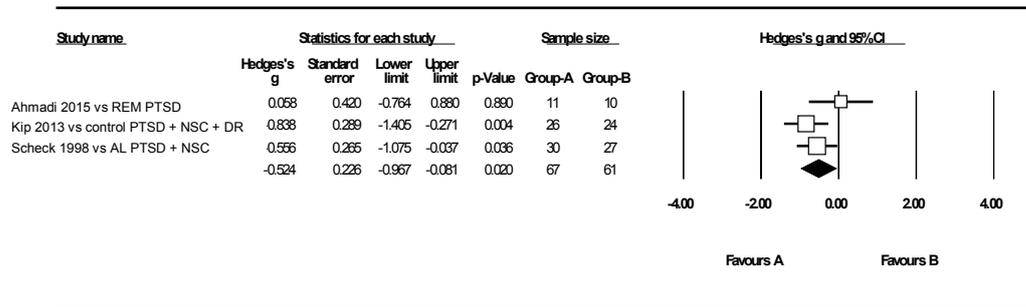
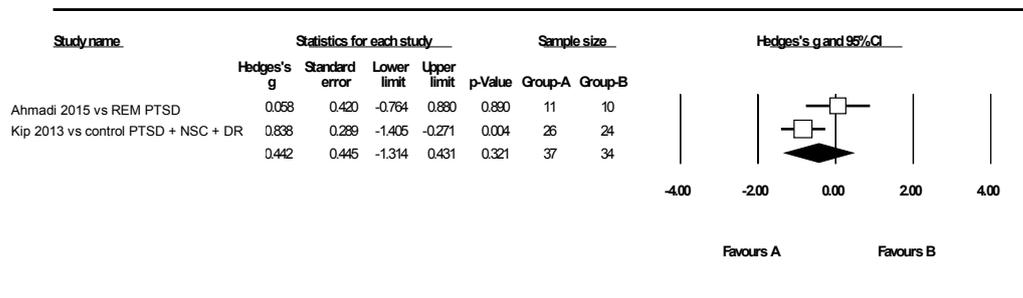


Fig. P.12. PTSD plus 2 or 3 CPTSD outcomes: EMDR vs non-specific control



Q. Forest Plots – Comparison of CBT, Exposure and EMDR

Fig. Q.1. Disturbances in relationships (DR): CBT vs Exposure alone

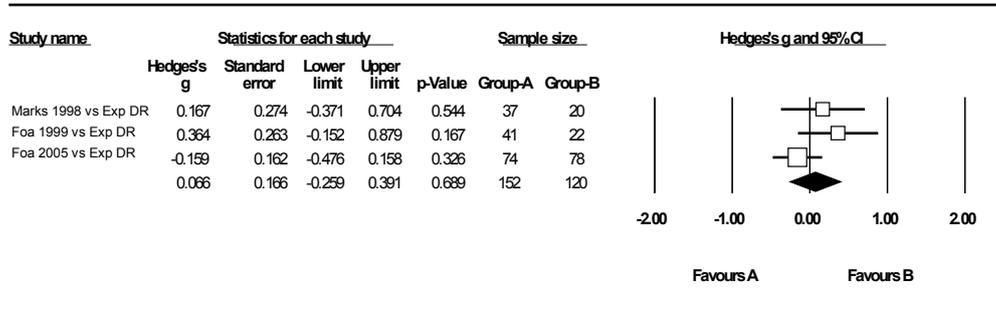


Fig. Q.2. Negative self-concept (NSC): CBT vs Exposure alone

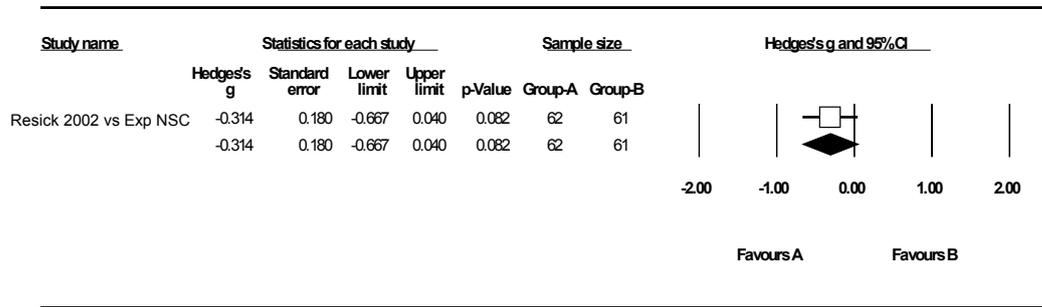


Fig. Q.3. PTSD: CBT vs Exposure alone

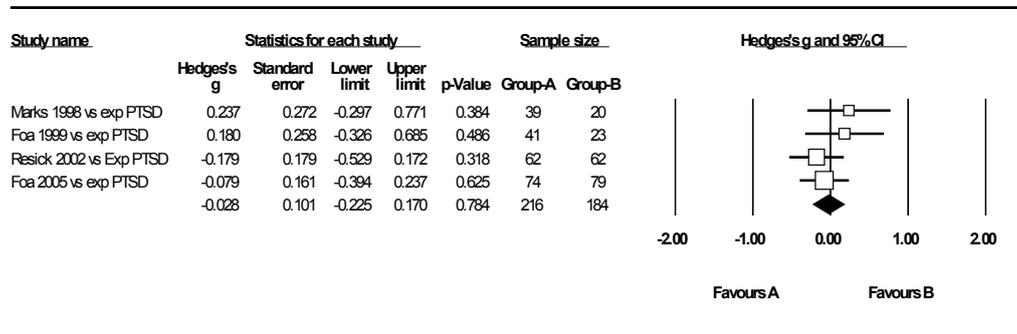


Fig. Q.4. PTSD plus 1, 2 or 3 CPTSD outcomes: CBT vs Exposure alone

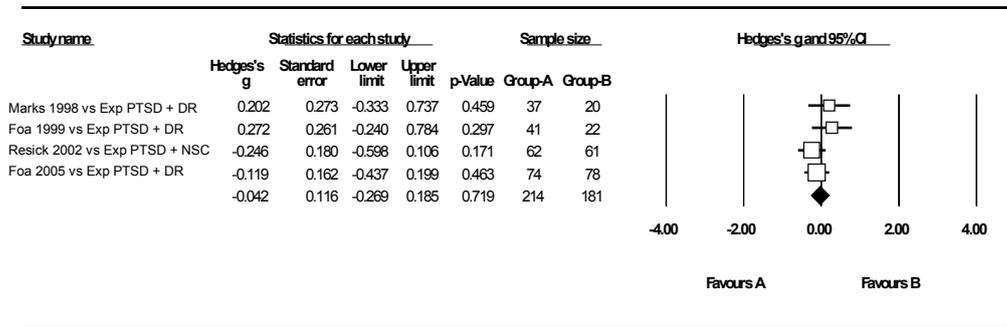


Fig. Q.5. Disturbances in relationships (DR): CBT vs EMDR

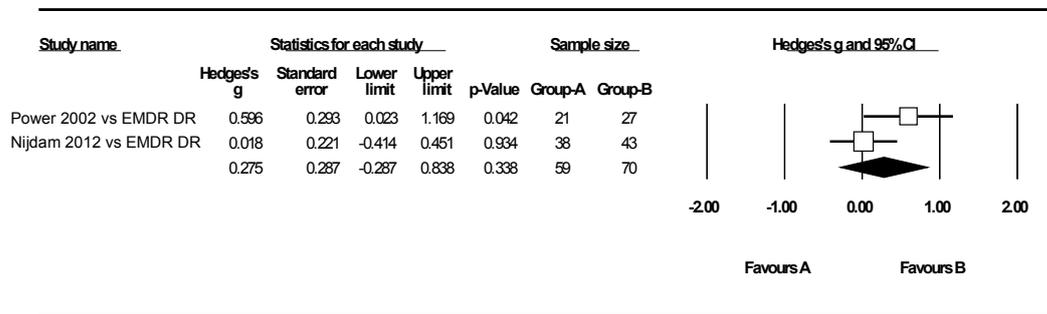


Fig. Q.6. PTSD: CBT vs EMDR

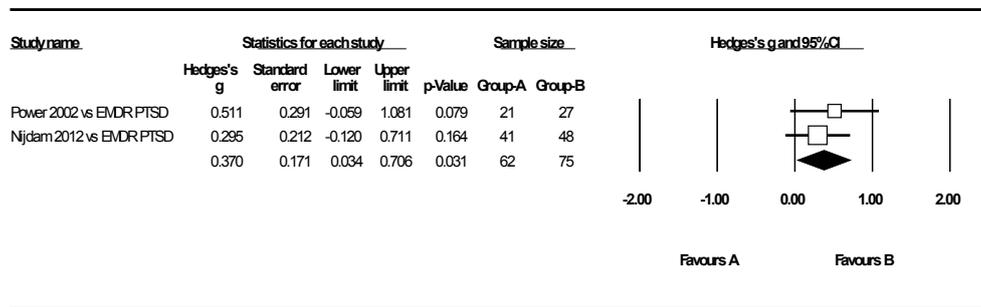


Fig. Q.7. PTSD plus 1, 2 or 3 CPTSD outcomes: CBT vs EMDR

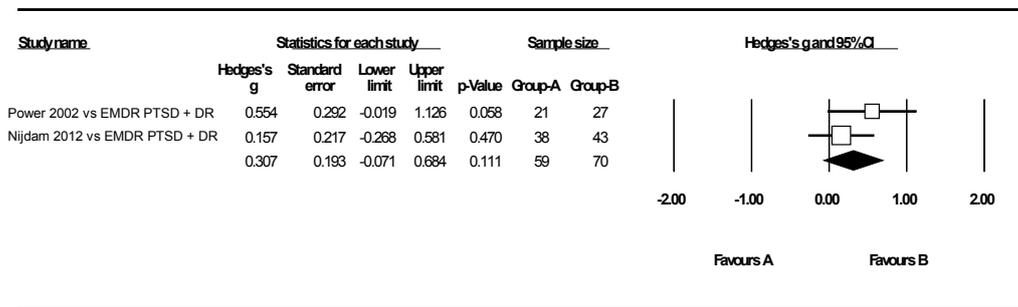


Fig. Q.8. Disturbances in relationships (DR): EMDR vs Exposure alone

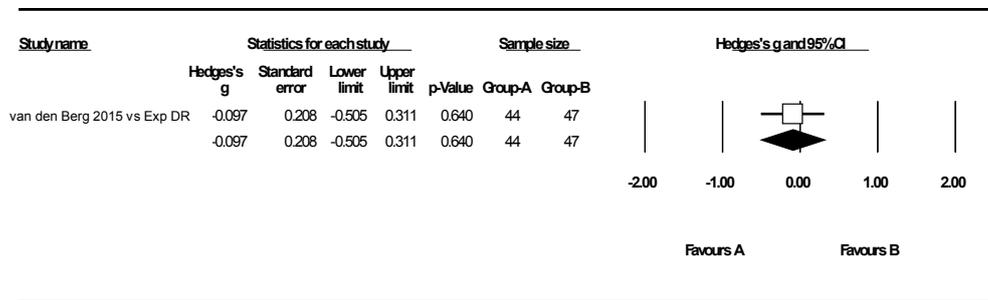


Fig. Q.9. Negative self-concept (NSC): EMDR vs Exposure alone

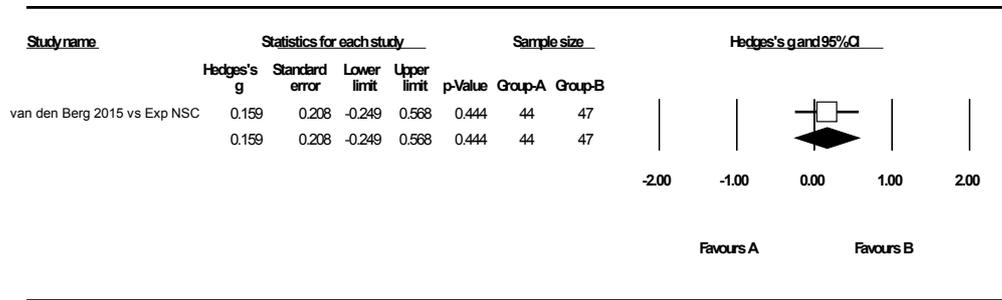


Fig. Q.10. PTSD: EMDR vs Exposure alone

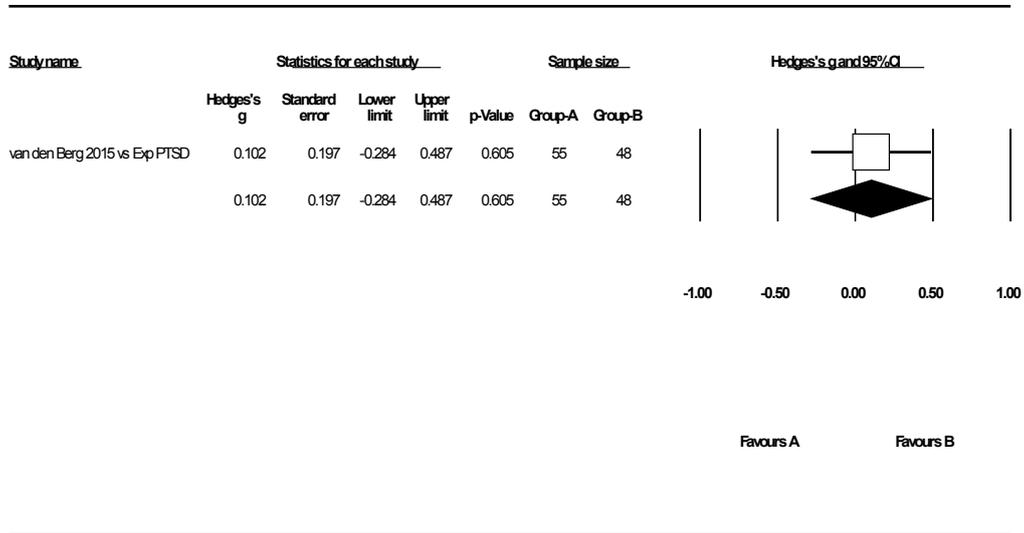


Fig. Q.11. PTSD plus 1, 2 or 3 CPTSD outcomes: EMDR vs Exposure alone

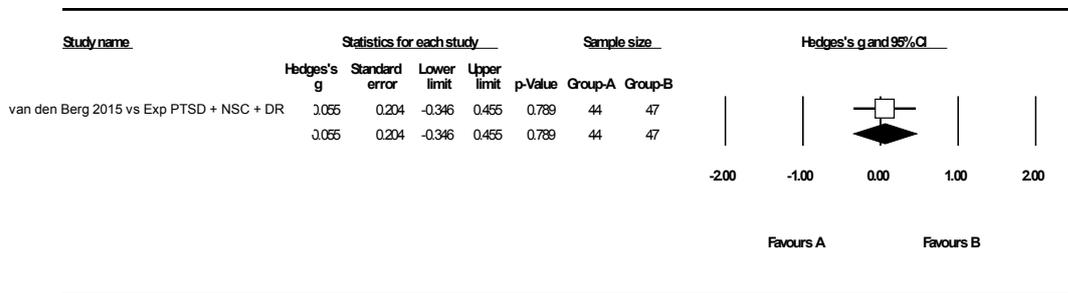
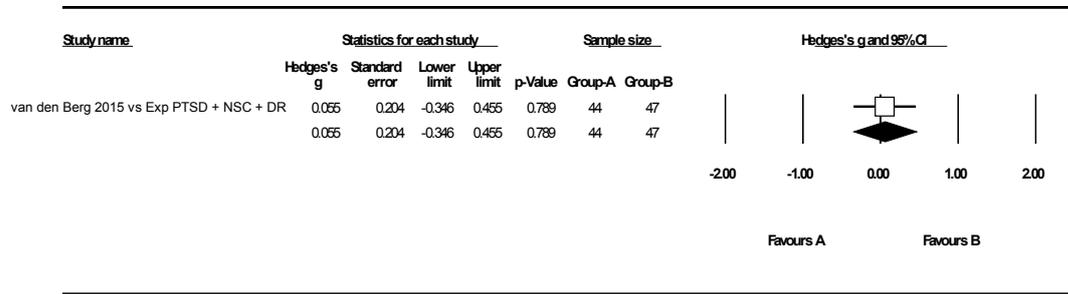


Fig. Q.12. PTSD plus 2 or 3 CPTSD outcomes: EMDR vs Exposure alone



R. Bubble Plots – Meta-regression Moderators (univariate)

Fig. R.1. Random sequence generation (low vs unclear or high risk of bias, k=52)

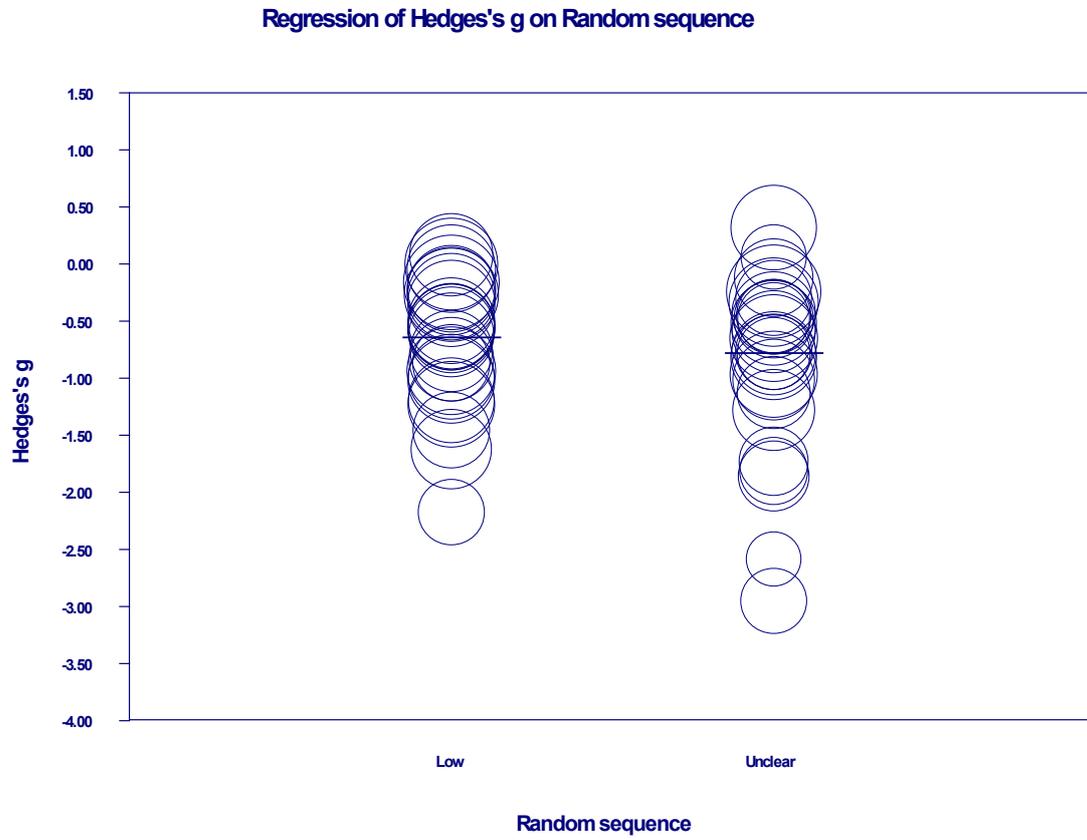


Fig. R.2. Allocation concealment (low vs unclear or high risk of bias, k=52)



Fig. R.3. Detection bias (low vs unclear or high risk of bias, k=52)

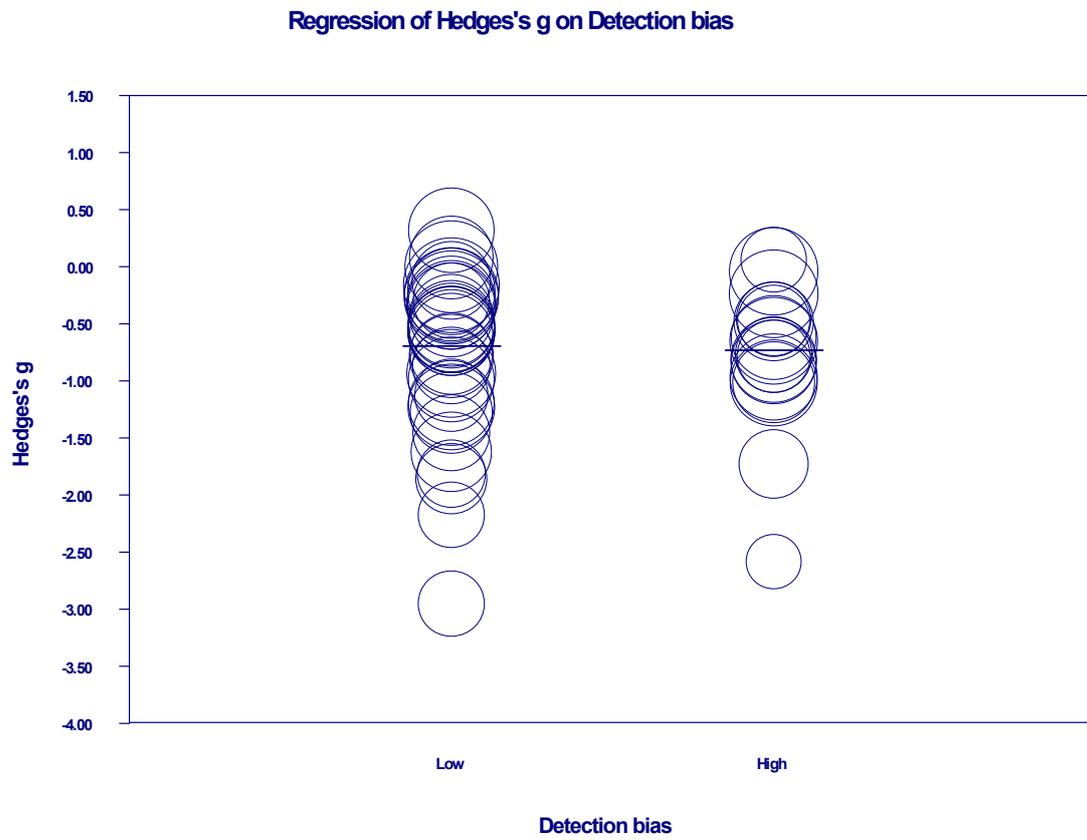


Fig. R.4. Selective reporting bias (low vs unclear or high risk of bias, k=52)

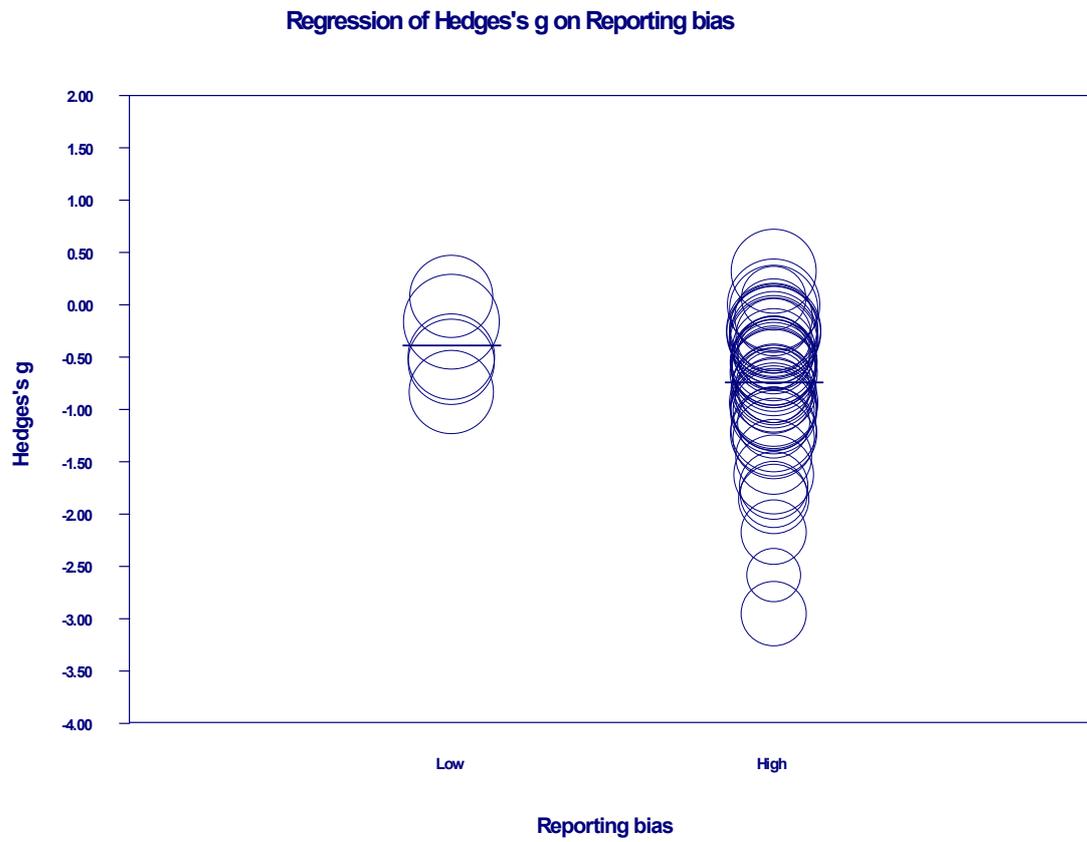


Fig. R.5. Attrition bias (low vs unclear or high risk of bias, k=52)

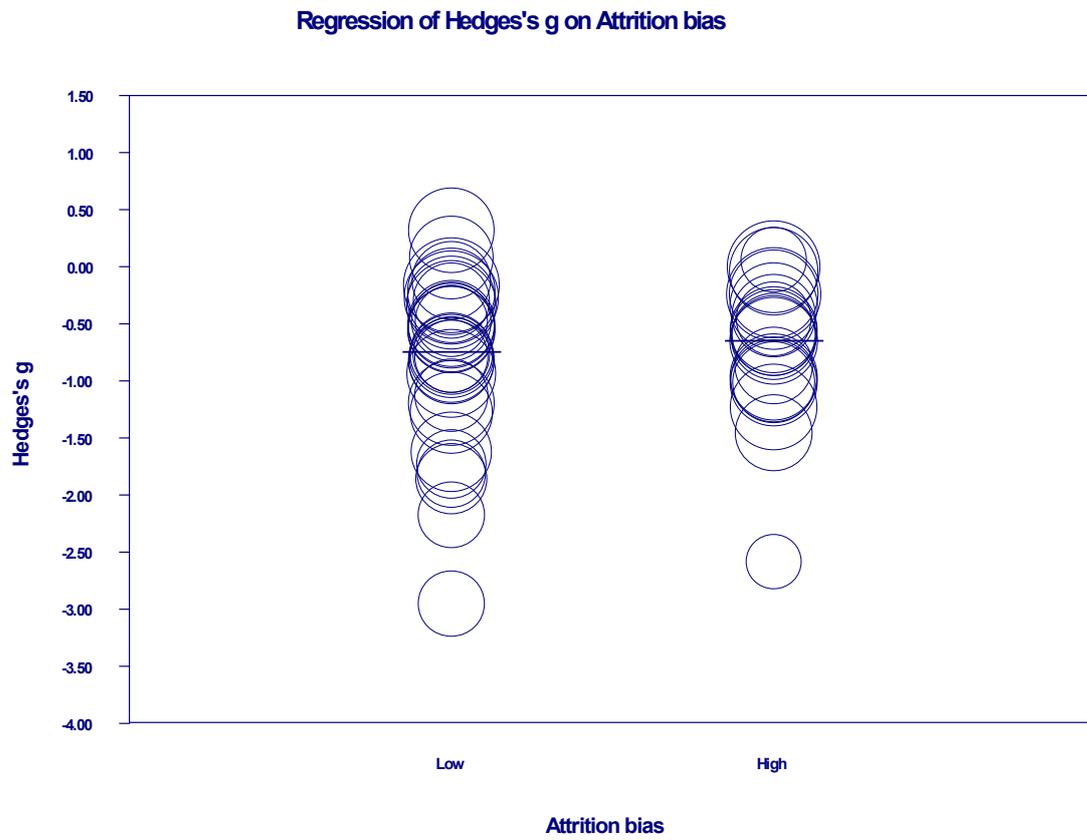


Fig. R.6. Overall quality (high quality vs low quality, k=52)

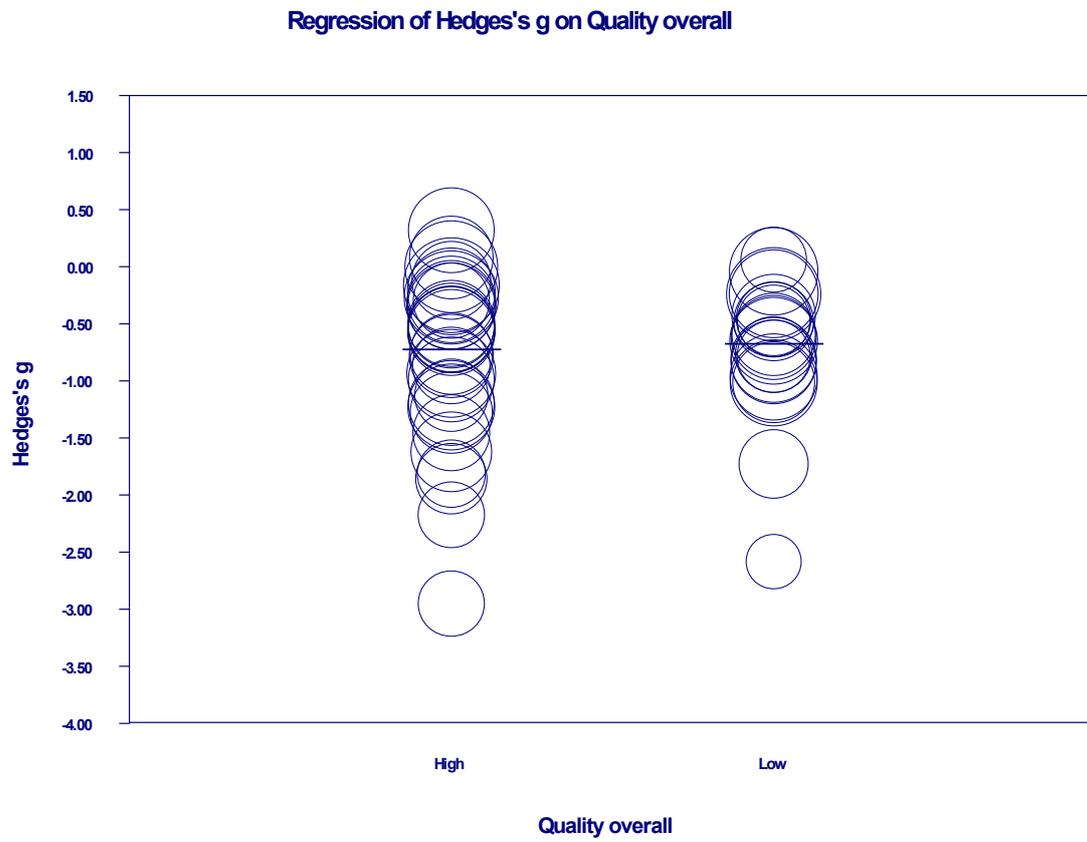


Fig. R.7. CPTSD symptoms (PTSD alone vs various CPTSD, k=52)

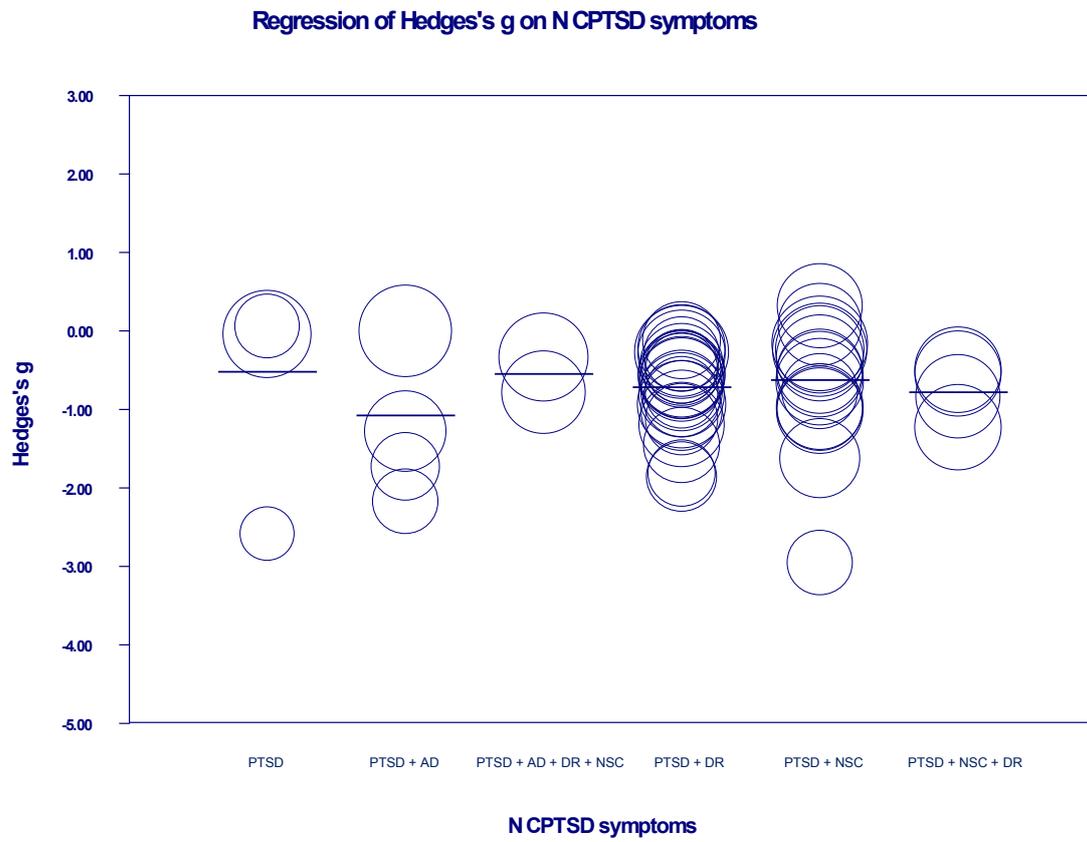


Fig. R.8. Comparator (TAU/WL vs control, k=52)

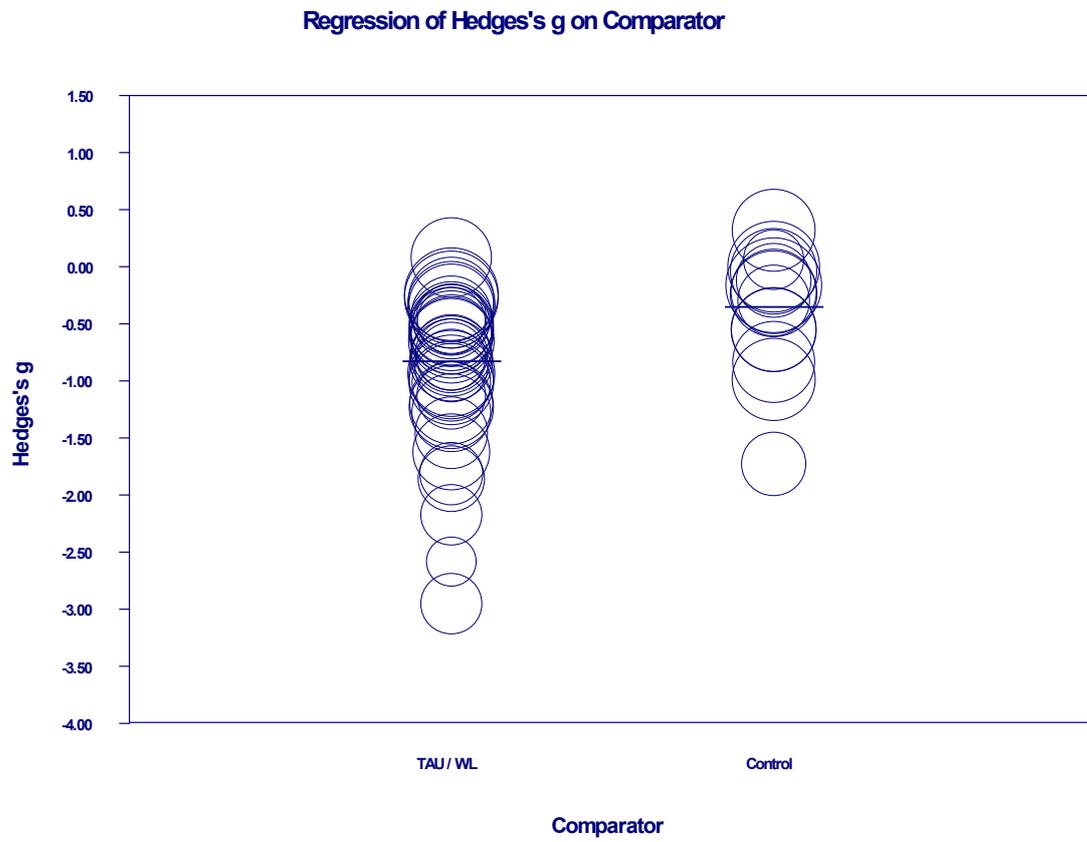


Fig. R.9. Treatments (individual CBT vs others, k=52)

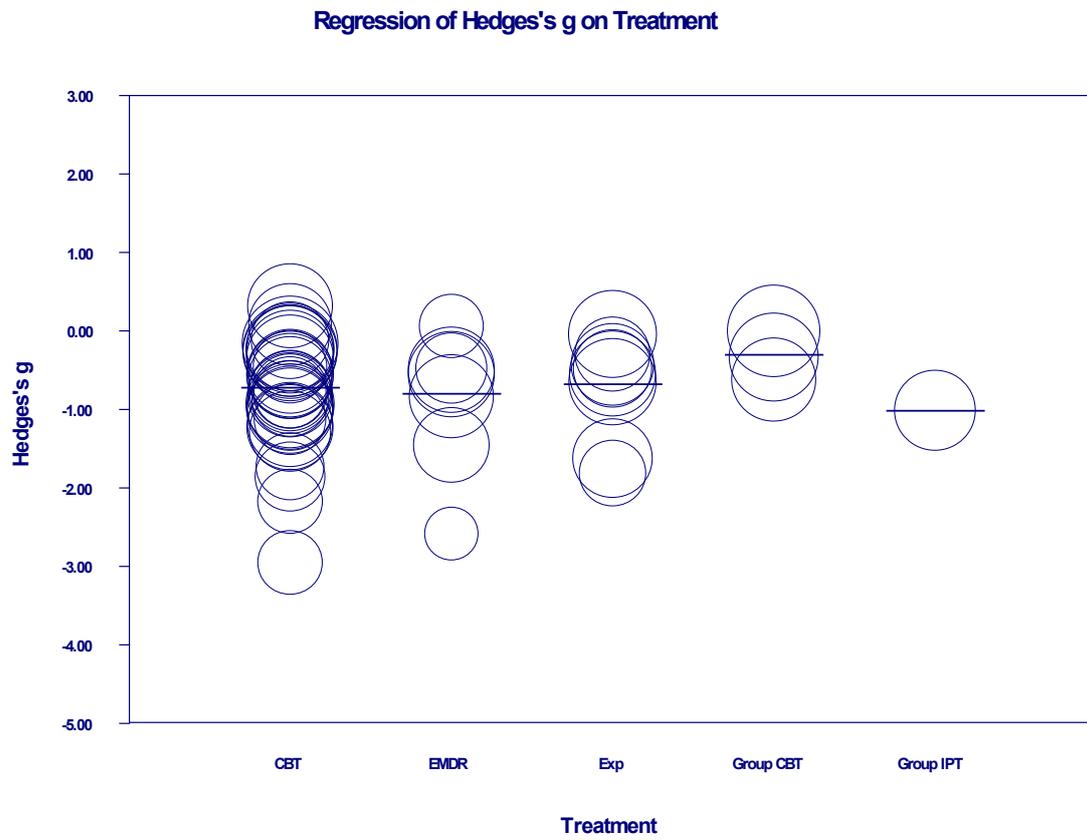


Fig. R.10. Therapy format (individual vs group, k=52)

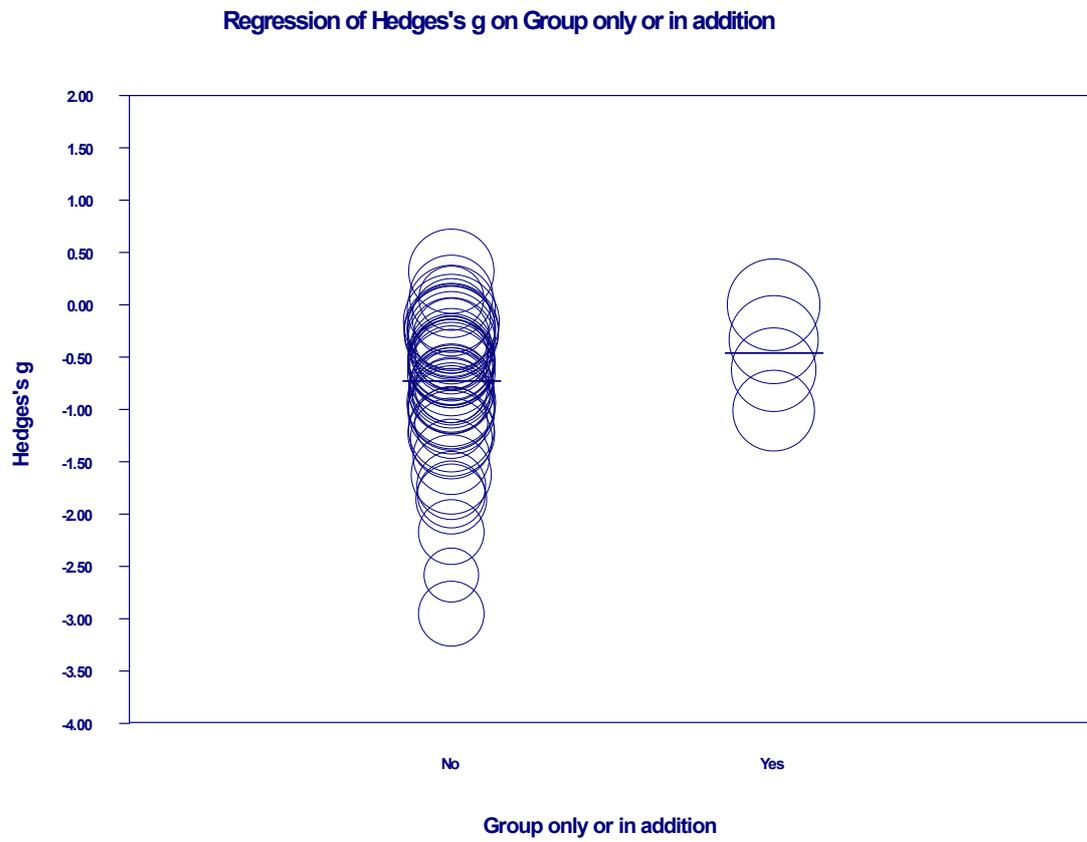
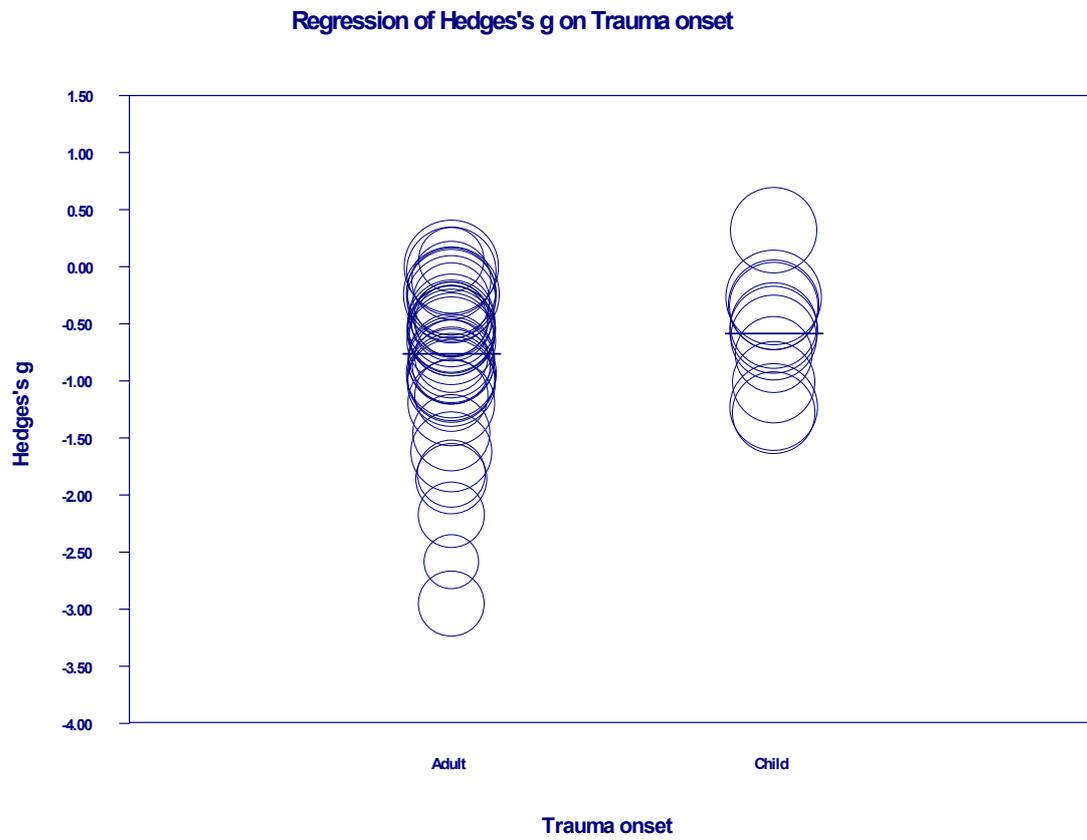


Fig. R.11. Trauma onset (Adult vs child, k=48)



S. Bubble Plots – Meta-regression Moderators (multivariate)

Fig. S.1. Overall quality (high vs low)

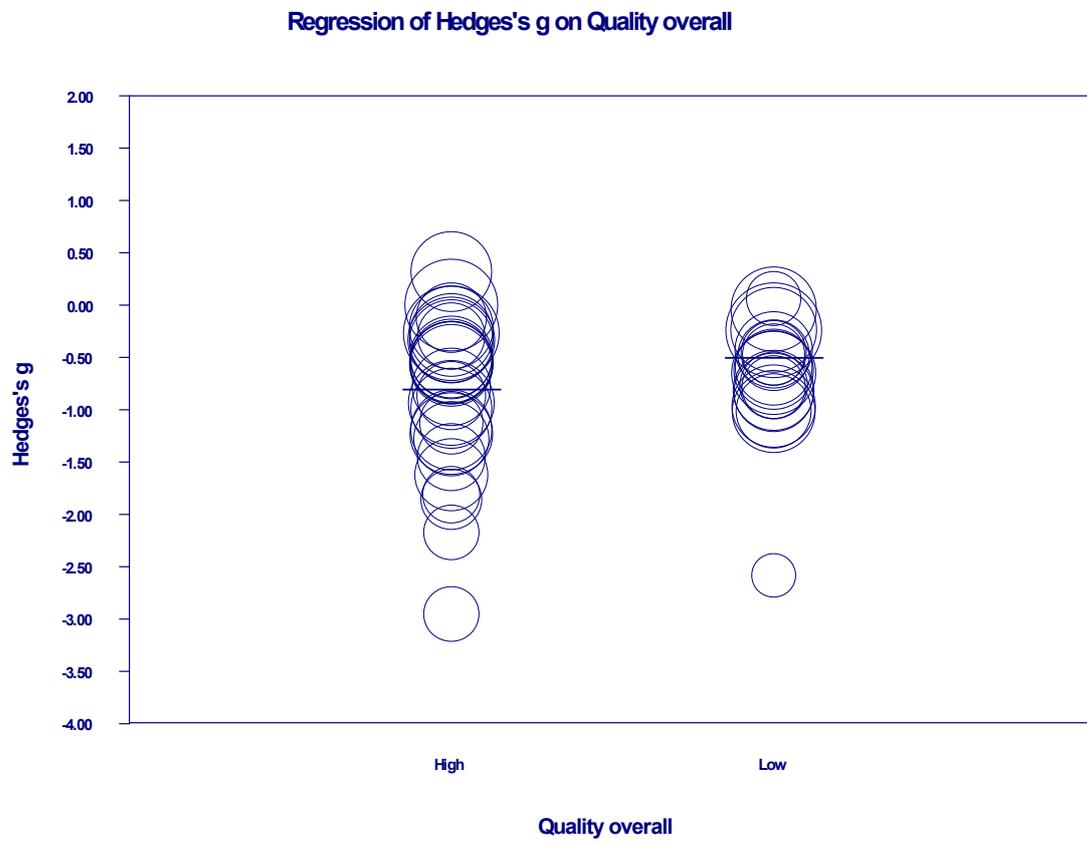


Fig. S.2. CPTSD symptoms (PTSD alone vs various CPTSD)

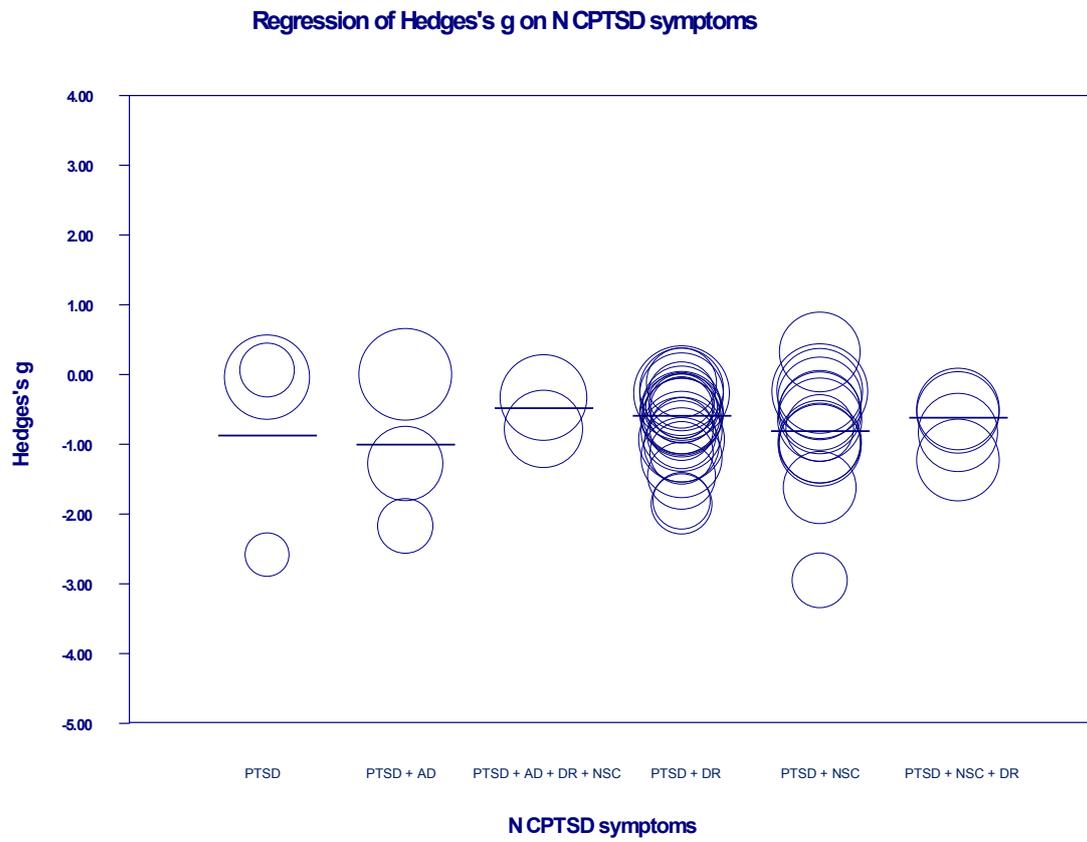


Fig. S.3. Comparator (TAU/WL vs control)

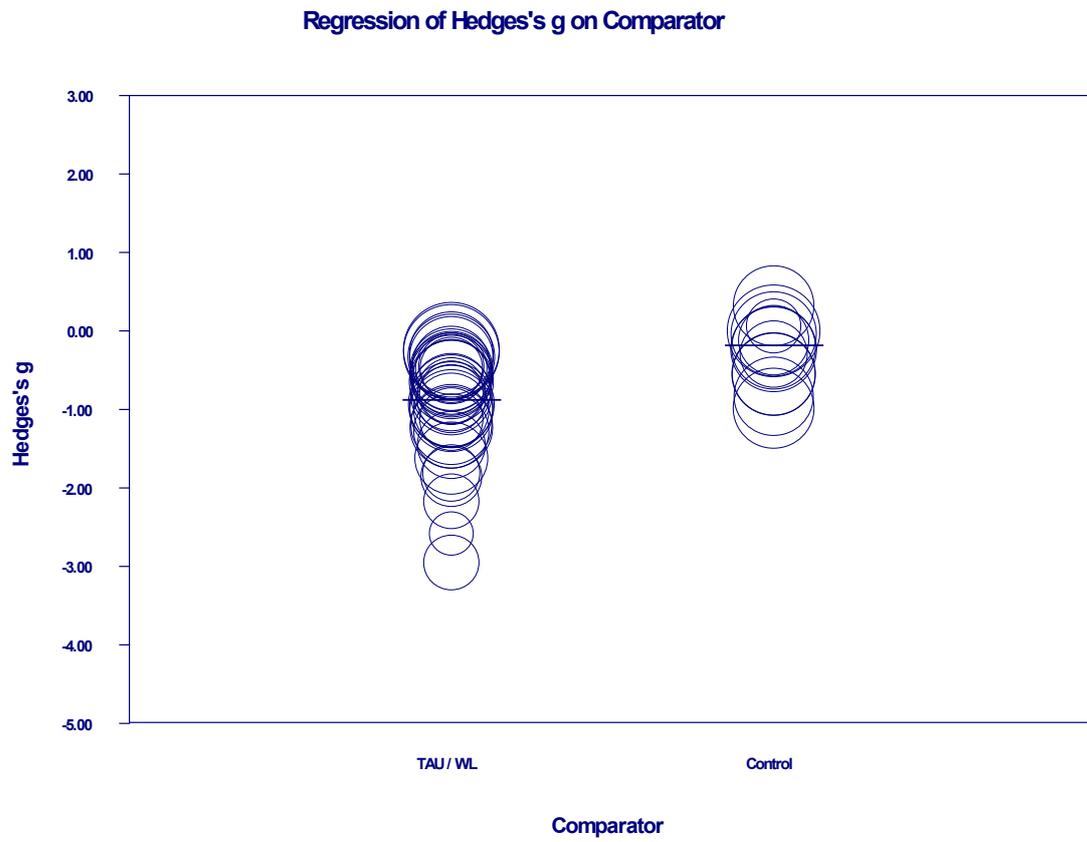


Fig. S.4. Treatments (individual CBT vs others)

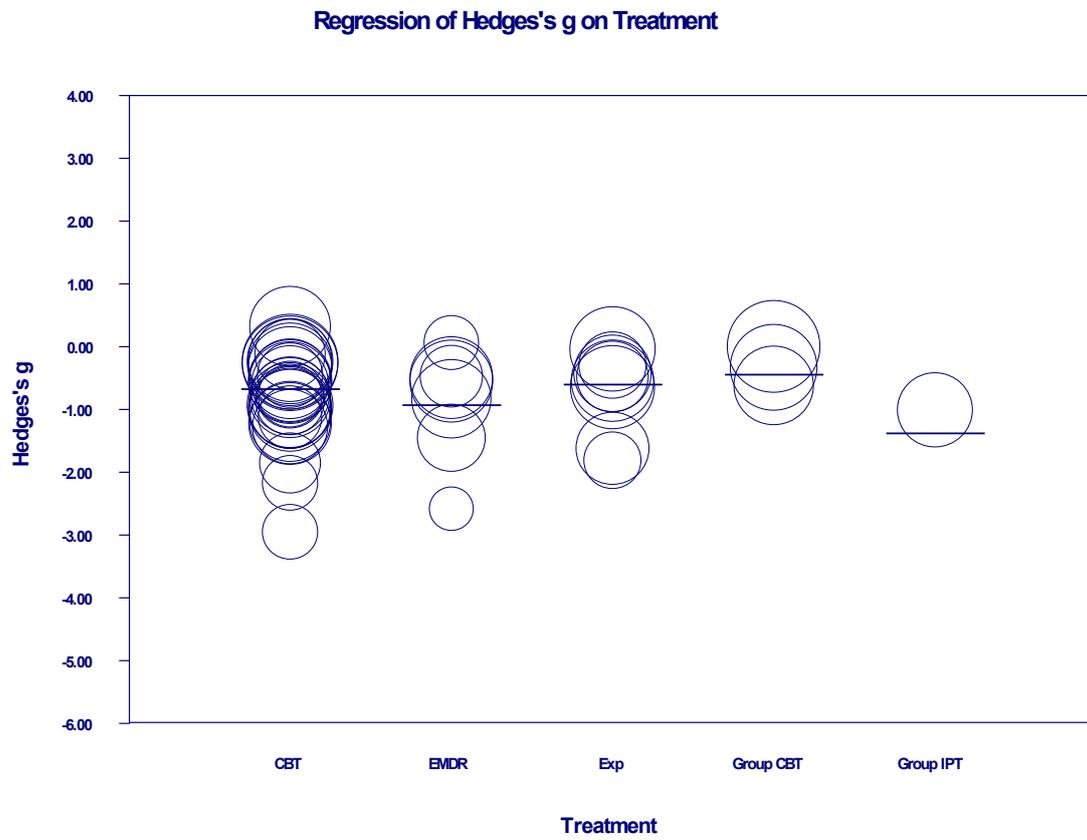
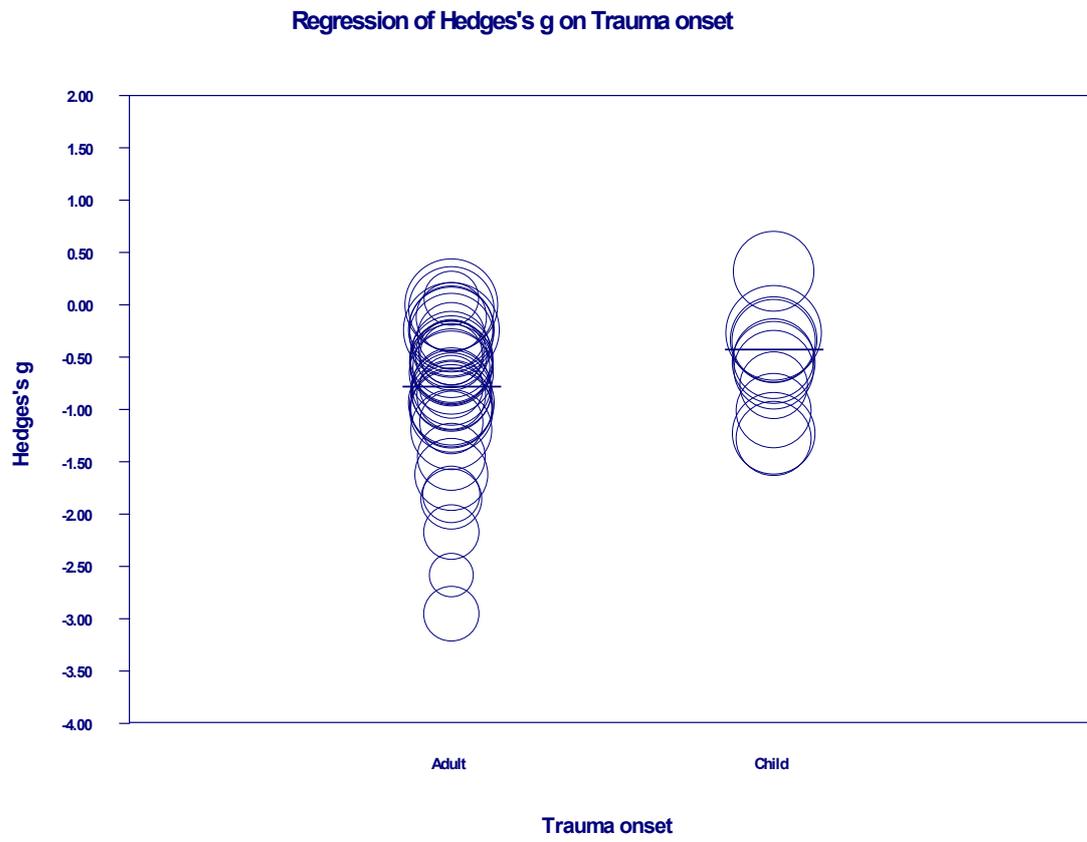


Fig. S.5. Trauma onset (adult vs child)



T. Funnel Plots for Meta-analyses (where publication bias is indicated)

Fig. T.1. Disturbances in relationships (DR): Cognitive/imagery modification with or without exposure vs TAU/WL

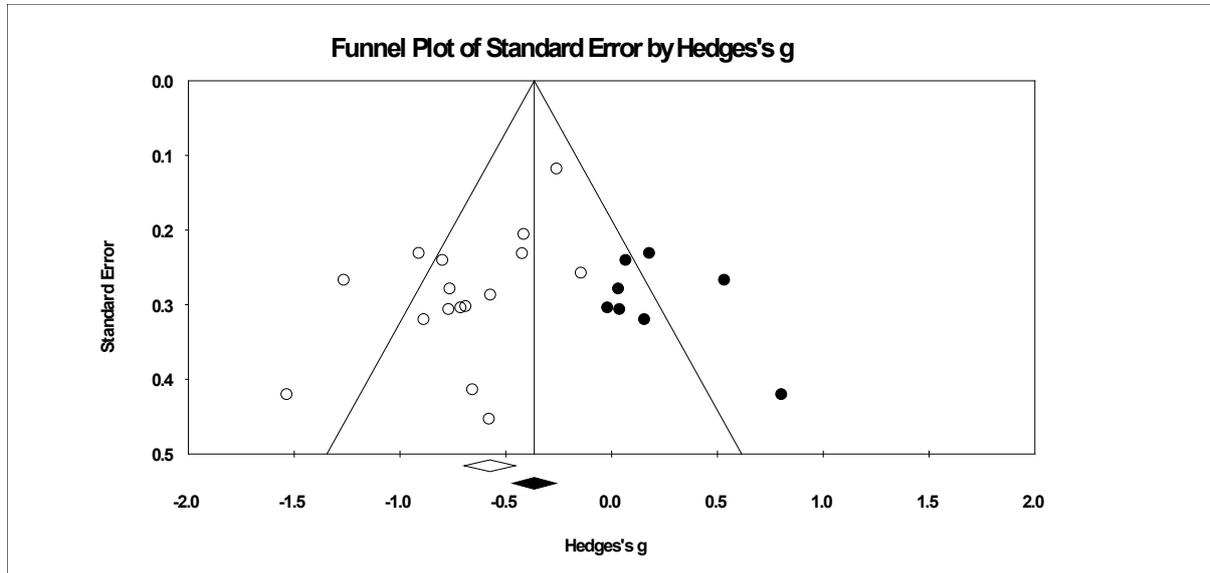


Fig. T.2. PTSD: Cognitive/imagery modification with or without exposure vs TAU/WL

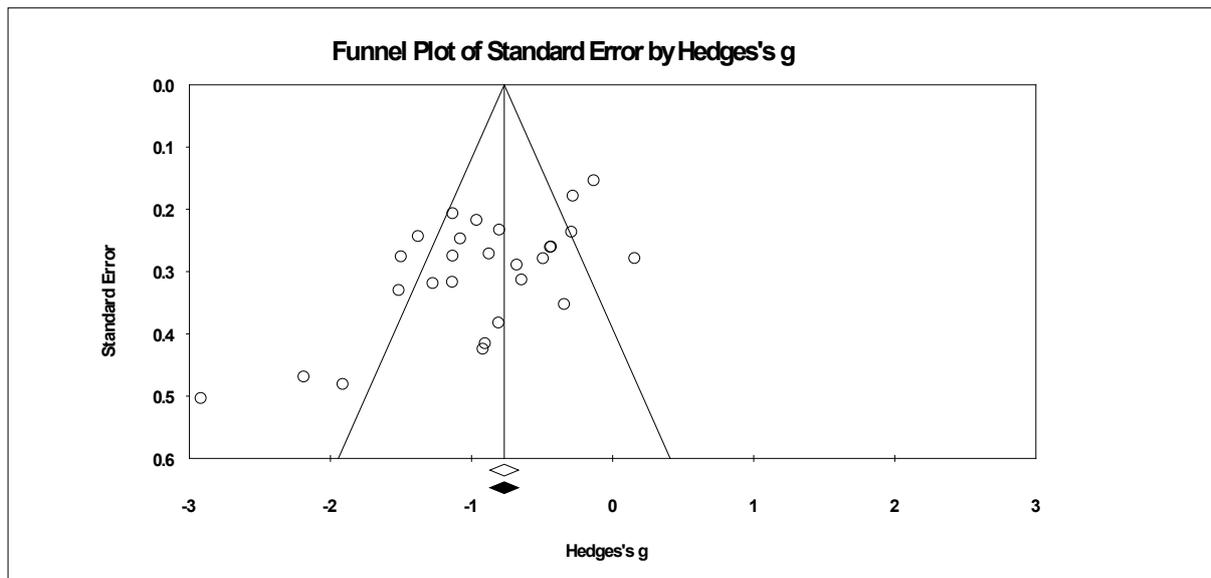
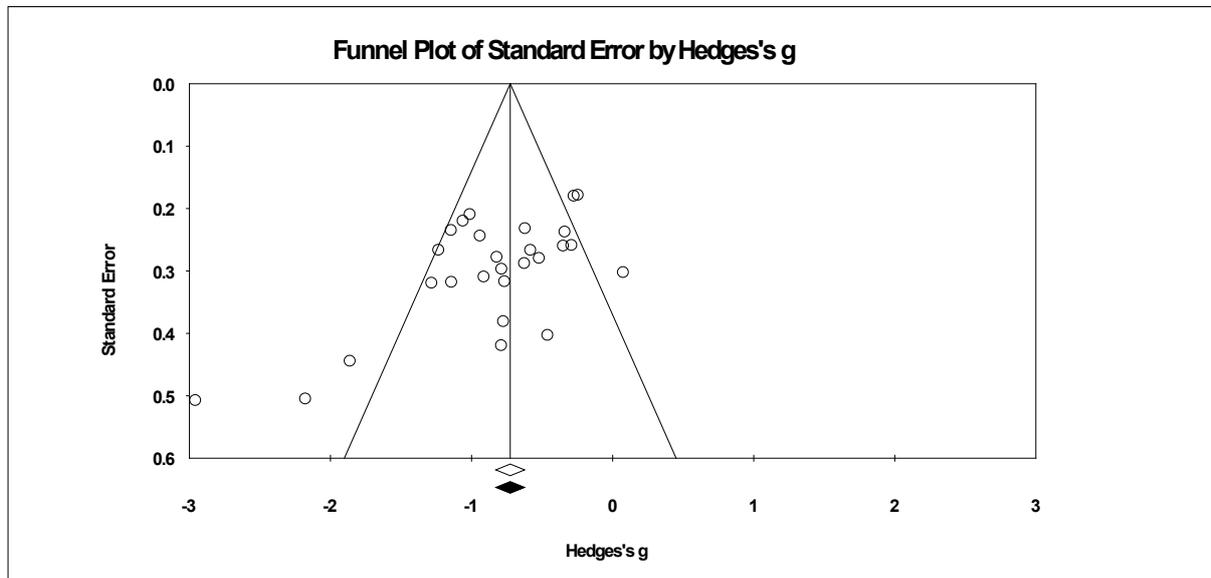


Fig. T.3. PTSD plus 1, 2 or 3 CPTSD outcomes: Cognitive/imagery modification with or without exposure vs TAU/WL



U. PRISMA Checklist

Section/topic	#	Checklist item	Reported
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	Yes
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	Yes
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	Yes
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	Yes
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	Yes
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	Yes
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	Yes
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Yes
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Yes
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	Yes
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	Yes

Section/topic	#	Checklist item	Reported
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	Yes
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	Yes
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	Yes

Section/topic	#	Checklist item	Reported
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	Yes
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	Yes

RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Yes
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Yes
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Yes
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Yes
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	Yes
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	Yes
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	Yes
DISCUSSION			

Section/topic	#	Checklist item	Reported
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	Yes
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	Yes
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	Yes
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

V. References for the 51 Included Studies

- Ahmadi K, Hazrati M, Ahmadizadeh M and Noohi S** (2015) REM desensitization as a new therapeutic method for post-traumatic stress disorder: a randomized controlled trial. *Acta Medica Indonesiana*, **47**, 111–119.
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- Cloitre M, Koenen KC, Cohen LR and Han H** (2002) Skills training in affective and interpersonal regulation followed by exposure: A phase-based treatment for PTSD related to childhood abuse. *Journal of Consulting and Clinical Psychology* **70**, 1067–1074.
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- Dorrepaal E, Thomaes K, Smit JH, Van Balkom AJLM, Veltman DJ, Hoogendoorn AW and Draijer N** (2012) Stabilizing group treatment for complex posttraumatic stress disorder related to child abuse based on psychoeducation and cognitive behavioural therapy: A multisite randomized controlled trial. *Psychotherapy and Psychosomatics* **81**, 217–225.
- Duffy M, Gillespie K and Clark DM** (2007) Post-traumatic stress disorder in the context of terrorism and other civil conflict in Northern Ireland: randomised controlled trial. *British Journal of Medicine* **334**, 1147. doi: 10.1136/bmj.39021.846852.BE.
- Dunn NJ, Rehm LP, Schillaci J, Soucek J, Mehta P, Ashton CM, Yanasak E and Hamilton JD** (2007) A randomized trial of self-management and psychoeducational group therapies for comorbid chronic posttraumatic stress disorder and depressive disorder. *Journal of Traumatic Stress* **20**, 221–237.
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Ehlers A, Clark DM, Hackmann A, McManus F and Fennell M (2005) Cognitive therapy for post-traumatic stress disorder: development and evaluation. *Behaviour Research and Therapy* **43**, 413–431.

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Figure 1. PRISMA diagram

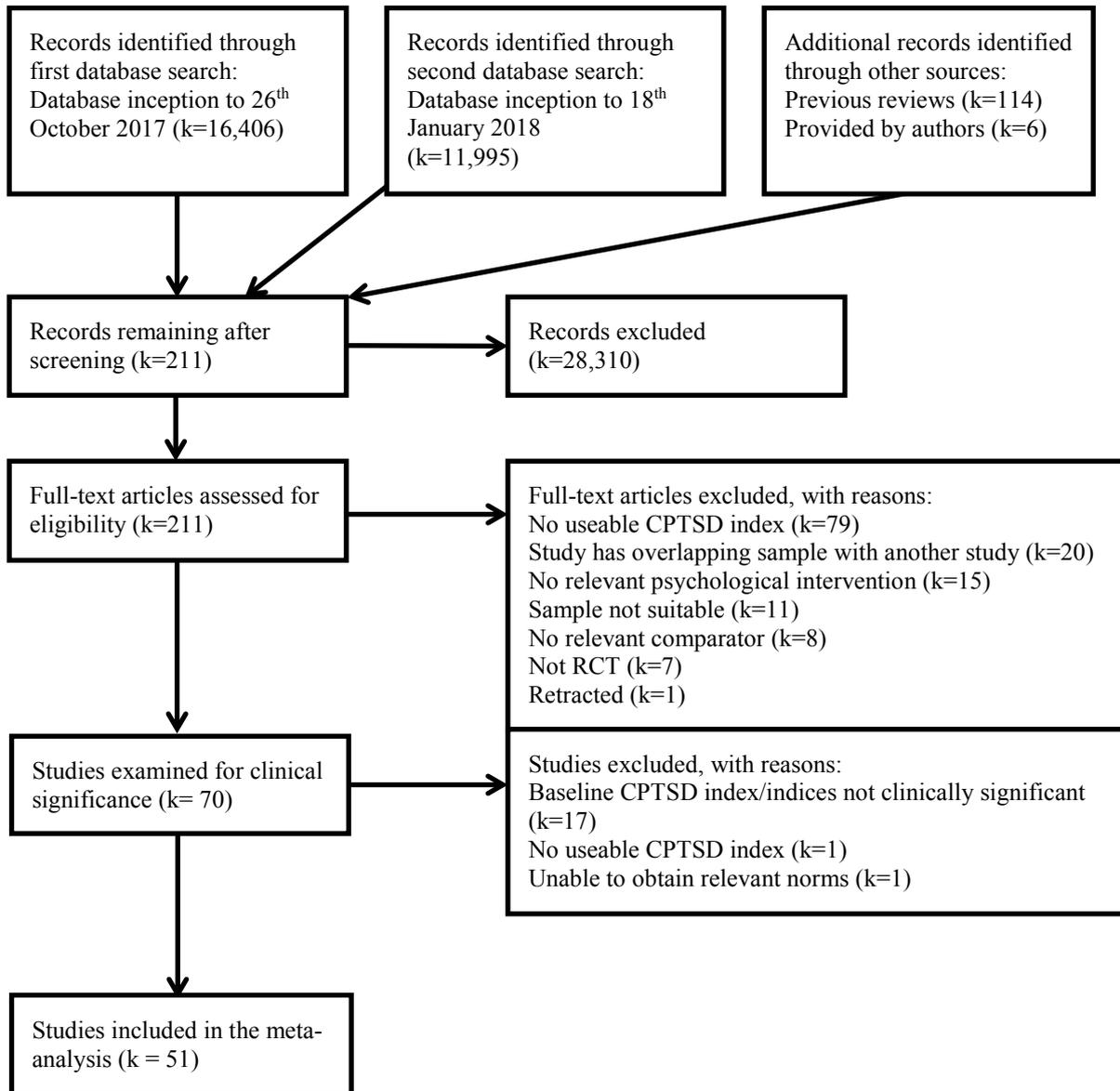
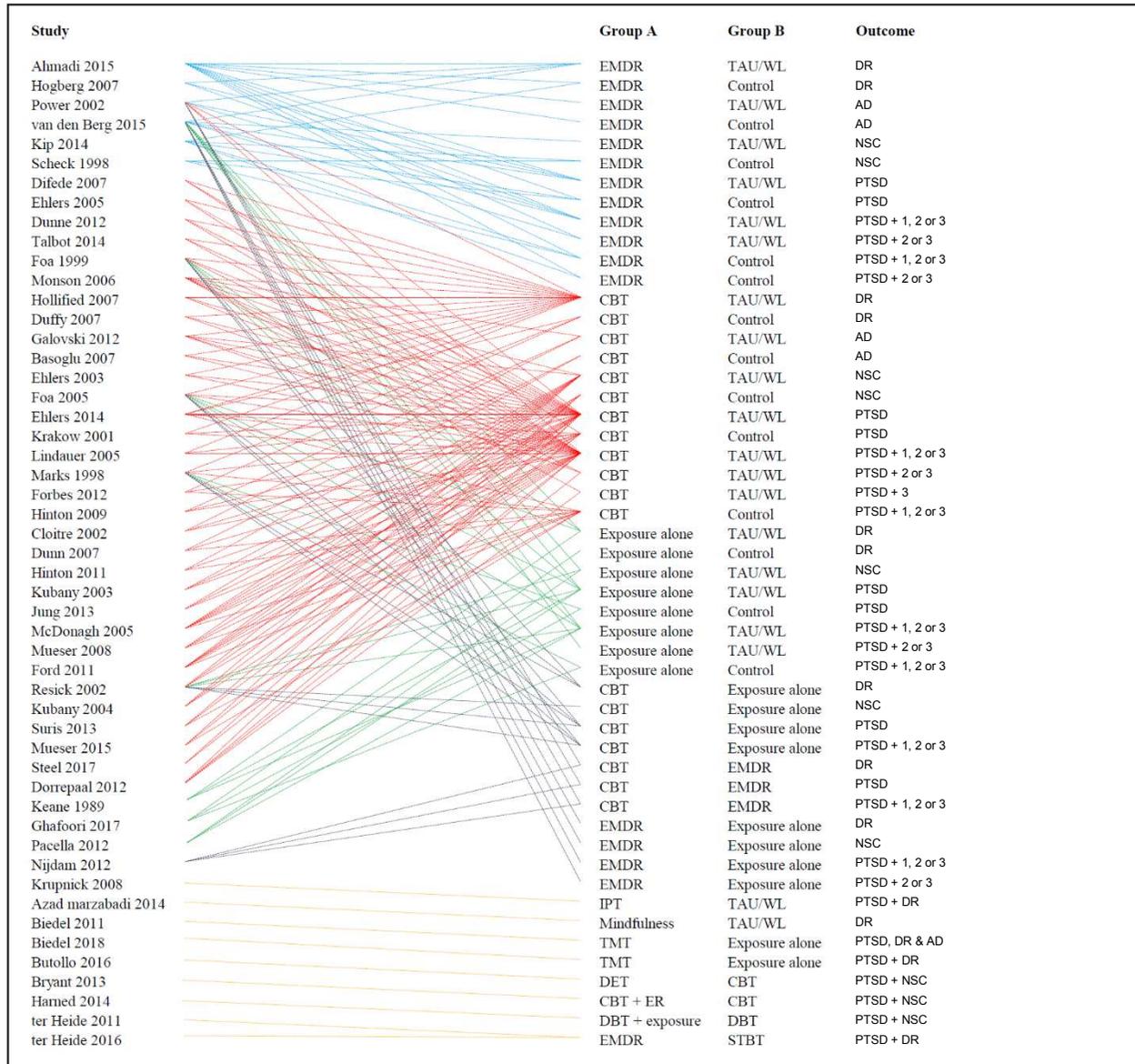


Figure 2. Overview of studies contributing to each analysis



Abbreviations: AD=affect dysregulation; CBT=cognitive behavioural therapy; CPTSD=complex posttraumatic stress disorder; DBT=dialectical behaviour therapy; DET=dialogical exposure therapy; DR=disturbances in relationships; DSO=disturbances in self-organisation; EMDR=eye-movement and desensitisation and reprocessing therapy; ER=emotion regulation (training); IPT=interpersonal psychotherapy; NSC=negative self-concept; PTSD=posttraumatic stress disorder; PTSD + 1, 2 or 3=PTSD + 1, 2 or 3 CPTSD (DSO) outcomes; PTSD + 2 or 3=PTSD + 2 or 3 CPTSD (DSO) outcomes; PTSD + 3=PTSD + all 3 CPTSD (DSO) outcomes; STBT=stabilisation treatment; TAU=treatment as usual; TMT=trauma management therapy; WL=waiting list.

Figure 3. Bubble plot of trauma onset (adult vs child) by Hedges' g, controlling for study quality, degree of CPTSD symptom severity, type of comparator, and type of treatment in multivariate meta-regression.

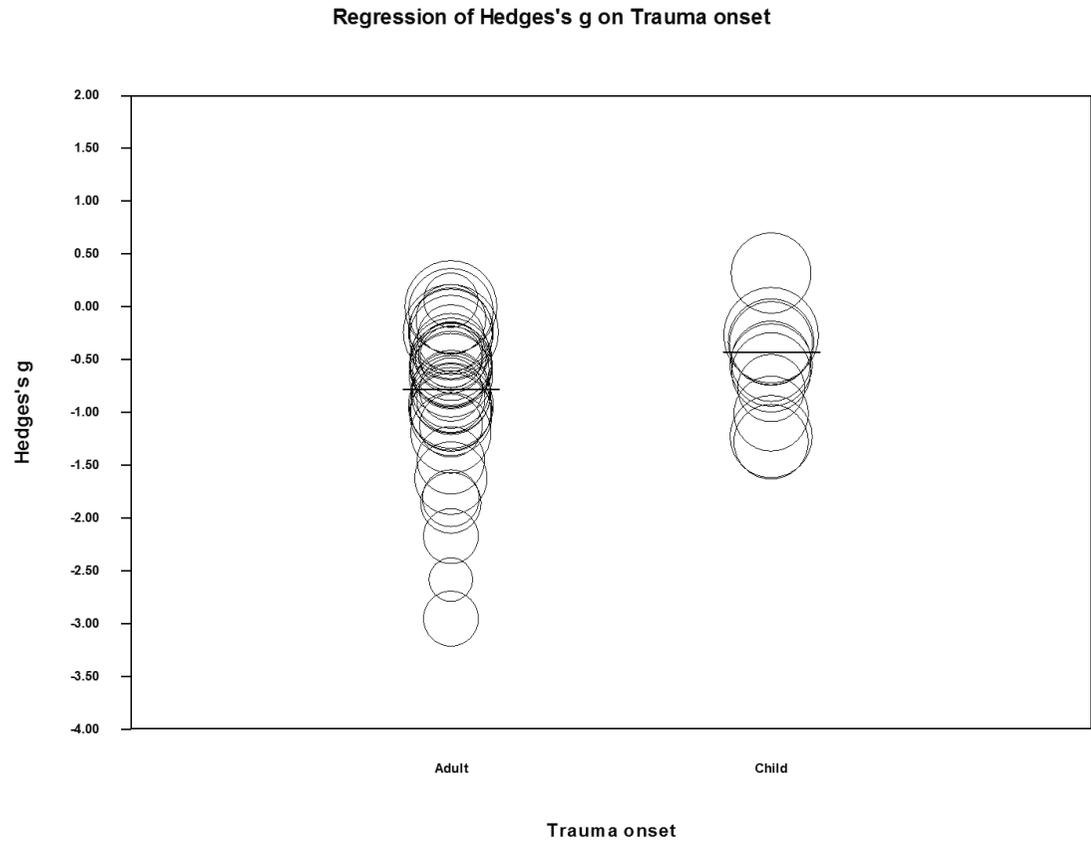


Table 1. Cognitive behavioural therapy with or without exposure vs TAU/WL or non-specific control

Outcome	Comparator	k included studies	Treatment N	Control N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
DR	vs TAU/WL	16	485	395	-0.66 (-0.84, -0.48), <0.001	45%, 0.021	0.007, -0.39 (-0.59, -0.20), 8	Moderate -1 publication bias
DR	vs control	3	128	79	-0.32 (-0.60, -0.03), 0.029	0%, 0.402	-	Moderate -1 imprecision
AD	vs TAU/WL	3	54	61	-1.42 (-2.20, -0.65), <0.001	71%, 0.033	-	Moderate -1 imprecision
AD	vs control	2	63	62	-0.82 (-2.91, 1.26), 0.440	94%, <0.001	-	Very low -1 inconsistency -2 imprecision
NSC	vs TAU/WL	9	320	281	-0.82 (-1.19, -0.44), <0.001	79%, <0.001	-	Moderate -1 inconsistency
NSC	vs control	4	207	163	-0.24 (-0.69, 0.21), 0.295	75%, 0.008	-	Low -1 inconsistency -1 imprecision

PTSD	vs TAU/WL	27	899	773	-0.90 (-1.11, -0.68), <0.001	76%, <0.001	0.002, -0.90 (-1.11, -0.68), 0	Moderate -1 inconsistency
PTSD	vs control	9	408	323	-0.37 (-0.66, -0.09), 0.011	71%, 0.001		Moderate -1 inconsistency
PTSD + 1, 2 or 3	vs TAU/WL	27	841	705	-0.81 (-1.00, -0.62), <0.001	68%, <0.001	0.003, -0.81 (-1.00, -0.62), 0	High
PTSD + 2 or 3	vs TAU/WL	3	92	90	-0.78 (-1.31, -0.24), 0.005	68%, 0.043		Moderate -1 imprecision
PTSD + 3	vs TAU/WL	2	58	58	-0.53 (-0.96, -0.09), 0.017	28%, 0.239		Low -2 imprecision
PTSD + 1, 2 or 3	vs control	9	398	314	-0.34 (-0.62, -0.06), 0.019	68%, 0.001		Low -1 imprecision -1 inconsistency
PTSD + 2 or 3	vs control	0	-	-	-	-		
PTSD + 3	vs control	0	-	-	-	-		

Abbreviations: AD=affect dysregulation; CPTSD=complex posttraumatic stress disorder; DR=disturbances in relationships; DSO=disturbances in self-organisation; NSC=negative self-concept; PTSD=posttraumatic stress disorder; PTSD + 1, 2 or 3=PTSD + 1, 2 or 3 CPTSD (DSO) outcomes; PTSD + 2 or 3=PTSD + 2 or 3 CPTSD (DSO) outcomes; PTSD + 3=PTSD + all 3 CPTSD (DSO) outcomes; TAU=treatment as usual; WL=waiting list.

Table 2. Exposure only vs TAU/WL or non-specific control

Outcome	Comparator	k included studies	Treatment N	Control N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
DR	vs TAU/WL	4	158	110	-0.59 (-1.12, -0.07), 0.028	73%, 0.011	-	Moderate -1 imprecision
DR	vs control	1	47	24	-0.12 (-0.60, 0.37), 0.642	-	-	Very low -2 RoB -2 imprecision
AD	vs TAU/WL	0	-	-	-	-	-	-
AD	vs control	0	-	-	-	-	-	-
NSC	vs TAU/WL	3	131	102	-0.73 (-1.03, -0.43), <0.001	21%, 0.283	-	Moderate -1 imprecision
NSC	vs control	0	-	-	-	-	-	-
PTSD	vs TAU/WL	6	246	190	-1.05 (-1.52, -0.58), <0.001	79%, <0.001	-	Low -2 imprecision
PTSD	vs control	2	67	42	-0.08 (-0.47, 0.30), 0.675	0%, 0.803	-	Low -2 imprecision

Outcome	Comparator	k included studies	Treatment N	Control N	Hedges' g (95% CI), p-value	Heterogeneity, I ² , p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
PTSD + 1, 2 or 3	vs TAU/WL	6	242	158	-0.86 (-1.25, -0.47), <0.001	69%, 0.006	-	High
PTSD + 2 or 3	vs TAU/WL	1	47	39	-0.56 (-0.99, -0.14), 0.009	-	-	Low -2 imprecision
PTSD + 3	vs TAU/WL	0	-	-	-	-	-	-
PTSD + 1, 2 or 3	vs control	2	67	42	-0.19 (-0.57, 0.20), 0.336	0%, 0.636	-	Low -2 imprecision
PTSD + 2 or 3	vs control	0	-	-	-	-	-	-
PTSD + 3	vs control	-	-	-	-	-	-	-

Abbreviations: AD=affect dysregulation; CPTSD=complex posttraumatic stress disorder; DSO=disturbances in self-organisation; DR=disturbances in relationships; NSC=negative self-concept; PTSD=posttraumatic stress disorder; PTSD + 1, 2 or 3=PTSD + 1, 2 or 3 CPTSD (DSO) outcomes; PTSD + 2 or 3=PTSD + 2 or 3 CPTSD (DSO) outcomes; PTSD + 3=PTSD + all 3 CPTSD (DSO) outcomes; TAU=treatment as usual; WL=waiting list.

Table 3. EMDR vs TAU/WL or non-specific control

Outcome	Comparator	k included studies	Treatment N	Control N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
DR	vs TAU/WL	4	94	84	-0.76 (-1.35, -0.16), 0.012	70%, 0.019	-	Moderate -1 imprecision
DR	vs control	2	37	34	-0.35 (-1.01, 0.31), 0.312	46%, 0.174	-	Very low -2 RoB -2 imprecision -1 inconsistency
AD	vs TAU/WL	1	11	12	-1.64 (-2.56, -0.72), 0.000	-	-	Very low -2 RoB -2 imprecision
AD	vs control	1	11	10	0.25 (-0.57, 1.08), 0.548	-	-	Very low -2 RoB -2 imprecision
NSC	vs TAU/WL	1	44	39	-0.61 (-1.04, -0.17), 0.006	-	-	Low -2 imprecision
NSC	vs control	2	56	53	-0.78 (-1.56, -0.01), 0.049	75%, 0.047	-	Very low -1 inconsistency

Outcome	Comparator	k included studies	Treatment N	Control N	Hedges' g (95% CI), p-value	Heterogeneity, I ² , p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
								-2 imprecision
PTSD	vs TAU/WL	4	105	92	-1.26 (-2.01, -0.51), 0.001	79%, 0.002	-	Low -1 inconsistency -1 imprecision
PTSD	vs control	3	70	65	-0.69 (-1.35, -0.03), 0.041	70%, 0.035	-	Very low -1 RoB -1 inconsistency -1 imprecision
PTSD + 1, 2 or 3	vs TAU/WL	4	94	84	-1.15 (-1.92, -0.37), 0.004	81%, 0.002	-	Low -1 inconsistency -1 imprecision
PTSD + 2 or 3	vs TAU/WL	2	55	51	-1.36 (-3.13, 0.42), 0.134	90%, 0.001	-	Very low -1 inconsistency -2 imprecision
PTSD + 3	vs TAU/WL	0	-	-	-	-	-	-

Outcome	Comparator	k included studies	Treatment N	Control N	Hedges' g (95% CI), p-value	Heterogeneity, I ² , p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
PTSD + 1, 2 or 3	vs control	3	67	61	-0.52 (-0.97, -0.08), 0.020	35%, 0.213	-	Low -1 RoB -1 imprecision
PTSD + 2 or 3	vs control	2	37	34	-0.44 (-1.31, 0.43), 0.321	68%, 0.079	-	Very low -2 RoB -1 inconsistency -2 imprecision
PTSD + 3	vs control	0	-	-	-	-	-	-

Abbreviations: AD=affect dysregulation; CPTSD=complex posttraumatic stress disorder; DR=disturbances in relationships; DSO=disturbances in self-organisation; EMDR=eye-movement and desensitisation and reprocessing therapy; NSC=negative self-concept; PTSD=posttraumatic stress disorder; PTSD + 1, 2 or 3=PTSD + 1, 2 or 3 CPTSD (DSO) outcomes; PTSD + 2 or 3=PTSD + 2 or 3 CPTSD (DSO) outcomes; PTSD + 3=PTSD + all 3 CPTSD (DSO) outcomes; TAU=treatment as usual; WL=waiting list.

Table 4. Comparison of CBT, Exposure and EMDR

Outcome	Comparison (A vs B)	k included studies	Group A N	Group B N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
DR	CBT vs exposure alone	3	152	120	0.07 (-0.26, 0.39), 0.689	38%, 0.200	-	Moderate -1 imprecision
AD	CBT vs exposure alone	0	-	-	-	-	-	-
NSC	CBT vs exposure alone	1	62	61	-0.31 (-0.67, 0.04), 0.082	-	-	Very low -2 RoB -2 imprecision
PTSD	CBT vs exposure alone	4	216	184	-0.03 (-0.23, 0.17), 0.784	0%, 0.493	-	Moderate -1 imprecision
PTSD + 1, 2 or 3	CBT vs exposure alone	4	214	181	-0.04 (-0.27, 0.19), 0.719	20%, 0.291	-	Moderate -1 imprecision
PTSD + 2 or 3	CBT vs exposure alone	0	-	-	-	-	-	-
PTSD + 3	CBT vs exposure alone	0	-	-	-	-	-	-

Outcome	Comparison (A vs B)	k included studies	Group A N	Group B N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
DR	CBT vs EMDR	2	59	70	0.28 (-0.29, 0.34), 0.338	60%, 0.115	-	Very low -2 imprecision -1 inconsistency
AD	CBT vs EMDR	0	-	-	-	-	-	-
NSC	CBT vs EMDR	0	-	-	-	-	-	-
PTSD	CBT vs EMDR	2	62	75	0.37 (0.03, 0.71), 0.031	0%, 0.548	-	Low -2 imprecision
PTSD + 1, 2 or 3	CBT vs EMDR	2	59	70	0.31 (-0.07, 0.68), 0.111	16%, 0.275	-	Low -2 imprecision
PTSD + 2 or 3	CBT vs EMDR	0	-	-	-	-	-	-
PTSD + 3	CBT vs EMDR	0	-	-	-	-	-	-
DR	EMDR vs exposure alone	1	44	47	-0.10 (-0.51, 0.31), 0.640	-	-	Low -2 imprecision
AD	EMDR vs exposure alone	0	-	-	-	-	-	-

Outcome	Comparison (A vs B)	k included studies	Group A N	Group B N	Hedges' g (95% CI), p-value	Heterogeneity, I², p-value	Publication bias, p-value, adjusted g (95% CI), k imputed studies	Quality (GRADE)
NSC	EMDR vs exposure alone	1	44	47	0.16 (-0.25, 0.57), 0.444	-	-	Low -2 imprecision
PTSD	EMDR vs exposure alone	1	55	48	0.10 (-0.28, 0.49), 0.604	-	-	Low -2 imprecision
PTSD + 1, 2 or 3	EMDR vs exposure alone	1	44	47	0.06 (-0.35, 0.46), 0.789	-	-	Low -2 imprecision
PTSD + 2 or 3	EMDR vs exposure alone	1	44	47	0.06 (-0.35, 0.46), 0.789	-	-	Low -2 imprecision
PTSD + 3	EMDR vs exposure alone	0	-	-	-	-	-	-

Abbreviations: AD=affect dysregulation; CPTSD=complex posttraumatic stress disorder; DR=disturbances in relationships; DSO=disturbances in self-organisation; EMDR=eye-movement and desensitisation and reprocessing therapy; NSC=negative self-concept; PTSD=posttraumatic stress disorder; PTSD + 1, 2 or 3=PTSD + 1, 2 or 3 CPTSD (DSO) outcomes; PTSD + 2 or 3=PTSD + 2 or 3 CPTSD (DSO) outcomes; PTSD + 3=PTSD + all 3 CPTSD (DSO) outcomes.