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Psychological therapies for post-traumatic stress disorder and comorbid substance use disorder (Review)

Roberts NP, Roberts PA, Jones N, Bisson JI

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[Intervention Review]

Psychological therapies for post-traumatic stress disorder and comorbid substance use disorder

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ABSTRACT

Background

Post-traumatic stress disorder (PTSD) is a debilitating mental health disorder that may develop after exposure to traumatic events. Substance use disorder (SUD) is a behavioural disorder in which the use of one or more substances is associated with heightened levels of distress, clinically significant impairment of functioning, or both. PTSD and SUD frequently occur together. The comorbidity is widely recognised as being difficult to treat and is associated with poorer treatment completion and poorer outcomes than for either condition alone. Several psychological therapies have been developed to treat the comorbidity, however there is no consensus about which therapies are most effective.

Objectives

To determine the efficacy of psychological therapies aimed at treating traumatic stress symptoms, substance misuse symptoms, or both in people with comorbid PTSD and SUD in comparison with control conditions (usual care, waiting-list conditions, and no treatment) and other psychological therapies.

Search methods

We searched the Cochrane Depression, Anxiety and Neurosis Group's Specialised Register (CCDANCTR) all years to 11 March 2015. This register contains relevant randomised controlled trials from the Cochrane Library (all years), MEDLINE (1950 to date), EMBASE (1974 to date), and PsycINFO (1967 to date). We also searched the World Health Organization International Clinical Trials Registry Platform and ClinicalTrials.gov, contacted experts, searched bibliographies of included studies, and performed citation searches of identified articles.

Selection criteria

Randomised controlled trials of individual or group psychological therapies delivered to individuals with PTSD and comorbid substance use, compared with waiting-list conditions, usual care, or minimal intervention or to other psychological therapies.

Data collection and analysis

We used standard methodological procedures expected by Cochrane.

Main results

We included 14 studies with 1506 participants, of which 13 studies were included in the quantitative synthesis. Most studies involved adult populations. Studies were conducted in a variety of settings. We performed four comparisons investigating the effects of psychological

therapies with a trauma-focused component and non-trauma-focused interventions against treatment as usual/minimal intervention and other active psychological therapies. Comparisons were stratified for individual- or group-based therapies. All active interventions were based on cognitive behavioural therapy. Our main findings were as follows.

Individual-based psychological therapies with a trauma-focused component plus adjunctive SUD intervention was more effective than treatment as usual (TAU)/minimal intervention for PTSD severity post-treatment (standardised mean difference (SMD) -0.41; 95% confidence interval (CI) -0.72 to -0.10; 4 studies; n = 405; very low-quality evidence) and at 3 to 4 and 5 to 7 months' follow-up. There was no evidence of an effect for level of drug/alcohol use post-treatment (SMD -0.13; 95% CI -0.41 to 0.15; 3 studies; n = 388; very low-quality evidence), but there was a small effect in favour of individual psychological therapy at 5 to 7 months (SMD -0.28; 95% CI -0.48 to -0.07; 3 studies; n = 388) when compared against TAU. Fewer participants completed trauma-focused therapy than TAU (risk ratio (RR) 0.78; 95% CI 0.64 to 0.96; 3 studies; n = 316; low-quality evidence).

Individual-based psychological therapy with a trauma-focused component did not perform better than psychological therapy for SUD only for PTSD severity (mean difference (MD) -3.91; 95% CI -19.16 to 11.34; 1 study; n = 46; low-quality evidence) or drug/alcohol use (MD -1.27; 95% CI -5.76 to 3.22; 1 study; n = 46; low-quality evidence). Findings were based on one small study. No effects were observed for rates of therapy completion (RR 1.00; 95% CI 0.74 to 1.36; 1 study; n = 62; low-quality evidence).

Non-trauma-focused psychological therapies did not perform better than TAU/minimal intervention for PTSD severity when delivered on an individual (SMD -0.22; 95% CI -0.83 to 0.39; 1 study; n = 44; low-quality evidence) or group basis (SMD -0.02; 95% CI -0.19 to 0.16; 4 studies; n = 513; low-quality evidence). There were no data on the effects on drug/alcohol use for individual therapy. There was no evidence of an effect on the level of drug/alcohol use for group-based therapy (SMD -0.03; 95% CI -0.37 to 0.31; 4 studies; n = 414; very low-quality evidence). A post-hoc analysis for full dose of a widely established group therapy called Seeking Safety showed reduced drug/alcohol use post-treatment (SMD -0.67; 95% CI -1.14 to -0.19; 2 studies; n = 111), but not at subsequent follow-ups. Data on the number of participants completing therapy were not for individual-based therapy. No effects were observed for rates of therapy completion for group-based therapy (RR 1.13; 95% CI 0.88 to 1.45; 2 studies; n = 217; low-quality evidence).

Non-trauma-focused psychological therapy did not perform better than psychological therapy for SUD only for PTSD severity (SMD -0.26; 95% CI -1.29 to 0.77; 2 studies; n = 128; very low-quality evidence) or drug/alcohol use (SMD 0.22; 95% CI -0.13 to 0.57; 2 studies; n = 128; low-quality evidence). No effects were observed for rates of therapy completion (RR 0.91; 95% CI 0.68 to 1.20; 2 studies; n = 128; very low-quality evidence).

Several studies reported on adverse events. There were no differences between rates of such events in any comparison. We rated several studies as being at 'high' or 'unclear' risk of bias in multiple domains, including for detection bias and attrition bias.

Authors' conclusions

We assessed the evidence in this review as mostly low to very low quality. Evidence showed that individual trauma-focused psychological therapy delivered alongside SUD therapy did better than TAU/minimal intervention in reducing PTSD severity post-treatment and at long-term follow-up, but only reduced SUD at long-term follow-up. All effects were small, and follow-up periods were generally quite short. There was evidence that fewer participants receiving trauma-focused therapy completed treatment. There was very little evidence to support use of non-trauma-focused individual- or group-based integrated therapies. Individuals with more severe and complex presentations (e.g. serious mental illness, individuals with cognitive impairment, and suicidal individuals) were excluded from most studies in this review, and so the findings from this review are not generalisable to such individuals. Some studies suffered from significant methodological problems and some were underpowered, limiting the conclusions that can be drawn. Further research is needed in this area.

PLAIN LANGUAGE SUMMARY

Psychological therapies for post-traumatic stress disorder and substance use disorder

Who may be interested in this review?

• Individuals with post-traumatic stress disorder (PTSD) and substance use disorder (SUD) and their families and friends.

• Healthcare providers for individuals with PTSD and SUD.

Why is this review important?

Many people have PTSD or SUD. Both conditions can impact everyday functioning. A number of different psychological therapies are successful at treating PTSD and SUD when they occur separately. However, PTSD and SUD often occur together, and it may be harder to treat individuals with both PTSD and SUD. A number of psychological therapies have been developed to treat people with both PTSD and SUD, but it is not clear how effective these therapies are.

What questions does this review aim to answer?

We sought to find out whether psychological therapies are effective in treating people with PTSD and SUD in comparison to control conditions and other psychological therapies.

Which studies were included in the review?

We searched scientific databases to find all published and unpublished studies of psychological therapies to treat people with PTSD and SUD up to 11 March 2015. We included 14 studies with 1506 participants.

What does the evidence from the review tell us?

The evidence showed that individual trauma-focused psychological therapy delivered alongside SUD therapies was more effective in reducing PTSD compared to treatment as usual. This result was found both straight after treatment and at long-term follow-up. However, SUD severity only declined at long-term follow-up. More people dropped out of the trauma-focused therapy compared with treatment as usual. Overall, the benefits of trauma-focused treatment were small.

We found little evidence for the benefit of individual- or group-based non-trauma-focused psychological therapies. For group-based therapies, we found that substance use was reduced post-treatment when participants were offered a full course of 25 sessions of the therapy 'Seeking Safety', which was delivered in a group setting. However, this positive effect did not continue at later follow-up points. The level of drop-out was high across all studies.

We graded the quality of evidence as low to very low. This review includes a small number of studies. Some included studies were poorly designed, and most studies were small. There was also considerable variation in the way that the therapies and control therapies were delivered. It is likely that participants in the included studies received a range of other stabilising interventions alongside trauma-focused treatment, and we found no evidence to support the delivery of trauma-focused therapies without SUD-focused therapies. It is therefore possible that our findings will change as further evidence of higher quality is accumulated. Healthcare providers should exercise caution when considering whether to provide therapies described in this review.

Summary of findings for the main comparison.

Trauma-focused psychological therapy compared to control intervention

Patient or population: Individuals with post-traumatic stress disorder and comorbid substance use disorder
Settings: Community addiction and mental health services
Intervention: Individual-based psychological therapy including a trauma-focused component
Comparison: Treatment as usual/minimal intervention/placebo intervention

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	TAU/ minimal intervention	Individual-based psychological therapyincluding a trauma-focused component				
PTSD severity following treatment completion As assessed by the CAPS, PSS-I, or IES-R. High scores indicate greater symptom severity	-	The mean PTSD severity following treatment completion in the intervention groups was 0.41 standard deviations lower (0.72 to 0.1 lower)	-	405 (4 studies)	⊕⊖⊖⊖ **very low** [1,2,3]	SMD -0.41 (-0.72 to -0.1) Effect sizes of the range 0.2 to 0.5 indicate a small treatment effect
Drug or alcohol use, or both following treatment completion As assessed by the TLFB or CIDI. High scores indicate greater symptom severity	-	The mean drug/alcohol use following treatment completion in the intervention groups was 0.13 standard deviations lower (0.41 lower to 0.15 higher)	-	388 (3 studies)	⊕⊖⊖⊖ **very low** [1,2,3]	SMD -0.13 (-0.41 to 0.15) Not significant
Treatment completers	**Study population**		**RR 0.80** (0.69 to 0.93)	316 (3 studies)	⊕⊕⊖⊖ **low** [1,3]	Indicates higher drop-out in the intervention group
	761 per 1000	609 per 1000 (525 to 708)				
	Moderate					
	718 per 1000	574 per 1000 (495 to 668)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CAPS: Clinician Administered PTSD Scale; **CI:** confidence interval; **CIDI:** Composite International Diagnostic Interview; **IES-R:** Impact of Events Scale-Revised; **PSS-I:** PTSD Symptom Scale-Interview; **PTSD:** post-traumatic stress disorder; **RR:** risk ratio; **SMD:** standardised mean difference; **TAU:** treatment as usual; **TLFB:** Timeline Followback Interview

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Quality of evidence downgraded by one point because the risk of bias in most trials was high or unclear in several domains.
[2]Quality of evidence downgraded by one point because of a high level of unexplained statistical heterogeneity.
[3]Quality of evidence downgraded by one point as a result of significant clinical heterogeneity.
SUD based adjunctive therapy was not a formal part of either the experimental or control condition in one study (Coffey 2006). However, participants were recruited through an SUD based service and it is likely that they would have had access to adjunctive SUD- based therapy on an informal basis. All other studies in this comparison included formal access SUD-based adjunctive therapy.

Summary of findings 2. Trauma-focused psychological intervention compared to active psychological intervention for SUD only

Trauma-focused psychological therapy compared to active psychological therapy for SUD only

Patient or population: Individuals with post-traumatic stress disorder and comorbid substance use disorder
Settings: Community addiction and mental health services
Intervention: Individual-based psychological therapy including a trauma-focused component
Comparison: Active psychological therapy for SUD only

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Active psychological therapyfor SUD only	Individual-based psychological therapyincluding a trauma-focused component				
PTSD severity following treatment completion As assessed by the CAPS. High scores indicate greater symptom severity	-	The mean PTSD severity following treatment completion in the intervention groups was **3.91 lower** (19.16 lower to 11.34 higher)	-	46 (1 study)	⊕⊕⊖⊖ **low** [1]	Not significant

Drug or alcohol use, or both following treatment completion As assessed by the TLFB. High scores indicate greater symptom severity	-	The mean drug/alcohol use following treatment completion in the intervention groups was **1.27 lower** (5.76 lower to 3.22 higher)	-	46 (1 study)	⊕⊕⊖⊖ **low** [1]	Not significant
Treatment completers	**Study population**		**RR 1** (0.74 to 1.36)	62 (1 study)	⊕⊕⊖⊖ **low** [1]	Not significant
	724 per 1000	**724 per 1000** (536 to 985)				
	Moderate					
	724 per 1000	**724 per 1000** (536 to 985)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CAPS: Clinician Administered PTSD Scale; **CI:** confidence interval; **PTSD:** post-traumatic stress disorder; **RR:** risk ratio; **SUD:** substance use disorder; **TLFB:** Timeline Follow-back Interview

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Quality of evidence downgraded by two points because findings were based on outcomes from one study with a small sample size.
SUD based adjunctive therapy was not a formal part of either the experimental or control condition in the study contributing to this comparison.

Summary of findings 3. Non-trauma-focused psychological intervention for PTSD and SUD or PTSD only compared to control intervention

Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only compared to control intervention

Patient or population: Individuals with post-traumatic stress disorder and comorbid substance use disorder
Settings: Community addiction services and prison service
Intervention: Group- and individual-based non-trauma-focused psychological therapy

Outcomes	Illustrative comparative risks* (95% CI)	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments

	Assumed risk	Corresponding risk				
	TAU/minimal intervention	**Group or Indvidual based non-trauma-focused psychological therapy**				
PTSD severity following treatment completion - Individual-based intervention As assessed by the CAPS. High scores indicate greater symptom severity	-	The mean PTSD severity following treatment completion in the intervention groups was **0.22 standard deviations lower** (0.83 lower to 0.39 higher)	-	44 (1 study)	⊕⊕⊝⊝ **low** [1]	SMD -0.22 (-0.83 to 0.39)
PTSD severity following treatment completion - Group-based intervention As assessed by the CAPS or IES-R. High scores indicate greater symptom severity	-	The mean PTSD severity following treatment completion in the intervention groups was **0.02 standard deviations lower** (0.19 lower to 0.16 higher)	-	513 (4 studies)	⊕⊕⊝⊝ **low** [2,3]	SMD -0.02 (-0.19 to 0.16)
Drug or alcohol use, or both following treatment completion - Individual-based intervention	-	No data	-	-	-	Not estimable
Drug or alcohol use, or both following treatment completion - Group-based intervention As assessed by the ASI, TLFB or CIDI. High scores indicate greater symptom severity	-	The mean drug/alcohol use following treatment completion in the intervention groups was **0.41 standard deviations lower** (0.97 lower to 0.14 higher)	-	464 (3 studies)	⊕⊝⊝⊝ **very low** [2,3,4]	SMD -0.41 (-0.97 to 0.14) Not significant
Treatment completers - Individual-based intervention	-	No data	-	-	-	Not estimable
Treatment completers - Group-based intervention	**Study population**		**RR 1.13** (0.88 to 1.45)	381 (2 studies)	⊕⊕⊝⊝ **low** [2,3]	-
	538 per 1000	**608 per 1000** (473 to 780)				
	Moderate					
	493 per 1000	**557 per 1000** (434 to 715)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
ASI: Addiction Severity Index; **CAPS:** Clinician Administered PTSD Scale; **CI:** confidence interval; **CIDI:** Composite International Diagnostic Interview; **IES-R:** Impact of Events Scale-Revised; **PTSD:** post-traumatic stress disorder; **RR:** risk ratio; **SMD:** standardised mean difference; **SUD:** substance use disorder; **TAU:** treatment as usual; **TLFB:** Timeline Followback Interview

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Quality of evidence downgraded by two points because findings were based on outcomes from one study with a small sample size.
[2]Quality of evidence downgraded by one point because the risk of bias in most trials was high or unclear in several domains.
[3]Quality of evidence downgraded by one point because of significant clinical heterogeneity.
[4]Quality of evidence downgraded by one point because of a high level of unexplained statistical heterogeneity.
The individual-based study (Mueser 2008) in this comparison did not include access to SUD based adjunctive therapy. Participants in all other studies were able to access SUD-based adjunctive therapy.

Summary of findings 4. Non-trauma-focused psychological intervention for PTSD and SUD or PTSD only compared to active psychological intervention for SUD only

Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only compared to active psychological therapy for SUD only

Patient or population: Individuals with post-traumatic stress disorder and comorbid substance use disorder
Settings: Community substance abuse treatment programs
Intervention: Individual-based combined non-trauma-focused psychological therapy
Comparison: Active psychological therapy for SUD only

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Active psychological therapyfor SUD only	Individual-based combined non-trauma-focused psychological therapy				
PTSD severity following treatment completion	-	The mean PTSD severity following treatment completion in the intervention groups was **0.26 standard deviations lower** (1.29 lower to 0.77 higher)	-	128 (2 studies)	⊕⊖⊖⊖ **very low** [1,2,3]	SMD -0.26 (-1.29 to 0.77) Not significant

As assessed by the CAPS. High scores indicate greater symptom severity						
Drug or alcohol use, or both following treatment completion As assessed by the SUI or ASI. High scores indicate greater symptom severity	-	The mean drug/alcohol use following treatment completion in the intervention groups was **0.22 standard deviations higher** (0.13 lower to 0.57 higher)	-	128 (2 studies)	⊕⊕⊖⊖ **low** [1,3]	SMD 0.22 (-0.13 to 0.57) Not significant
Treatment completers	**Study population**		**RR 0.91** (0.68 to 1.20)	128 (2 studies)	⊕⊖⊖⊖ **very low** [1,3]	Not significant
	618 per 1000	**563 per 1000** (420 to 742)				
	Moderate					
	591 per 1000	**538 per 1000** (402 to 709)				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
ASI: Addiction Severity Index; **CAPS:** Clinician Administered PTSD Scale; **CI:** confidence interval; **PTSD:** post-traumatic stress disorder; **RR:** risk ratio; **SMD:** standardised mean difference; **SUD:** substance use disorder; **SUI:** Substance Use Inventory

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

[1]Quality of evidence downgraded by one point because the risk of bias in most trials was high or unclear in several domains.
[2]Quality of evidence downgraded by two points because of a high level of unexplained statistical heterogeneity.
[3]Quality of evidence downgraded by one point because findings were based on outcomes from two studies with small sample sizes.
Both studies in this comparison involved access to adjunctive SUD-based therapy.

BACKGROUND

Description of the condition

Post-traumatic stress disorder (PTSD) is a relatively common and well-recognised psychiatric disorder that occurs following a major traumatic event (NCCMH 2005). Characteristic symptoms include re-experiencing phenomena such as nightmares and recurrent distressing thoughts of the event, avoidance and numbing of general responsiveness such as trying not to talk about or be reminded of the traumatic event, experiencing detachment and estrangement from other people, and hyperarousal symptoms including sleep disturbance, increased irritability, and hypervigilance (APA 2013).

Substance use disorder (SUD) is defined as a complex behavioural disorder characterised by preoccupation with obtaining alcohol or other drugs and a narrowing of behavioural repertoire towards excessive consumption and loss of control over consumption. It is usually also accompanied by the development of tolerance to the substances being consumed and withdrawal and impairment in social and occupational functioning (APA 2013). In diagnostic terms, SUD is characterised by maladaptive misuse of substances (such as alcohol, amphetamines, cannabis, cocaine, hallucinogens, opioids, inhalants, phencyclidine, sedatives, hypnotics, and anxiolytics), which leads to clinically significant impairment or distress (APA 2013). Impairment might include increased tolerance, excessive prolonged usage, recurrent failure to meet important responsibilities, recurrent use in situations when this is likely to be physically dangerous, inability to reduce or limit usage, and considerable time spent obtaining substances or recovering from their effects.

Comorbidity between PTSD and SUD is common (Chilcoat 2003; Ford 2007; Reynolds 2005; Schäfer 2007). Epidemiological studies show significantly increased rates of PTSD amongst individuals with SUD (for example Chilcoat 1998a; Chilcoat 1998b; Cottler 1992; Dragan 2007; Driessen 2008; Helzer 1987; Mills 2006; Najavits 1998; Reynolds 2005; Reynolds 2011; Schäfer 2010), with the prevalence of lifetime PTSD ranging from 26% to 52% and prevalence of current PTSD from 15% to 42% (Driessen 2008; Reynolds 2011; Schäfer 2007; Schäfer 2010). In the Australian National Survey of Health and Wellbeing, Mills 2006 found opiates, sedatives, and amphetamines to be the drug groups to have most frequent comorbid PTSD. SUDs have also been found to be prevalent amongst individuals with PTSD (Chilcoat 2003; Jacobsen 2001; Mills 2006). In PTSD-diagnosed samples, prevalence rates of comorbid substance abuse range from 19% to 35% and comorbid alcohol abuse from 36% to 52% (Breslau 1992; Kessler 1995; Pietrzak 2011), with estimates being even higher in some clinical populations, such as military veterans (Jacobsen 2001; Keane 1990; Kulka 1990; McDevitt-Murphy 2010; Ruzek 2003). In a large epidemiological study of over 34,000 individuals in a community sample in the USA, Pietrzak 2011 found that 6.4% of the sample met lifetime diagnosis for full PTSD. Comorbidity was common across the PTSD sample (some 2463 individuals), with 46.4% meeting diagnosis for any alcohol or drug use disorder, 41.8% meeting diagnosis for alcohol abuse or dependence, and 22.3% meeting diagnosis for drug use or dependence. In another large epidemiological study, Kulka 1990 found that 73% of Vietnam veterans who met the diagnosis for PTSD qualified for a lifetime diagnosis of alcohol abuse or dependence. The Australian National Survey of Health and Wellbeing found that 34.4% of those with PTSD also had an SUD, most commonly an alcohol use disorder (24.1%) (Mills 2006). A number of other subgroups have been found to have particularly high rates of comorbidity of PTSD and SUD. Such groups include women, adolescents, the homeless, prisoners, gays and lesbians, rescue workers, sex workers, and victims of domestic violence (Najavits 2006).

Individuals with both disorders have also been found to have a more severe clinical profile than those with either disorder alone, lower general functioning, poorer well-being, and worse outcomes across a variety of measures (Schäfer 2007). Such individuals are also more likely to meet additional criteria for other psychiatric disorders, such as affective disorders, anxiety disorders, and personality disorders (Mills 2006; Schäfer 2007). For these reasons, randomised controlled trials evaluating PTSD treatment therapies routinely exclude individuals with substance misuse-related problems (Ouimette 2003b). A number of authors have called for greater understanding of the impact of this comorbidity on treatment outcomes and research to determine which therapies are most effective in treating these comorbid conditions (for example Mills 2006; Ouimette 2003a; Ouimette 2003b; Ouimette 2003c).

Description of the intervention

There are a number of established and evidence-based forms of psychological therapies for both PTSD and SUD (van Dam 2012). Several forms of trauma-focused cognitive behavioural therapy (TF-CBT) have been demonstrated to be effective in treating PTSD (Bisson 2013; Bradley 2005). Evidence-based therapies include prolonged exposure, cognitive processing therapy, brief eclectic psychotherapy, and cognitive therapy. A common component of these trauma-focused therapies is that they include some form of guided exposure to the traumatic memory. For example, prolonged exposure involves asking the patient to relive the trauma imaginally. This is often conducted by creating a detailed present-tense account of exactly what happened during the traumatic event, making an audio recording of it, and asking the individual to listen to this over and over again. Other common components of TF-CBT include in vivo exposure to feared situations and cognitive therapy focused on distorted thinking and beliefs. Variants of these TF-CBT models have been developed for specific subgroups. For example, narrative exposure therapy was developed for use with refugees and those who have been exposed to war and violent conflict, and skills training in affective and interpersonal regulation and narrative story telling (STAIR/NST) was developed for individuals with a history of childhood trauma. Eye movement desensitisation and reprocessing (EMDR) has also been well established as an intervention for PTSD (Bisson 2013). EMDR involves the PTSD sufferer focusing on a traumatic image, thought, emotion, and a bodily sensation whilst receiving bilateral stimulation most commonly in the form of eye movements. There is also evidence for the efficacy of stress management training in the treatment of PTSD, although treatment effects have not been demonstrated to be as great as for TF-CBT-based interventions or EMDR (Bisson 2013). Concerns remain about the applicability of these types of treatments to complex cases (Ruscio 2006). Studies evaluating interventions for PTSD have typically excluded those individuals with certain complexities such as SUD, suicidality, serious self harm, homelessness, and serious mental illness, and a recent meta-analysis suggests that the benefits of specific interventions are smaller for individuals with more complex clinical problems (Gerger 2014). This study also highlighted the possible

benefits gained from non-specific interventions. A key principle of treatment that is endorsed by many expert clinicians in the trauma field is that treatment for individuals with complex PTSD presentations should be phased (Herman 1992), with an emphasis on interventions aimed at promoting a sense of safety and stabilisation of symptoms through improving self management and emotional regulation prior to the onset of trauma-focused intervention (Cloitre 2011).

Cognitive behavioural therapies are also considered to be effective for SUD (Knapp 2007; van Dam 2012). A number of interventions based on the principles of CBT or behaviour therapy have been found to be effective for those with drug and alcohol problems. These include coping-skills training, relapse prevention, contingency management, and behavioural couples therapy. Coping-skills training and relapse prevention approaches are aimed at strengthening adaptive coping skills and reducing the risk of relapse in high-risk or challenging situations. Contingency management is based on principles of operant conditioning. It aims to encourage adaptive abstinence-focused behaviours through means of positive incentives. Contingency management has been found to be effective in the treatment of cocaine and stimulant misuse (Knapp 2007), and there is some evidence of effectiveness with opioid users (Mayet 2004). Behavioural couples therapy (BCT) recognises that interpersonal and relationship factors are often associated with relapse. In common with other cognitive behavioural therapies, BCT seeks to improve behavioural self control and develop new coping skills to facilitate and maintain abstinence. It also seeks to improve general relationship functioning and partners' coping with drinking or drug use-related situations. BCT has been found to be effective at reducing frequency of usage, reducing negative consequences of use, and increasing relationship satisfaction in a number of studies with alcohol, opiate, and poly-substance users (Powers 2008). Other popular psychosocial models for treating addiction include motivational interviewing (MI) and 12-step approaches. MI is a widely used intervention in many addiction services. MI is a semi-directive method for enhancing intrinsic motivation to change by exploring and resolving ambivalence through Socratic questioning and cognitive behavioural strategies. There is some evidence for the effectiveness of MI in reducing substance use in a number of studies (Smedslund 2011). One of the most widely used intervention programmes for alcohol misuse and dependence is the 12-step approach, originally developed by Alcoholics Anonymous. The 12-step approach consists of a brief, structured, manual-driven approach to facilitating recovery from alcohol abuse, intended to be implemented over 12 to 15 sessions. Some 12-step approaches include a spiritual approach, some are led by a professional, and others are led by former alcohol dependents. In a Cochrane review of the 12-step approach, Ferri 2006 concluded that there was no strong evidence for effectiveness in reducing alcohol dependence, although the programme remains popular.

For various reasons, individuals with PTSD and SUD comorbidity are perceived as being more difficult to treat than individuals with either condition alone (Najavits 2002a; Schäfer 2007). This comorbidity is associated with poorer recruitment and retention in treatment programmes (Foa 2010; Najavits 2002a; Schäfer 2007), poorer treatment outcomes (Berenz 2012; Najavits 2002a; Ouimette 2003a; Ouimette 2003b; Reynolds 2005; Schäfer 2007), poorer treatment adherence, and shorter periods of abstinence post-treatment (Brown 2003). Despite high prevalence levels, adults in treatment for SUD are frequently not assessed for PTSD (Mills 2006), or offered PTSD-based interventions (Ford 2007; Ouimette 2003b; Reynolds 2005). There is a paucity of evidence for recommendations about treatment interventions for affective or anxiety disorders that are comorbid with SUD (Watkins 2005; Wilson 2008). In practice, a wide range of pharmacological and psychological therapies are used to treat the comorbidity. A concern for many treating clinicians related to intervention with some pharmacological agents such as benzodiazepines, is that patients might abuse these agents. In recognition of the clinical challenges involved in treating individuals with comorbid PSTD and SUD, a number of specialised psychological therapy approaches have been developed over the past 15 years or so. Three different types of treatment approach are identified in the literature (Gulliver 2010; Weiss 1995a): sequential, concurrent, and integrated. In sequential approaches, one comorbidity - usually substance misuse - is treated first, and the other - usually PTSD - afterwards. One sequential model to have received some attention is 'Transcend', a partially inpatient hospital-based model (Donovan 2001). With concurrent approaches, each condition is treated separately but simultaneously using established evidence-based interventions for each condition (Brady 2001; Triffleman 1999). One example of a concurrent approach is concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE) (Back 2001; Mills 2007). COPE uses cognitive behavioural therapy for substance use throughout the duration of the 13 treatment sessions and prolonged exposure for PTSD from around session five (Foa 1998). Integrative approaches treat both conditions together using interventions to address both disorders at the same time. Amongst integrative models, 'Seeking Safety' has probably received the most attention, with a number of randomised and non-randomised evaluative studies (Najavits 2002b; Najavits 2007). Seeking Safety is a skills-based therapy that aims to develop adaptive cognitive, behavioural, and interpersonal coping. Seeking Safety can be delivered on an individual basis or via groups.

Treatment interventions for PTSD and comorbid SUD have recently become a topic for review, in Berenz 2012 and Najavits 2013, and systematic review (Torchalla 2012; van Dam 2012). These reviews suggest some positive preliminary findings in relation to integrated and trauma-focused psychological therapies for comorbidity. Najavits 2013, Torchalla 2012, and van Dam 2012 based their conclusions on evidence from both controlled and non-controlled trials. All of these reviews identified significant methodological limitations in the studies reviewed. Several recently published controlled trials were not included in any of these reviews.

How the intervention might work

A number of different explanations for the relationship between SUD and PTSD have been proposed (Meyer 1986; Schäfer 2007). The most widely supported explanation is that PTSD influences the development of SUD, through means such as self medication (Schäfer 2007). Other explanations include the possibility that problematic substance use increases the risk of being exposed to trauma and increases psychological vulnerability to the effects of trauma (Meyer 1986; Schäfer 2007).

psychological therapies may therefore effect change in symptoms and functioning in such individuals through a number of different mechanisms. One potential mechanism by which psychological therapies might work is the development of enhanced coping skills which may increase the ability to regulate negative emotions

(Busuttil 2009), leading to increased capacity to tolerate traumatic memories and craving urges. Another potential mechanism is the processing of trauma memories (Ehlers 2000; Foa 1998) leading to a decreased need to 'self medicate'. Psychological therapies such as those based on cognitive behavioural therapy (CBT) are also likely to promote changes in thinking and belief systems underlying trauma memories, and beliefs and ideas about substance use (Ehlers 2000; Najavits 2002b). For example, such interventions may facilitate attitudinal change to substance misuse and aid increased understanding of cognitive and situational risk factors associated with patterns of drug taking or problematic drinking, particularly those associated with past trauma. Other change mechanisms might include the development and reinforcement of adaptive coping skills which support constructive coping with both conditions (Brown 2003). It is likely that different interventions will operate though different means of change.

Why it is important to do this review

A number of systematic reviews of interventions for PTSD have been published in the Cochrane Library. As already noted, Bisson 2013 (along with other reviews, for example Bradley 2005) has described fairly robust evidence for trauma-focused CBT and EMDR as treatments for chronic PTSD, with emerging evidence for some non-trauma-focused CBT-based interventions and trauma-focused CBT-based group interventions. Other Cochrane reviews have considered single-session psychological 'debriefing' to prevent PTSD (Rose 2002), multiple-session early psychological therapies for the prevention of PTSD (Roberts 2009), early psychological therapies to treat acute traumatic stress symptoms (Roberts 2010), pharmacological treatments (Stein 2006), combined pharmacotherapy and psychological therapies for PTSD (Hetrick 2010), and psychological therapies for the treatment of PTSD in children and adolescents (Gillies 2012). Over 70 systematic reviews of interventions for SUD have been published in the Cochrane Library. Reviews of psychological therapies have considered psychosocial interventions for cocaine and psychostimulant amphetamines-related disorders (Knapp 2007), psychosocial interventions for opiate abuse and dependence (Mayet 2004), motivational interviewing for substance abuse (Smedslund 2011), 12-step programmes for alcohol dependence (Ferri 2006), and psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users (Klimas 2014).

The issue of how best to manage or plan intervention for individuals with comorbid PTSD and SUD is a challenging one for clinicians (Najavits 2002a), and there is no real consensus about best practice. Most diagnosis-specific guidelines for PTSD and other mental health disorders are silent as to whether the specific treatment recommendation applies to co-occurring disorders (Watkins 2005). As we have discussed, comorbidity is a frequent problem, and those individuals with comorbidity are more challenging for general mental health services, trauma specialists, and addiction services to treat (Schäfer 2007). In clinical practice, many clinicians still argue the addiction should be treated first (for example Busuttil 2009; Foa 2000; Zayfert 2007), or that abstinence is necessary before diagnosis and a management plan can be made (see Watkins 2005). The reality for many people with comorbidity is that they can frequently get passed between services with little co-ordination of care (Najavits 2006). Watkins 2005 argues that there has been a broad shift in the literature towards more co-ordinated treatment plans over recent years, although it is far from clear that there is strong evidence to support this shift or that it has translated into change in routine clinical practice. There is also contention about perceived high risk of adverse effects of psychological evidence-based treatment therapies, such as eye movement desensitisation and reprocessing and prolonged exposure, with comorbid groups (see Watkins 2005). We hope this review will be able to shed some light on what evidence there is to support these different models and treatment approaches, in order to aid clinician decision making.

OBJECTIVES

To determine the efficacy of psychological therapies aimed at treating traumatic stress symptoms, substance misuse symptoms, or both in people with comorbid PTSD and SUD in comparison with control conditions (including usual care, waiting-list conditions, and no treatment) and other psychological therapies.

METHODS

Criteria for considering studies for this review

Types of studies

Any randomised or cluster-randomised controlled trial that considers one or more defined psychological therapy aimed at reducing traumatic stress symptoms, SUD symptoms, or both. We did not use sample size and publication status to determine whether or not a study should be included. Studies published in all languages were eligible for inclusion.

We were willing to include for consideration studies using a cross-over design (for example specified intervention aimed at reducing traumatic stress symptoms followed by intervention aimed at reducing substance use and vice versa), as we felt that this addresses issues of clinical debate. However, we identified no such studies.

Types of participants

Participant characteristics

We made no restriction on age, although we anticipated that most studies would focus on adult populations. We did not make decisions about inclusion or exclusion on the basis of gender or ethnicity.

Diagnosis

Any individual suffering from comorbid PTSD and SUD. Treatment studies of individuals with PTSD and associated disorders such as acute stress disorder have sometimes included individuals who met most but not all criteria for the condition. In light of this, a previous Cochrane review of psychological therapies for PTSD, Bisson 2013, specified that at least 70% of participants had to be diagnosed as suffering from PTSD according to the International Classification of Diseases (ICD), WHO 1993, or Diagnostic and Statistical Manual of Mental Disorders (DSM), APA 2013. We believe that the issue of inclusion of some individuals with subthreshold diagnosis is likely to occur in comorbid studies as well. For this review, we decided to set a more conservative limit that at least 80% of participants will have been diagnosed as suffering from PTSD according to DSM or ICD criteria. Similarly, at least 80% of participants met formal diagnostic criterion for a substance misuse

disorder according to DSM, APA 2013, or equivalent ICD definitions, WHO 1993, based on codes F10 to F19, excluding F15 (caffeine) and F17 (tobacco). Codes F10 to F19 include mental and behavioural disorders due to use of alcohol (F10), opioids (F11), cannabinoids (F12), sedatives or hypnotics (F13), cocaine (F14), other stimulants (amphetamine) (F15), hallucinogens (F16), volatile solvents (F18), and multiple drug use and use of other psychoactive substances (F19). There was no restriction on the basis or severity of PTSD symptoms, type of traumatic event, or nature of substance use (including alcohol).

Comorbidities

We made no restriction on other comorbidity.

Setting

There was no restriction on the setting in which a study took place.

Subset data

Although we applied an 80% threshold for diagnosis of PTSD and SUD, we also decided that when we identified studies where a significant subset of participants met our inclusion criteria (below the 80% threshold), we would approach the study authors to see if we could obtain outcome data for the subset who met inclusion, if such information was not available in the study report. If we were able to obtain these data and other inclusion criteria were met, we would then include the data in the review. We made the decision to potentially include studies on this basis after the review protocol was published.

Types of interventions

Experimental interventions

We considered any experimental psychological therapy designed to reduce symptoms of PTSD, substance usage, or both.

For the purposes of this review, a psychological therapy included any specified non-pharmaceutical intervention aimed at reducing traumatic stress symptoms, SUD, or both, offered by one or more health professional or layperson. Potential therapy categories included any of the following.

1. Trauma-focused psychological therapy: any psychological therapy including trauma-focused cognitive behavioural therapy (TF-CBT) and eye movement desensitisation and reprocessing (EMDR), delivered to individuals with comorbidity. TF-CBT includes any intervention that uses predominantly trauma-focused cognitive, behavioural, or cognitive-behavioural techniques. This category includes individual exposure therapy and specialised treatment packages such as concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE), which include interventions for SUD (Back 2001; Mills 2007), and group approaches such as 'Transcend' (Donovan 2001). Individual trauma-focused interventions for PTSD have been found to be more effective than group-based intervention (Bisson 2013). We therefore made a post hoc decision to present and analyse individual- and group-based trauma-focused approaches separately.
2. Non-trauma-focused therapy for both PTSD and SUD or PTSD or SUD only: any psychological therapy including CBT aimed at addressing symptoms of PTSD and SUD on a sequential or integrated basis that does not include treatment of PTSD symptoms through a trauma-focused or exposure-based therapy. Interventions are likely to be targeted at increasing knowledge through psychoeducation and on improving coping skills. This category includes Seeking Safety (Najavits 2002b), which can be delivered on an individual basis or through groups. Group interventions are generally considered to show weaker effects than individual interventions (Najavits 2014 [personal communication]). We made a post hoc decision to present and analyse individual- and group-based non-trauma-focused approaches separately.
3. Active psychological therapy for SUD only. This includes structured therapeutic programmes based on CBT, 12-step, contingency management, and reinforcement-based therapies. It also includes interventions based on motivational interviewing and psychological therapies aimed at management of cravings or to achieve abstinence.

The experimental intervention could be delivered as a monotherapy or as an adjunct to an established treatment that was received (in an identical way) by participants in both the experimental and the comparator group, for example TF-CBT plus CBT for SUD versus CBT for SUD alone.

Comparator interventions

1. A control intervention included no intervention or any minimal intervention such as a waiting-list control, treatment as usual, minimal or placebo condition.
2. An alternative active psychological therapy as described above.

Types of outcome measures

Primary outcomes

1. Severity of traumatic stress symptoms using a standardised measure such as the Clinician Administered PTSD Symptom Scale (CAPS) (Blake 1995), the Impact of Event Scale (Horowitz 1979), the Davidson Trauma Scale (Davidson 1997), or the Post-Traumatic Diagnostic Scale (Foa 1997a). In circumstances where an individual study utilised both a clinician-administered and a self report measure, primacy was given to outcomes using the clinician-administered measure, as such measures are considered to provide the 'gold standard' in the traumatic stress field (for example Foa 1997b).

2. Reduction in drug use, alcohol use, or both as measured by a standardised measure such as the Addiction Severity Index (ASI) (McLellan 1992), the Substance Use Inventory (Weiss 1995b), the Opiate Treatment Index (Darke 1992), the Severity of Drug Dependence Scale (Gossop 1995), or the Substance Abuse Module (Haro 2006), or biological markers of drug and alcohol use, such as urine, saliva, and hair analysis, or self reported days of substance use/abstinence within a specified period such as the Timeline Followback Interview (Sobell 1995). There is less consensus about gold-standard outcomes in the addiction field. We prioritised outcomes in the order of standardised instruments, followed by biological markers, followed by self report measures.

3. Treatment completion as measured by number of participants who were identified as treatment completers by study authors. We undertook to interpret drop-out data with caution, as it is recognised that participants can withdraw from studies for various and complex reasons and reported drop-out can be influenced by

experimental factors related to practice of the research team (Loke 2011).

Secondary outcomes

4. PTSD diagnosis after treatment.

5. SUD diagnosis after treatment.

6. Adverse events reported by number and type.

7. Compliance, as measured by proportion of treatment sessions attended.

8. General functioning, including quality of life measures such as the 36-Item Short Form Survey (SF-36) (Ware 2003).

9. Use of health-related resources (e.g. hospital admission, outpatient contacts, visits to primary care).

Timing of outcome assessment

When information was available primary outcomes were analysed at the following time points.

- Immediately post-treatment
- 3 to 4 months post-treatment
- 5 to 7 months post-treatment
- 8 to 11 months post-treatment
- 12 months and beyond post-treatment

Our primary outcome point was immediately post-treatment. We analysed secondary outcomes only at this time point.

Search methods for identification of studies

The Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (CCDANCTR)

The Cochrane Depression, Anxiety and Neurosis Group (CCDAN) maintains two clinical trials registers at their editorial base in Bristol, UK: a references register and a studies-based register. The CCDANCTR-References Register contains over 39,500 reports of randomised controlled trials (RCTs) in depression, anxiety, and neurosis. Approximately 60% of these references have been tagged to individual, coded trials. The coded trials are held in the CCDANCTR-Studies Register, and records are linked between the two registers through the use of unique Study ID tags. Coding of trials is based on the EU-Psi coding manual, using a controlled vocabulary; please contact the CCDAN Trials Search Co-ordinator for further details. Reports of trials for inclusion in the Group's registers are collated from routine (weekly), generic searches of MEDLINE (1950-), EMBASE (1974-), and PsycINFO (1967-); quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL); and review-specific searches of additional databases. Reports of trials are also sourced from international trials registers c/o the World Health Organization's trials portal (the International Clinical Trials Registry Platform (ICTRP)), pharmaceutical companies, and the handsearching of key journals, conference proceedings, and other (non-Cochrane) systematic reviews and meta-analyses.

Details of CCDAN's generic search strategies (used to identify RCTs) can be found on the Group's website.

Electronic searches

We conducted searches for Condition (PTSD) and Population (patients with comorbid substance abuse) to 11 March 2015.

1. CCDANCTR-Studies Register

We searched the studies register using the following terms:

Condition = ("post-traumatic stress disorders") AND Comorbidity = ("alcohol dependence" or "substance related disorders" or "substance abuse")

2. CCDANCTR-References Register

We searched the references register using a more sensitive set of free-text terms:

[Condition]
1. (PTSD or post-trauma* or "post trauma*" or posttrauma* or "stress disorder*" or "combat disorder*" or "war neuros*")
2. (trauma* and (psycho* or stress*))
3. (stress* and (extreme or disorder*))
4. DESNOS
5. (1 or 2 or 3 or 4)
[Population: comorbid substance abuse]
6. ("substance use disorder*" or SUD)
7. "drug abuse"
8. (abuser* or abusing or addict* or depend* or habit* or misuse or user*)
9. (abuse and not (child* or sex*))
[Common drugs of abuse]
10. (adinazolam or aerosol* or alcohol* or alprazolam or amphetamin* or anthramycin or anxiolytic* or ativan or barbituat* or bentazepam or benzodiazepin* or bromazepan or brotizolam or buprenorphin* or camazepam or cannabi* or chlordiazepoxid* or cinolazepam or clobazam or clonazepam or clorazepam or clotiazepam or cloxazolam or cocaine* or codeine or crack or crystal or cyprazepam or depressant* or diacetylmorphin* or diazepam* or doxefazepam or ecstasy or estazolam or etizolam or fentanyl or flunitrazepam or flurazepam or flutazoram or flutoprazepam or fosazepam or gases or GHB or girisopam or halazepam or hallucinogen* or haloxazepam or heroin* or hydromorphone or hydroquinone or hypnotic* or inhalant* or ketamin* or ketazolam or librium or loflazepate or loprazolam or lorazepam or lormetazepam or LSD or marihuana* or marijuana* or MDMA or meclonazepam or medazepam or meperidine or mephedrone or mescalin* or metaclazepam or methadone or methamphetamin* or methaqualone or mexazolam or midazepam or midazolam or morphine* or narcotic* or nerisopam or nimetazepam or nitrazepam or nitrites or "nitrous oxide" or "n-methyl-3,4-methylenedioxyamphetamine" or nordazepam or opiate* or opiod* or opium or oxazepam or oxazolam or oxazypam or oxycodone or oxzepam or painkiller* or "pain killer*" or PCP or pethidin* or phencyclidin* or pinasepam or prazepam or propazepam or propoxyphene or psilocybin or psychedelic* or psychoactive* or psychostimulant* or quinazolinone or ripazepam or ritalin or sedative* or serazepin* or solvent* or steroid* or stimulant* or substance* or temazepam or tetrazepam or tofisopam or tramadol or triazolam or triflubazam or valium or vicodin)
11. (drug* and (recreational or street))
12. (6 or 7 or 8 or 9 or 10 or 11)
[Condition + Population]

13. (5 and 12)

We performed a further search on 4 December 2015 (prior to publication). We screened results and placed studies of interest in those awaiting classification; we may include or exclude these in a future update to this review (as appropriate).

3. Cochrane Central Register of Controlled Trials (CENTRAL)

We also searched the Cochrane Central Register of Controlled Trials (CENTRAL) to 3 January 2015 (Appendix 1).

4. International trial registries

We searched the World Health Organization's trials portal (ICTRP) and ClinicalTrials.gov to identify additional unpublished or ongoing studies (11 March 2015 and 4 December 2015).

Searching other resources

We also checked reference lists of studies identified in the search, as well as related review articles and management guidelines. We conducted Internet searches of known websites, conference proceedings, and discussion for the following: American Association for the Treatment of Opioid Dependence (http://www.aatod.org/), DrugScope (http://www.drugscope.org.uk/), European Society for Traumatic Stress Studies (https://www.estss.org), International Harm Reduction Association (http://www.ihra.net/), International Society for Traumatic Stress Studies (http://www.istss.org), Society for the Study of Addiction (http://www.addiction-ssa.org/), and the United Kingdom Psychological Trauma Society (http://www.ukpts.co.uk). We also searched studies included in the Cochrane review 'Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults' (Bisson 2013), and reviews of psychological therapies undertaken for the Cochrane Drug and Alcohol Group. We searched studies within these reviews on the basis that a significant subset of participants might warrant inclusion.

Data collection and analysis

Selection of studies

Two review authors (NPR and PAR) independently read the abstracts of all potential trials. If an abstract appeared to represent an RCT, the two review authors independently read the full report to determine if the trial met the inclusion criteria. In case of disagreement, a third review author was consulted (JIB).

Data extraction and management

We used a data extraction sheet to capture data, which we then entered into Review Manager 5 software (RevMan 2011). Information extracted included demographic details of participants, details of the traumatic event, type of substance use, the randomisation process, the interventions used, drop-out rates, and outcome data. Three review authors (NPR, PAR, and NJ) independently extracted data. In case of disagreement, the fourth review author was consulted (JIB).

Main planned comparisons

1. Trauma-focused psychological therapy versus control intervention
2. Trauma-focused psychological therapy versus non-trauma-focused psychological therapy for PTSD and SUD or PTSD only
3. Trauma-focused psychological therapy versus active psychological therapy for SUD only
4. Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only versus control intervention
5. Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only versus active psychological therapy for SUD only
6. Active psychological therapy for SUD only versus control intervention

We undertook to present and analyse data for individual- and group-based interventions separately.

Assessment of risk of bias in included studies

We assessed risk of bias using The Cochrane Collaboration's 'Risk of bias' tool and reported the results in a standard 'Risk of bias' table. We assessed the following domains:

1. Sequence generation: Was the allocation sequence adequately generated?
2. Allocation concealment: Was allocation adequately concealed?
3. Blinding of participants, personnel, and outcome assessors for each main outcome or class of outcomes: Was knowledge of the allocated intervention adequately prevented during the study?
4. Incomplete outcome data for each main outcome or class of outcomes: Were incomplete outcome data adequately addressed?
5. Selective outcome reporting: Are reports of the study free of suggestion of selective outcome reporting?
6. Other sources of bias: Was the study apparently free of other problems that could put it at a high risk of bias?

We judged the risk of bias for each domain within and across studies, based on the following three categories:

- low risk of bias;
- unclear risk of bias;
- high risk of bias.

Three review authors (NPR, PAR, and NJ) independently assessed risk of bias for each study. Any disagreements were initially to be discussed between the three rating review authors. Where disagreement persisted, advice was sought from the fourth review author (JIB).

Measures of treatment effect

We analysed continuous outcomes using mean difference when all trials had measured outcome on the same scale. When trials measured outcomes on different scales, we used the standardised mean difference. We used risk ratio as the main categorical outcome measure, as this is more widely used than odds ratio in health-related practice. We presented all outcomes using 95% confidence intervals.

Unit of analysis issues

Cross-over trials

We did not identify any cross-over trials. However, we specified at the protocol stage that if we included such trials, we would include final outcomes from these trials where the study addressed order of intervention for trauma-related intervention and control

or management of SUD symptoms. For trials that had a cross-over design that did not address these clinical pathway issues, we would only consider results from the first randomisation period. We decided that each stage of analysis would be stratified by treatment type and that further analysis would include follow-up data where these were available. We would only make comparisons involving follow-up data when outcome data were available for similar time points.

Studies with multiple treatment groups

We specified that if the trial had three (or more) arms, we would consider undertaking pair-wise meta-analysis with each arm, depending upon the nature of the intervention in each arm and its relevance to the review objectives. We aimed to avoid multiple comparisons to limit the risk of false-positive results. When a study had three or more arms that were relevant to the review, we would consider the appropriateness of combining data from two arms if interventions were sufficiently similar or of using data from the arms of the trial that fit closest to the review objective. Decisions would follow the guidance provided in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), and we would report the rationale for any decisions made. In actuality, only one study included in the review had more than two treatment arms, and for reasons described below we only included two arms in comparisons.

Cluster-randomised trials

We specified that management of cluster-randomised trials would follow the guidance provided in the *Cochrane Handbook*. We identified no cluster-randomised trials.

Dealing with missing data

When intention-to-treat (ITT) data were available, we reported this in the results. We attempted to access ITT data wherever possible. For dichotomous outcomes, we conducted ITT analysis by making imputations based on the assumption that all missing participants had a negative outcome. We included completer-only data when this was the only data source available. In cases where there was inadequate information within a particular paper to undertake analysis, we made attempts to compute missing data from other information available within the paper, using guidance provided by Higgins 2011. For continuous data when only the standard error, t-statistics, or P values were reported, we calculated standard deviations using the guidance provided by Higgins 2011. When imputation was not possible or when further clarification was required, we attempted to contact the authors to request additional information. In cases where no further useable data was available, we did not include the study in further analysis.

Assessment of heterogeneity

We initially used visual inspection of the forest plots to explore for possible heterogeneity. We also examined heterogeneity between studies by observing the I^2 statistic and Chi^2 test ($P < 0.10$). As suggested in the *Cochrane Handbook* (Higgins 2011), we took an I^2 of less than 30% to indicate mild heterogeneity, and we used a fixed-effect model to synthesise the results. We considered an I^2 of 30% to 60% to indicate moderate heterogeneity and an I^2 of 60% to 90% substantial heterogeneity (Higgins 2011). Due to the level of clinical heterogeneity in the included studies, we decided to use a random-effects model to summarise results including more than one study. We specified that where significant heterogeneity was present, we would attempt to explain the variation.

Assessment of reporting biases

We specified that if sufficient studies (10 or more) were available in a meta-analysis, we would prepare funnel plots and examine them for signs of asymmetry (Egger 1997). We specified that if asymmetry was identified, we would consider possible reasons for this.

Data synthesis

In recognition of the substantial clinical heterogeneity between included studies, we pooled all data using a random-effects model.

Subgroup analysis and investigation of heterogeneity

We specified that we would explore the following possible causes of clinical heterogeneity if data were sufficient to allow.

1. Specified treatment intervention model (e.g. Seeking Safety, Transcend, concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE)).
2. Specified treatment plans (e.g. sequential versus concurrent versus integrated approaches).
3. Participant subgroup (e.g. veterans versus victims of sexual, physical, and domestic violence versus childhood trauma versus rescue workers).
4. Specific substances of misuse (e.g. alcohol versus opioids versus cocaine versus amphetamines).
5. Intervention objectives (treating symptoms of PTSD versus SUD versus general well-being/coping).

Sensitivity analysis

We specified that we would consider sensitivity analysis to explore possible causes of methodological heterogeneity if data were sufficient to allow. We would base analyses on the following criteria.

We would exclude trials considered most susceptible to bias based on the following quality assessment criteria:

1. those judged to be at high risk of bias or unclear risk of bias for allocation concealment;
2. high levels of postrandomisation losses (more than 40%) or exclusions;
3. unblinded outcome assessment or blinding of outcome assessment uncertain.

Summary of findings

We evaluated the quality of the available evidence of our findings using the GRADE approach (Guyatt 2011; Langendam 2013). We generated 'Summary of findings' tables using GRADEprofiler software (http://tech.cochrane.org/revman/gradepro) using data imported from Review Manager 5.3 (RevMan 2011). These tables provide outcome-specific information concerning the overall quality of evidence from studies included in the comparison, the magnitude of effect of the interventions examined, and the sum of available data on the outcomes that were considered. We assessed the quality of evidence using five factors:

- Limitations in study design and implementation of available studies;

- Indirectness of evidence;
- Unexplained heterogeneity or inconsistency of results;
- Imprecision of effect estimates;
- Potential publication bias.

For each outcome that included pooled data, we classified the quality of evidence for each outcome according to the following categories.

- High quality: further research is very unlikely to change our confidence in the estimate of effect.
- Moderate quality: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
- Low quality: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
- Very low quality: we are very uncertain about the estimate.

We downgraded the evidence from 'high quality' by one level for serious (or by two for very serious) study limitations (risk of bias), indirectness of evidence, serious inconsistency, imprecision of effect estimates, or potential publication bias. We included the primary outcomes of PTSD severity, drug and/or alcohol use, and treatment completion in the 'Summary of findings' tables.

RESULTS

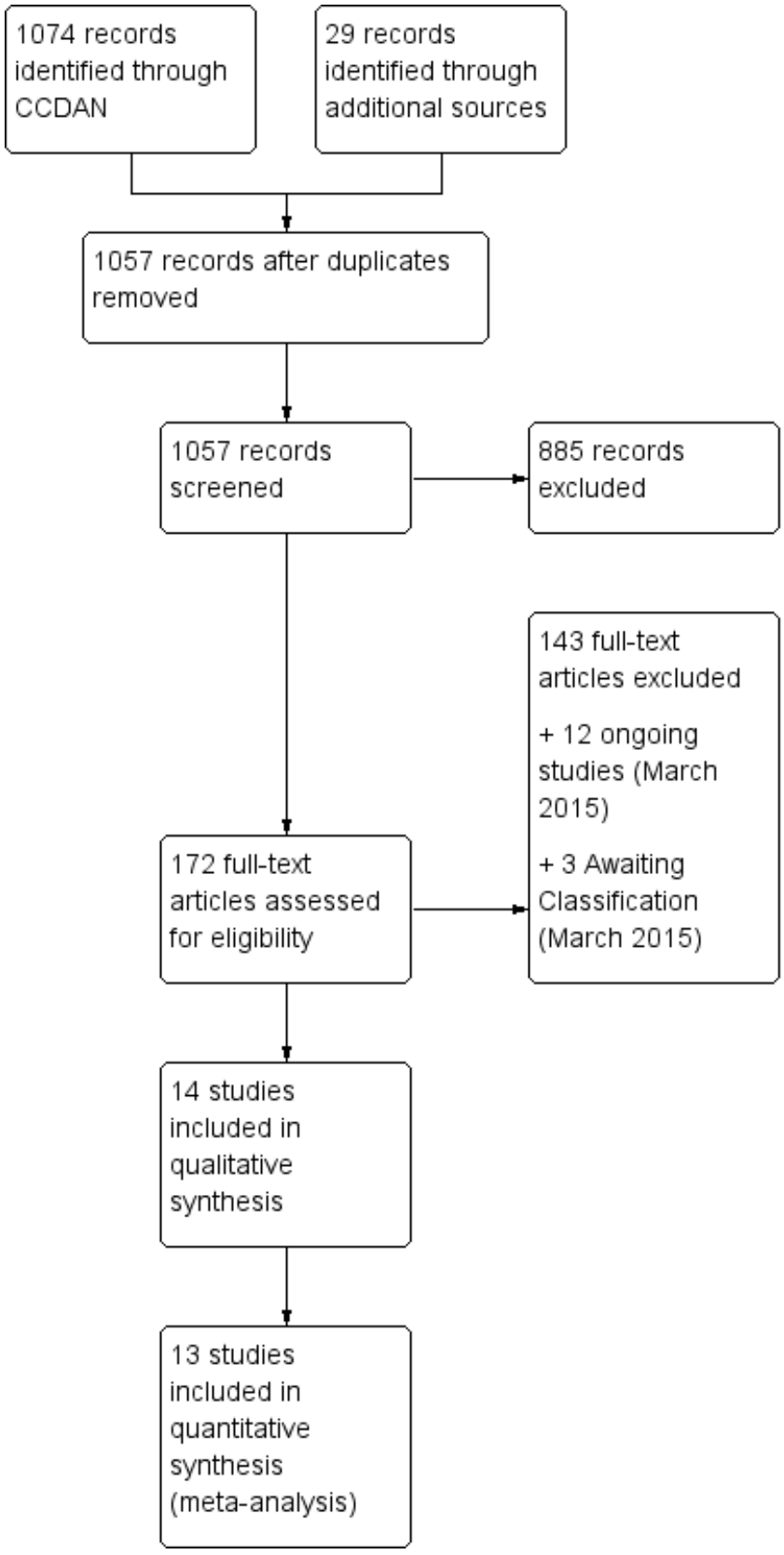
Description of studies

Results of the search

We conducted electronic searches to 11 March 2015 (with results fully incorporated into the review). We also contacted 42 trial investigators; see Appendix 2.

We identified 1099 references, 1057 of which remained after de-duplication. Two review authors (NPR and PAR) independently screened the titles and abstracts of these records and excluded 885 that did not meet the inclusion criteria. For 3 of the remaining 172 study reports we were only able to obtain conference abstracts. We judged these studies as potentially relevant to the review, but were unable to undertake classification of these abstracts. Twelve references were for ongoing studies. We retrieved and inspected the full-text papers for the remaining 157 reports, excluding 143 of them as not meeting our inclusion criteria. Thirteen of the remaining studies met the full inclusion criteria and so were included in the review. We also identified a number of studies with a significant subset of individuals who met all inclusion criteria. We were able to obtain data on this subset from the authors of one study (Mueser 2008), resulting in a total of 14 studies being included in the review. Thirteen of these 14 studies contributed to the quantitative synthesis. The study selection process is also detailed in our PRISMA flow diagram (see Figure 1).

Figure 1. Study flow diagram.



Note: We conducted a further search on 4 December 2015, prior to publication, but did not incorporate results at this time. We screened the abstracts (n = 72) and identified 4 new studies, which we've added to those awaiting classification. Two of these studies meet the eligibility criteria for this review (McGovern 2015; Perez-Dandieu 2015), and a further two will do so if subset data is available (Barrett 2015; Wolf 2015). The December search also identified Stappenbeck 2015 (NCT00760994), which after contacting the trialists was confirmed to be the same trial as Simpson 2011 (already awaiting classification). We also identified an additional five ongoing study protocols (NCT01211106; NCT01457404; NCT01663337; NCT01849029; NCT02335125).

Included studies

We included 14 studies in this review, with characteristics as follows (see also Characteristics of included studies).

Design

All of the included studies were randomised controlled trials or pilot randomised controlled trials. One study was described as a laboratory-based study investigating the effects of trauma-focused intervention on alcohol craving elicited by trauma cues (Coffey 2006). One study had two intervention arms in which allocation was randomised (Hien 2004); a third control arm was added part way through the study, and allocation to this arm was made on a non-randomised basis. We have not included data from this third arm in the review. Studies were randomised at the participant level and used a parallel-group design.

Sample sizes

A total of 1506 participants were allocated to groups across the 14 included studies. The number of participants ranged from 29, in Norman unpublished, to 353, in Hien 2009. Three other studies had fewer than 50 participants (Coffey 2006; Najavits 2006a; Zlotnick 2009), with the subsample of 44 from a cohort of 108 in Mueser 2008. Three studies had 50 to 100 participants (Hien 2004 - excluding the arm that was non-randomised; McGovern 2011; Sannibale 2013), and the remaining six studies included more than 100 participants (Boden 2012; Coffey submitted; Foa 2013; Frisman 2008; Hien 2009; Mills 2012).

Setting

Twelve studies were conducted in the USA; the remaining two studies were carried out in Australia (Mills 2012; Sannibale 2013). The majority of studies recruited individuals from community outpatient substance abuse services. One study recruited from veteran outpatient substance abuse services (Boden 2012). Four studies also made use of advertisements or flyers (Foa 2013; Hien 2004; Mills 2012). Najavits 2006a also recruited from hospitals and schools. Sannibale 2013 recruited from a range of services. Coffey submitted recruited from a residential substance misuse service, and Zlotnick 2009 from the minimum-security wing of a female prison. Mueser 2008 recruited from community mental health services. All participants were seen on an outpatient basis, apart from those in Zlotnick 2009, who received most of their intervention in prison, with some follow-up on release.

Participants

All studies were of adults, apart from Najavits 2006a, who investigated intervention for adolescent girls with a mean age of 16.06 years. One study recruited from veteran populations with an all-male cohort (Boden 2012). Zlotnick 2009 recruited female prisoners. Other studies with a female-only cohort were Hien 2004, Hien 2009, Najavits 2006a, and Norman unpublished. All other studies were of mixed gender and from community groups. All studies met the minimum threshold of 80% of participants meeting full diagnosis for PTSD. Across all studies, 1387 (92.1%) of participants met full diagnosis for PTSD, with the remaining group being described as having subthreshold PTSD. All participants in all studies met minimum criteria for a substance use disorder. Coffey 2006, Coffey submitted, and Foa 2013 included people with alcohol dependence, and Norman unpublished and Sannibale 2013 included people with alcohol use disorder. The majority of participants in Coffey submitted were also drug dependent. The other 10 studies included people with substance abuse. Substance use in these studies was typically polydrug use, with many participants using multiple drugs. None of the included studies targeted one specific substance other than alcohol. The subsample in Mueser 2008 excluded people with substance dependence. Hien 2004 and Mills 2012 only included people with substance dependence, and the majority (93.9%) of participants in Najavits 2006a were also substance dependent.

Exclusion criteria were not identified in Frisman 2008. Most other studies excluded on the basis of current or acute psychosis, current suicidal/homicidal ideation, and significant cognitive impairment (for example resulting from dementia or brain injury). Hien 2009 also excluded on the grounds of past history of psychosis. Mueser 2008 was a study that was primarily interested in intervention for individuals with severe mental illness, and they only excluded individuals who were in psychiatric hospital. In recruiting participants with alcohol dependence, Foa 2013 excluded people with other substance dependence conditions. Sannibale 2013 excluded people with severe substance dependence. Mills 2012 excluded people who had a history of self harm in the past six months. Coffey 2006 excluded people with combat-related PTSD. Coffey submitted excluded those who were in an abusive relationship at the time of recruitment, and Norman unpublished only included participants who had been out of an abusive relationship for at least a month. Hien 2004 and Hien 2009 excluded people with advanced-stage medical diseases. Hien 2009 and McGovern 2011 excluded those involved in ongoing legal disputes. Najavits 2006a also excluded if people were mandated to treatment, or had characteristics that would interfere with treatment completion (mental retardation, homelessness, impending incarceration, or a life-threatening illness). This was the only study to report on exclusion on the basis of homelessness. However, it is argued that people who are homeless are routinely excluded from these kinds of studies (Najavits 2014 [personal communication]).

Interventions

All of the experimental interventions included in the review were based on some form of cognitive behavioural therapy (CBT). Following van Dam 2012, these interventions can perhaps best be summarised and divided into trauma-focused approaches - some of which included combined interventions for SUD - and non-trauma-focused interventions, which mainly involved integrated treatment of PTSD and SUD.

Trauma-focused/combined interventions

Individual-based trauma-focused/combined interventions

Five studies included trauma-focused/exposure-based components as a part of the intervention program, delivered individually. Four studies tested combined coping skills-focused intervention for SUD with exposure-based interventions for PTSD as the experimental condition (Coffey submitted; Foa 2013; Mills 2012; Sannibale 2013). Coffey submitted compared 9 to 12 sessions imaginal and in vivo exposure plus treatment as usual against an equivalent health-related psycho-education intervention. Foa 2013 was a 2x2 study examining the effects of prolonged exposure and naltrexone. For psychological therapies, prolonged exposure plus supportive counselling was compared with supportive counselling alone. The supportive counselling intervention combined medication management with compliance enhancement techniques based on motivational interviewing. We considered this to be equivalent to a treatment-as-usual intervention. For medication, naltrexone was compared against a placebo. The numbers of participants receiving the two psychological therapies were equal in the two medication groups. Mills 2012 compared concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE) against treatment as usual for substance abuse only. COPE includes motivational enhancement and CBT for substance use; psycho-education relating to both disorders and their interaction; in vivo exposure; imaginal exposure; and cognitive therapy for PTSD. Finally, Sannibale 2013 evaluated integrated CBT for PTSD and alcohol use disorder against CBT for alcohol use disorder and supportive counselling. The experimental condition in this trial included cognitive behavioural exposure-based therapy for PTSD, based on a prolonged exposure model with cognitive restructuring, in addition to cognitive therapy for problem drinking. The control intervention had no PTSD components in it. Coffey 2006 tested an exposure-based intervention that has been established for the treatment of PTSD, but recruited from within alcohol abuse services. They compared six sessions of imaginal exposure with six sessions of imagery-based relaxation training, with the primary aim of evaluating effects on alcohol-related craving.

Group-based trauma-focused/combined interventions

We identified no studies offering trauma-focused intervention through groups.

Non-trauma-focused intervention

Individual-based non-trauma-focused interventions

Four studies evaluated individual integrated PTSD/SUD intervention. One study compared an integrated PTSD/SUD intervention against treatment as usual for SUD (Najavits 2006a). The active condition in this trial was Seeking Safety plus treatment as usual. One study evaluated individual CBT against participants' usual psychiatric care (Mueser 2008). Treatment components included psycho-education, cognitive restructuring, and generalisation training. As described previously, this study evaluated treatment of PTSD for people with serious mental illness and did not include a component focusing on SUD. Two studies evaluated an integrated PTSD/SUD intervention delivered on an individual basis against an alternative psychological therapy for SUD alone (Hien 2004; McGovern 2011). Hien 2004 compared Seeking Safety plus treatment as usual to a relapse prevention comparison condition and a non-randomised treatment-as-usual arm, which we have not included in this review. McGovern 2011 compared integrated CBT plus treatment as usual (ICBT) with individual addiction counselling plus treatment as usual (IAC) as the control condition. There was no PTSD component to the IAC, which at 10 to 12 sessions was shorter than the 12- to 14-session ICBT intervention, which included psycho-education, cognitive restructuring, and generalisation training in relation to PTSD and SUD.

Group-based non-trauma-focused interventions

Five studies evaluated group interventions, four of which included Seeking Safety, Najavits 2002b, plus treatment as usual as the active treatment condition (Boden 2012; Hien 2009; Norman unpublished; Zlotnick 2009). Seeking Safety is a structured cognitive behavioural treatment with both safety/trauma and substance use components integrated into each session. Its primary goal is to reduce both PTSD and SUD by focusing on safe coping skills addressed through cognitive, behavioural, interpersonal, and case management domains over 24 to 25 sessions. In two of these trials (Boden 2012; Zlotnick 2009), treatment as usual was the control condition. The intervention in Hien 2009 provided a partial dose of Seeking Safety with 12 sessions to cover the core components of the model. This study used a female health psycho-education (Women's Health Education) comparison condition, which was delivered over the same number of sessions with the same level of attention given to participants. Norman unpublished included some components from cognitive trauma therapy for battered women with PTSD (CTT-BW) (Kubany 2004). The control condition in this study was a minimal-intervention therapist-led supportive 12-step group. The fifth study to evaluate a group-based integrated program was Frisman 2008. This study compared TARGET, an 8- to 9-week intervention that aims to improve adaptive coping skills, with treatment as usual for SUD only.

A fuller description of interventions can be found in the Characteristics of included studies tables.

Comparisons

The included studies compared:

1. psychological therapy versus 'control' (as defined in Types of interventions);
2. psychological therapy versus other psychological therapy (as defined in Types of interventions).

We made the following specific comparisons:

1. Trauma-focused psychological therapy versus control intervention
   a. Individual-based therapy: Coffey 2006; Coffey submitted; Foa 2013; Mills 2012.
   b. Group-based therapy: No studies.
2. Trauma-focused psychological therapy versus active psychological therapy for SUD only
   a. Individual-based intervention: Sannibale 2013.
   b. Group-based intervention: No studies.

3. Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only versus control intervention
   a. Individual-based intervention: Mueser 2008; Najavits 2006a.
   b. Group-based intervention: Boden 2012; Frisman 2008; Hien 2009; Norman unpublished; Zlotnick 2009.
4. Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only versus active psychological therapy for SUD only
   a. Individual-based intervention: Hien 2004; McGovern 2011.
   b. Group-based intervention: No studies.

Outcomes

PTSD outcomes

Of the 14 studies, 10 used a clinician-administered measure of PTSD (Coffey submitted; Foa 2013; Hien 2004; Hien 2009; McGovern 2011; Mills 2012; Mueser 2008; Norman unpublished; Sannibale 2013; Zlotnick 2009). In nine cases, this was the Clinician Administered PTSD Symptom Scale (CAPS) (Blake 1995). The Impact of Event Scale - Revised (IES-R), Weiss 1997, was the primary PTSD outcome measure in two studies (Boden 2012; Coffey 2006). Frisman 2008 used the Post-Traumatic Cognitions Inventory, which is a measure of trauma-related beliefs. We considered this to be a reasonable proxy to a PTSD outcome measure.

SUD outcomes

A range of measures were used to assess outcomes for SUD. These included the Timeline Followback Interview (Sobell 1995), which was used in five studies (Coffey submitted; Foa 2013; Norman unpublished; Sannibale 2013; Zlotnick 2009); the Addiction Severity Index (ASI) (McLellan 1992), used in three studies (Boden 2012; McGovern 2011; Zlotnick 2009); the Composite International Diagnostic Interview for DSM–IV (Robins 1989), used in three studies (Hien 2009; Mills 2012; Mueser 2008); and the Substance Use Inventory (Weiss 1995b), used in two studies (Hien 2004; Hien 2009). Toxicology screens were administered in Hien 2009 and McGovern 2011. Some studies used several SUD measures. In meta-analysis we included outcomes according to the specifications described in Types of outcome measures. Some studies also included outcomes for both alcohol use and drug use. In such cases we included the outcome that was most associated with the treatment condition (that is where alcohol was identified as the key comorbidity, we included the alcohol outcome, and where SUD was identified as the key comorbidity, we included the SUD outcome).

Treatment completion

Many of the included studies recognised high levels of treatment drop-out as a pervasive problem in the field (for example Hien 2004; Mills 2012). Definitions of the number of sessions attended for a participant to be considered a completer varied across studies. We used the definition of treatment completer provided by each study to undertake analyses of treatment acceptability. Boden 2012, Foa 2013, Mills 2012, Najavits 2006a, and Zlotnick 2009 provided no definition, although Mills 2012 provided data on the number of participants who attended at least one exposure session and the number attending all 13 treatment sessions. Hien 2004 and Norman unpublished identified a "minimum dose" as 25% of sessions attended. Hien 2009, Mueser 2008, and Sannibale 2013 specified a completer as an participants who had attended 50% of sessions. Definitions in the range of 70% to 80% of sessions were described in Coffey submitted, Frisman 2008, and McGovern 2011, and 100% of sessions was described in Coffey 2006.

Secondary outcomes

PTSD diagnostic status was reported in Coffey submitted, McGovern 2011, Mills 2012, Norman unpublished, Sannibale 2013, and Zlotnick 2009. SUD diagnostic status was reported only in Mills 2012. Adverse effects were reported by Boden 2012, Foa 2013, Hien 2009 (see Killeen 2008), Mills 2012, and Norman unpublished. Compliance as measured by the mean number of sessions attended was frequently reported, although some studies only reported attendance for the experimental group (Hien 2004; Najavits 2006a; Zlotnick 2009). General functioning was not evaluated in any study. Use of health-related resources (other service utilisation) was evaluated in Najavits 2006a, but was not clearly reported.

Timing of outcome assessment

All included trials apart from Frisman 2008 reported PTSD and SUD as a continuous outcome at the end of treatment. Long-term follow-up data ranging from 3 to 12 months was reported in all studies except Coffey 2006. Follow-up data was available at 3 months from the end of treatment in Boden 2012, Coffey submitted, Hien 2004, Hien 2009, McGovern 2011, Mueser 2008, Najavits 2006a, and Zlotnick 2009; at 5 to 6 months post-treatment in Coffey submitted, Foa 2013, Frisman 2008, Hien 2004, Hien 2009, Mills 2012, Mueser 2008, Sannibale 2013, and Zlotnick 2009; at 9 months in Sannibale 2013; and at 12 months in Frisman 2008 and Hien 2009. We note that Mills 2012 reported their follow-up points at 6 weeks, 3 months, and 9 months from baseline. As the planned intervention period was 3 months, we took the 3-month follow-up point as the end of treatment and the 9-month follow-up point as 6-month follow-up post-treatment. However, some participants did continue to receive therapy more than three months after baseline assessment.

Excluded studies

See Characteristics of excluded studies.

We identified 172 studies as being potentially eligible for this review after initial screening, of which 143 were excluded after closer examination. Of these, 21 did not meet study design criteria (that is not RCTs). We excluded 49 on the basis that less that 80% of the sample met diagnosis for PTSD. In some of these studies PTSD was not assessed at all. Five of these 49 studies assessed for traumatic stress symptoms, but a formal and reliable diagnosis of PTSD was not established (for example Ford 2011; Ghee 2009). We excluded 12 studies because less than 80% of the sample met diagnosis for SUD. We excluded seven studies evaluating interventions in trauma-exposed people with significant SUD history (for example van Dam 2013) on the basis that less than 80% of the sample met diagnosis for PTSD and SUD. Four studies did not provide outcomes that were either PTSD or SUD related, three studies did not evaluate a psychological therapy, and one study evaluated the addition of sertraline to a psychological therapy (Hien 2015). Twenty-seven studies were companion papers to studies included in this review. The remaining 19 studies were conference abstracts related to other studies that were either included in or excluded from the review.

Ongoing studies

See Characteristics of ongoing studies.

We identified 12 ongoing studies as being of potential relevance to this review (to March 2011) via the World Health Organization's

trials portal (ICTRP) and ClinicalTrials.gov and through a published protocol (DRKS00004288; NCT00946322; NCT01029197; NCT01186315; NCT01274741; NCT01338506; NCT01357577; NCT01365247; NCT01597856; NCT01693978; NCT02081417; NTR3084). Interventions currently being evaluated include Seeking Safety plus treatment as usual (TAU) in a Dutch population (planned recruits 130) (NTR3084), a multicentre trial of Seeking Safety versus structured relapse prevention versus TAU (DRKS00004288), a trial of Seeking Safety versus a past-focused integrated CBT-based therapy for PTSD and SUD (planned recruits 52) (NCT01274741), a trial of peer-led versus clinician-led Seeking Safety (NCT02081417), a trial of CBT in 160 military veterans (NCT01357577), a 3-arm trial comparing CBT (including prolonged exposure) with relapse prevention and TAU for PTSD and SUD (planned recruits 168) (NCT01365247), a trial of COPE in military veterans (planned recruits 90) (NCT01338506), a trial of prolonged exposure versus prolonged exposure with contingency management for drug users with PTSD (NCT01693978), a trial of prolonged exposure versus prolonged exposure plus virtual reality-based exposure to addiction cues (NCT01186315), a trial of group and individual CBT and exposure for people with serious mental illness (NCT01029197), a phase 1 trial of couple-based treatment of PTSD and alcohol use disorder (NCT00946322), and a phase 1 trial evaluating a screening, motivation enhancement, and referral program for US veterans seeking pension and compensation benefits (NCT01597856).

A further search of the trial registries (4 December 2015), prior to publication, identified five additional ongoing studies (NCT01211106; NCT01457404; NCT01663337; NCT01849029; NCT02335125).

Studies awaiting classification

See Characteristics of studies awaiting classification.

We identified these studies through records in clinical trial registries and conference abstracts, but could not identify or access full-text reports (to 11 March 2015). We have not yet formally evaluated these studies for eligibility, and may include or exclude them in a future update of this review. We initially identified three such studies (Park 2012; Simpson 2011; Skidmore 2013). Park 2012 have evaluated an integrated chronic disease management intervention in a primary care setting for people with SUD and a range of co-occurring mental disorders. Of the 553 total participants, 204 are reported to have met diagnosis for PTSD at baseline. Simpson 2011 sought to evaluate the feasibility of a methodology focused on deciphering mechanisms of change for decreasing alcohol use and PTSD symptomatology in people with current PTSD and alcohol dependence. Participants were assigned to one of three brief interventions (acceptance, cognitive restructuring, or attention placebo); 84 participants were reported to have been randomised (a report describing the main outcomes of this study has subsequently been published (Stappenbeck 2015)). Skidmore 2013 evaluated integrated cognitive behavioural therapy (ICBT) versus cognitive processing therapy, an established and evidence-based intervention for PTSD, in a group of 153 participants with co-occurring alcohol or substance dependence, depression, and trauma exposure. It is unclear whether a subgroup of participants met diagnosis for PTSD.

A further search of the Cochrane Depression, Anxiety and Neurosis Review Group's Specialised Register (4 December 2015), prior to publication, identified four additional studies (added to those awaiting classification). Two met the eligibility criteria for this review (McGovern 2015; Perez-Dandieu 2015), and a further two will also meet the eligibility criteria if subset data are available (Barrett 2015; Wolf 2015).

Risk of bias in included studies

For details of the 'Risk of bias' judgements for each study, see Characteristics of included studies. Graphical representations of the overall risk of bias in included studies are presented in Figure 2 and Figure 3.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

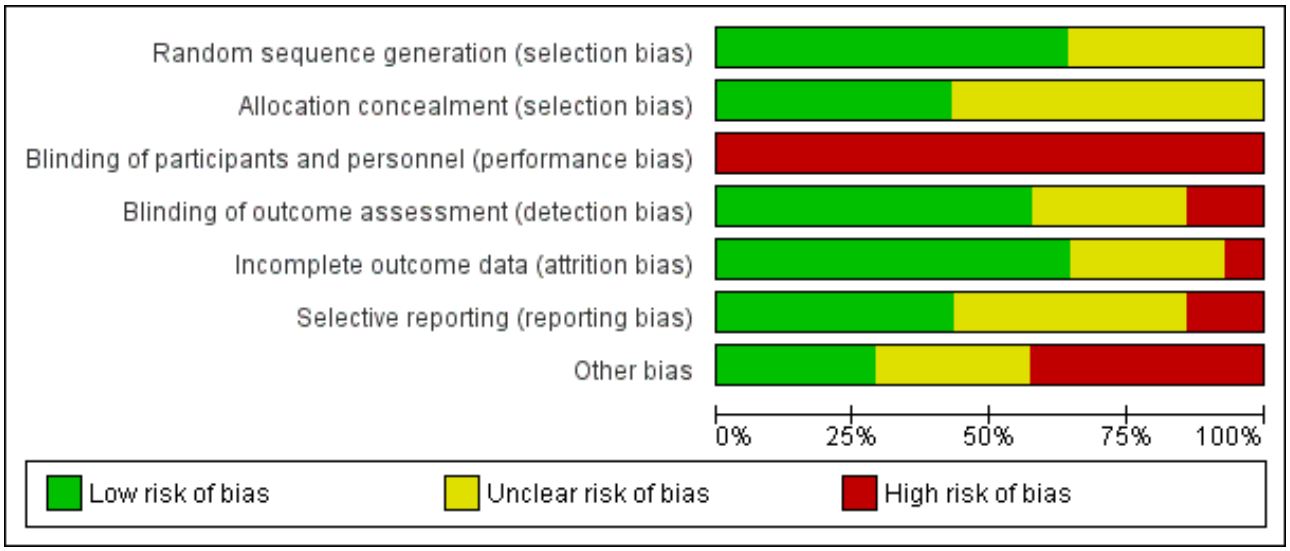
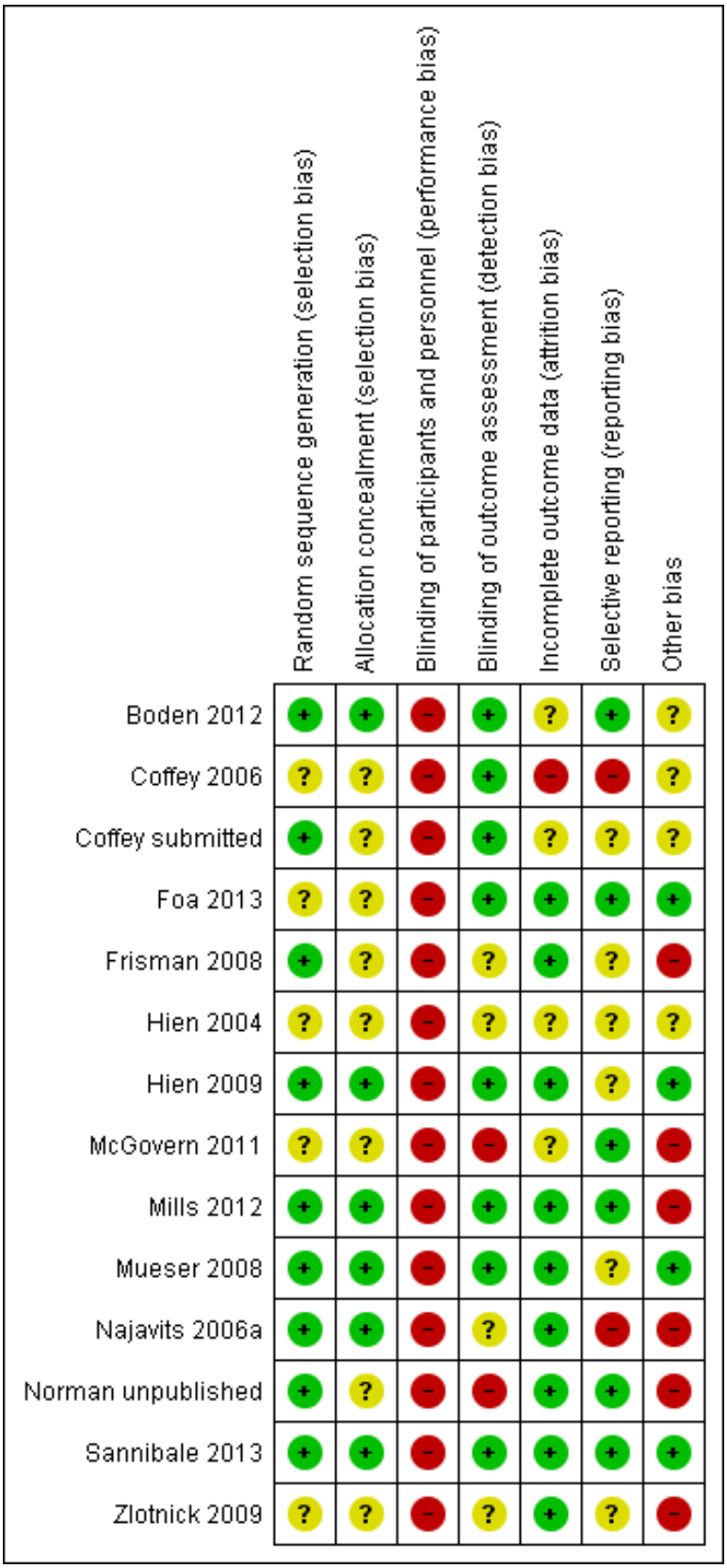


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Eight studies specified the method of sequence generation and were judged as being at low risk of bias (Boden 2012; Coffey submitted; Frisman 2008; Hien 2009; Mills 2012; Mueser 2008; Norman unpublished; Sannibale 2013). The method of allocation was unclear in the remaining studies. Of the nine studies that adequately reported method of sequence generation, we judged five as also describing their method of allocation adequately (Boden 2012; Hien 2009; Mills 2012; Mueser 2008; Sannibale 2013). We were unclear about the process of sequence generation and allocation for Najavits 2006a, but received additional information from the lead author that allowed us to judge that these were of low risk. The process of sequence generation and allocation were unclear in the remaining studies.

Blinding

In trials of psychological therapy participants cannot normally be blind to the treatment allocation. We therefore classified all trials as being at high risk of performance bias. Eight trials included blinding of the outcome assessor and so were rated as being at low risk of bias (Boden 2012; Coffey 2006; Coffey submitted; Foa 2013; Hien 2009; Mills 2012; Mueser 2008; Sannibale 2013). Research interviewers were not blinded to treatment assignment at the follow-up assessments in McGovern 2011 and Norman unpublished, which we therefore rated as high risk. We were unclear about the blinding of assessors in the remaining studies.

Incomplete outcome data

Seven studies reported drop-out and loss to follow-up clearly and performed intention-to-treat (ITT) analyses on all participants who were randomised, so that missing outcome data were replaced using a recognised statistical method, for example last observation carried forward (Foa 2013; Frisman 2008; Hien 2009; Mills 2012; Mueser 2008; Najavits 2006a; Sannibale 2013). We also judged Zlotnick 2009 as low risk because loss to follow-up was low. Three studies undertook ITT analysis by including participants in analyses if they had attended at least one treatment session, following randomisation (Coffey submitted; Hien 2004; Norman unpublished). For Norman unpublished, people who did not attend any treatment sessions remained blind to their allocation, and based on guidance provided by Fergusson 2002, we judged this study to be of low risk. We were unclear about whether participants in Coffey submitted and Hien 2004 were aware of their allocation and whether this might have influenced drop-out; we therefore judged these studies to be of unclear risk. We judged that methods of analysis were at high risk of bias in Coffey 2006.

Selective reporting

We were able to identify protocols with prespecified outcome measures for six trials (Boden 2012; Foa 2013; McGovern 2011; Mills 2012; Norman unpublished; Sannibale 2013). We checked that all prespecified outcomes were reported, and rated these studies as being at low risk of bias. We identified two trials as being at high risk (Coffey 2006; Najavits 2006a). We were able to extract only minimal data from Najavits 2006a because all outcomes were not fully reported and tabular data were mainly reported only for positive outcomes. We were unable to make a judgement about reporting bias for the other six trials.

Other potential sources of bias

We could identify no other potential sources of bias in four studies (Foa 2013; Hien 2009; Mueser 2008; Sannibale 2013). We judged that there was a high risk of bias because of additional factors in six studies (Frisman 2008; McGovern 2011; Mills 2012; Najavits 2006a; Norman unpublished; Zlotnick 2009). We were unable to make informed judgements about the remaining trials (Boden 2012; Coffey 2006; Coffey submitted; Hien 2004), and therefore rated them as unclear.

Effects of interventions

See: **Summary of findings for the main comparison**; **Summary of findings 2** Trauma-focused psychological intervention compared to active psychological intervention for SUD only; **Summary of findings 3** Non-trauma-focused psychological intervention for PTSD and SUD or PTSD only compared to control intervention; **Summary of findings 4** Non-trauma-focused psychological intervention for PTSD and SUD or PTSD only compared to active psychological intervention for SUD only

We have grouped results according to the intervention characteristics identified above in the Interventions section of Included studies.

Comparison 1: Trauma-focused psychological therapy versus control intervention

Four studies contributed to this comparison. These studies either evaluated trauma-focused CBT-based interventions in combination with SUD-focused interventions, or in the context of a substance abuse setting where SUD interventions were already being received. All studies evaluated interventions delivered individually.

Primary outcomes

1.1 PTSD severity

Four studies including 405 participants reported severity of PTSD symptoms at post-treatment (Analysis 1.1). We noted a small effect in favour of individual psychological therapy (standardised mean difference (SMD) -0.41; 95% confidence interval (CI) -0.72 to -0.10), although heterogeneity was moderate (I^2 = 49%). One study with 120 participants reported follow-up at 3 to 4 months (Analysis 1.2); we again noted a small effect in favour of individual psychological therapy (mean difference (MD) -9.83; 95% CI -17.11 to -2.55). Three studies including 388 participants reported follow-up at 5 to 7 months (Analysis 1.3). There was a small effect in favour of individual psychological therapy (SMD -0.34; 95% CI -0.58 to -0.10), and we noted no important heterogeneity (I^2 = 26%).

1.2 Drug or alcohol use, or both

Three studies including 388 participants reported severity of SUD symptoms post-treatment (Analysis 1.4). We found no significant difference (SMD -0.13; 95% CI -0.41 to 0.15). We noted a moderate level of heterogeneity (I^2 = 45%). One study with 120 participants reported SUD symptom severity at 3 to 4 months (Analysis 1.5). No significant difference was found (MD -2.33; 95% CI -12.87 to 8.21). Three studies including 388 participants reported follow-up at 5 to 7 months (Analysis 1.6). There was a small effect in favour of individual psychological therapy (SMD -0.28; 95% CI -0.48 to -0.07), and we noted no heterogeneity (I^2 = 0%).

1.3 Treatment completion

Three studies including 316 participants reported treatment completers (Analysis 1.7). We found a significant difference in favour of the control condition (risk ratio (RR) 0.78; 95% CI 0.64 to 0.96). We noted a moderate level of heterogeneity (I^2 = 41%).

Secondary outcomes

1.4 PTSD diagnosis after treatment

Only one study with 120 participants reported outcomes for PTSD diagnosis (Analysis 1.8). There was a small treatment effect in favour of individual psychological therapy (RR 0.71; 95% CI 0.51 to 1.00).

1.5 SUD diagnosis after treatment

No data were available for diagnostic status for substance use.

1.6 Adverse events

Two studies provided data on adverse events (Analysis 1.9). These two studies reported a total of 20 events. None of these events were attributed to treatment interventions provided in the studies. We found no significant differences between the two groups (RR 0.81; 95% CI 0.34 to 1.90), noted no heterogeneity (I^2 = 0%) (Analysis 1.10).

1.7 Compliance, as measured by proportion of treatment sessions attended

Three studies reported data on the mean number of treatment sessions attended by participants in the experimental group (Analysis 1.11), with participants attending a mean of 6.89 (standard deviation (SD) = 4.63) sessions. The proportions of available sessions attended per study varied from 35.2% to 68.0%.

1.8 General functioning

No data were available.

1.9 Use of health-related resources

No data were available.

Comparison 2: Trauma-focused psychological therapy versus active psychological therapy for SUD only

One study with 62 participants contributed to the comparison. Intervention in this study was delivered individually.

Primary outcomes

2.1 PTSD severity

One study reported severity of PTSD symptoms. No significant difference was found post-treatment (MD -3.91; 95% CI -19.16 to 11.34; n = 46; Analysis 2.1), at 5 to 7 months' follow-up (MD -9.32; 95% CI -22.89 to 4.25; n = 45; Analysis 2.2), or at 8 to 10 months' follow-up (MD 2.11; 95% CI -16.10 to 20.32; n = 47; Analysis 2.3). Differences in the numbers of participants contributing to each analysis were a result of the numbers available to follow-up at each time point.

2.2 Drug or alcohol use, or both

One study reported severity of PTSD symptoms. No significant difference was found post-treatment (MD -1.27; 95% CI -5.76 to 3.22; n = 46; Analysis 2.4), at 5 to 7 months' follow-up (MD 1.90; 95% CI -1.65 to 5.45; n = 45; Analysis 2.5), or at 8 to 10 months' follow-up (MD -0.93; 95% CI -4.04 to 2.18; n = 47; Analysis 2.6).

2.3 Treatment completion

Data on treatment completers were available from one study (Analysis 2.7). No difference was found between the two groups on rate of treatment completion (RR 1.00; 95% CI 0.74 to 1.36).

Secondary outcomes

2.4 PTSD diagnosis after treatment

One study reported data on PTSD diagnosis post-treatment (Analysis 2.8). No difference was found between the two groups (RR 1.04; 95% CI 0.67 to 1.62).

2.5 SUD diagnosis after treatment

One study reported data on SUD diagnosis post-treatment (Analysis 2.9). No difference was found between the two groups (RR 1.16; 95% CI 0.83 to 1.60).

2.6 Adverse events

Adverse events were not reported.

2.7 Compliance, as measured by proportion of treatment sessions attended

No data were available for the mean number of treatment sessions attended.

2.8 General functioning

No data were available.

2.9 Use of health-related resources

No data were available.

Comparison 3: Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only versus control intervention

One study evaluated non-trauma-focused psychological therapy delivered individually (Mueser 2008). Five studies evaluated group-based interventions. Four studies evaluated Seeking Safety as the experimental condition. Frisman 2008 evaluated an alternative group-based intervention (Frisman 2008 also had a far lower rate of completion than other studies).

Primary outcomes

3.1 PTSD severity

Individual-based intervention

One study with 44 participants reported severity of PTSD symptoms. No significant difference was found post-treatment (SMD -0.22; 95% CI -0.83 to 0.39; Analysis 3.1), at 3 to 4 months' follow-up (SMD -0.25; 95% CI -0.86 to 0.36; Analysis 3.2), or at 5 to 7 months' follow-up (SMD -0.20; 95% CI -0.81 to 0.41; Analysis 3.3).

Group-based intervention

Post-treatment data were available from 4 studies including 513 participants. All 4 studies evaluated Seeking Safety or partial-dose Seeking Safety as the experimental condition. We found no significant difference between the two groups (SMD -0.02; 95% CI -0.19 to 0.16; Analysis 3.1). There was general consistency in study results (I^2 = 0%). Data were also available from the same

four studies at 3 to 4 months' follow-up (Analysis 3.2); again, we found no significant differences (SMD 0.00; 95% CI -0.17 to 0.18; n = 499) and noted no heterogeneity (I^2 = 0%). Data at 5 to 7 months' follow-up were available from 4 studies including 566 participants. We identified no effect (SMD -0.14; 95% CI -0.31 to 0.03) and noted no heterogeneity (I^2 = 0%) (Analysis 3.3). Two studies with 518 participants provided data at 12 months' follow-up (Analysis 3.4). No effect was evident (SMD -0.07; 95% CI -0.25 to 0.10). There was general consistency in study results (I^2 = 0%).

3.2 Drug or alcohol use, or both

Individual-based intervention

No data were available.

Group-based intervention

Post-treatment data were available from 3 studies including 464 participants (Analysis 3.5). All three studies evaluated Seeking Safety or partial-dose Seeking Safety as the experimental condition. We found no significant difference between the two conditions (SMD -0.41; 95% CI -0.97 to 0.14). The degree of heterogeneity was substantial (I^2 = 79%). It should be noted that there was a significant difference in favour of the Seeking Safety intervention for two studies post-treatment (Boden 2012; Norman unpublished), but not for the third study (Hien 2009), which was much larger. Hien 2009 differed from Boden 2012 and Norman unpublished in that intervention was based on a partial-dose programme. This is addressed further under 'Subgroup analyses' below. Data at 3 to 4 months' follow-up were available from the 4 Seeking Safety or partial-dose Seeking Safety studies with 499 participants (Analysis 3.6). We found no significant differences (SMD -0.08; 95% CI -0.40 to 0.23). The degree of heterogeneity post-treatment was moderate (I^2 = 48%). Data at 5 to 7 months' follow-up were available from 4 studies with 572 participants (Analysis 3.7). We found no differences (SMD -0.06; 95% CI -0.23 to 0.11) and noted no heterogeneity (I^2 = 0%). Two studies with 528 participants provided data at 12 months (Analysis 3.8). We found no differences (SMD 0.02; 95% CI -0.15 to 0.20) and noted no heterogeneity (I^2 = 0%).

3.3 Treatment completion

Individual-based intervention

Data on treatment completion were available from one study only for participants receiving the experimental intervention (Analysis 3.9); 70.6% of participants attended a minimum of 6 of the 16 available treatment sessions and were considered treatment completers; 52.9% attended 12 or more sessions.

Group-based intervention

Two studies including 381 participants reported data on treatment completers for both the experimental and control condition (Analysis 3.10). We found no significant difference between the two conditions (RR 1.13; 95% CI 0.88 to 1.45). There was general consistency in study results (I^2 = 0%). One study only provided data about the number of participants in the experimental group considered to be completers (Analysis 3.9). At 28%, treatment adherence for the group intervention in this study was very low.

Secondary outcomes

3.4 PTSD diagnosis after treatment

Individual-based intervention

No data were available.

Group-based intervention

Two studies with 77 participants provided data on PTSD diagnosis post-treatment (Analysis 3.11). We found no differences (RR 1.01; 95% CI 0.66 to 1.54) and noted no heterogeneity (I^2 = 0%). Both studies evaluated full-dose Seeking Safety interventions as the experimental condition.

3.5 SUD diagnosis after treatment

No data were available.

3.6 Adverse events

Individual-based intervention

No data were available.

Group-based intervention

Three studies reported on adverse events (Analysis 3.12). Two of the studies reported no adverse events. The third study reported 83 study-related adverse events from 353 participants (Analysis 3.13). We found no differences in the number of events experienced between the two conditions (RR 1.03; 95% CI 0.71 to 1.50).

3.7 Compliance, as measured by proportion of treatment sessions attended

Individual-based intervention

No data were available.

Group-based intervention

Five studies reported data on the mean number of treatment sessions attended by participants in the experimental group (Analysis 3.14; Analysis 3.15), with participants attending a mean of 6.31 (SD = 5.71) sessions. The proportions of available sessions attended for the experimental group per study ranged from 37.9% to 62.4%.

3.8 General functioning

No data were available.

3.9 Use of health-related resources

No data were available.

Comparison 4: Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only versus active psychological therapy for SUD only

Two studies including 128 participants contributed to this comparison. Both studies evaluated interventions delivered individually.

Primary outcomes

4.1 PTSD severity

Two studies including 128 participants reported severity of PTSD symptoms. We found no significant difference post-treatment (SMD -0.26; 95% CI -1.29 to 0.77; Analysis 4.1). The level of heterogeneity

was considerable (I^2 = 87%). There was a significant difference in favour of the combined intervention post-treatment (MD -16.52; 95% CI -27.99 to -5.05) for one of these two studies, McGovern 2011, although it was noted that the two groups in this study were not well matched for PTSD severity at baseline. The same studies including 128 participants reported follow-up at 3 to 4 months, finding no significant difference between the two conditions (SMD 0.12; 95% CI -0.31 to 0.55; Analysis 4.2). We noted a moderate level of heterogeneity (I^2 = 33%). One study with 75 participants reported severity of PTSD symptoms at 5 to 7 months, finding no significant difference (MD 7.52; 95% CI -3.78 to 18.82; Analysis 4.3).

4.2 Drug or alcohol use, or both

Two studies including 128 participants reported severity of SUD symptoms. We found no significant differences post-treatment (SMD 0.22; 95% CI -0.13 to 0.57; Analysis 4.4), or at 3 to 4 months' follow-up (SMD 0.18; 95% CI -0.18 to 0.53; Analysis 4.5); we noted no heterogeneity at either follow-up point (I^2 = 0%). One study with 75 participants reported severity of SUD symptoms at 5 to 7 months' follow-up (Analysis 4.6); we found no significant difference (MD 0.10; 95% CI -0.20 to 0.40).

4.3 Treatment completion

Data on treatment completers were available from 2 studies with 128 participants. We found no difference between the two groups on rate of treatment completion (RR 0.91; 95% CI 0.68 to 1.20; Analysis 4.7).

Secondary outcomes

4.4 PTSD diagnosis after treatment

One study reported data on PTSD diagnosis post-treatment (Analysis 4.8). No difference was found between the two groups (RR 0.94; 95% CI 0.68 to 1.30).

4.5 SUD diagnosis after treatment

No data were available.

4.6 Adverse events

Adverse events were not reported.

4.7 Compliance, as measured by proportion of treatment sessions attended

Data were available from 1 study with 75 participants (Analysis 4.9). There was no difference between the two groups for treatment attendance (MD -0.10; 95% CI -3.75 to 3.55), with attendance of 48.0% at the experimental group sessions and 48.4% at control group sessions.

4.8 General functioning

No data were available.

4.9 Use of health-related resources

No data were available.

Reporting bias

Twelve of the 14 studies included in this review were published, and one study completed recently, Coffey submitted, was in the process of seeking publication. We followed up all appropriate trials registered with World Health Organization's trials portal (ICTRP) and ClinicalTrials.gov and made attempts to contact authors known to be active in this field. We identified one unpublished study that we were able to include. The numbers of studies in each comparison were insufficient to allow for meaningful consideration of publication bias using funnel plots (Lau 2006).

Subgroup analyses

Comparison 3: Group-based combined non-trauma-focused psychological therapy for PTSD and SUD versus waiting list/ treatment as usual/minimal intervention/placebo intervention

We reported analysis for the effects of group-based interventions on PTSD severity and drug/alcohol use at initial post-treatment follow-up above (Analysis 3.1; Analysis 3.5). Seeking Safety is widely used as a group-based intervention for treatment of comorbid PTSD and SUD. All studies contributing to these analyses evaluated Seeking Safety. Other analyses in Comparison 3 included one study that did not evaluate Seeking Safety (Frisman 2008). We therefore undertook subgroup analyses of PTSD severity and drug/alcohol use at later follow-up points excluding Frisman 2008. There was no evidence of an effect of Seeking Safety on PTSD severity at 5 to 7 months (SMD -0.12; 95% CI -0.34 to 0.10; k = 3; n = 425; Analysis 3.16) or at 12 months (SMD -0.04; 95% CI -0.25 to 0.17; k = 1; n = 353; Analysis 3.17). There was also no evidence of an effect on drug/ alcohol use at either 5 to 7 months (SMD -0.11; 95% CI -0.30 to 0.08; k = 3; n = 425; Analysis 3.18) or at 12 months (SMD 0.00; 95% CI -0.21 to 0.21; k = 1; n = 353; Analysis 3.19).

As we noted, the study by Hien 2009 included a 12-session partial dose of Seeking Safety. We therefore undertook post hoc analyses including only data from the full-dose Seeking Safety studies. These analyses showed no effect post-treatment (SMD -0.02; 95% CI -0.19 to 0.16; k = 3; n = 160), at 3 to 4 months (SMD 0.09; 95% CI -0.24 to 0.42; k = 3; n = 146), or at 5 to 7 months (SMD 0.13; 95% CI -0.35 to 0.60; k = 2; n = 72) for PTSD severity. We did find a moderate effect in favour of full-dose Seeking Safety post-treatment for drug/alcohol use (SMD -0.67; 95% CI -1.14 to -0.19; k = 2; n = 111). We noted no important heterogeneity (I^2 = 20%). There was no effect at 3 to 4 months (SMD -0.03; 95% CI -0.62 to 0.56; k = 3; n = 146) or at 5 to 7 months (SMD 0.03; 95% CI -0.45 to 0.51; k = 2; n = 72) for drug/ alcohol use.

Sensitivity analyses

Comparison 1: Individual-based psychological therapy including a trauma-focused component plus SUD intervention versus waiting list/treatment as usual/minimal intervention/placebo intervention

Coffey 2006 provided outcome data only on the basis of participants who were available for follow-up, and loss to follow-up was high. We therefore undertook a sensitivity analysis for PTSD severity (Analysis 1.1) excluding this study. We continued to find a small effect post-treatment in favour of individual-based psychological therapy, although this effect was reduced (SMD -0.33; 95% CI -0.56 to -0.10; Analysis 1.12). We noted no important heterogeneity (I^2 = 19%). Coffey 2006 did not contribute to analysis at other follow-up points.

DISCUSSION

Summary of main results

We included 14 studies including 1506 participants in this review. It was apparent that research attention is mainly focused on two broad types of intervention for PTSD and SUD comorbidity (van Dam 2012). These are CBT-based interventions delivered on an individual basis consisting of a significant trauma-focused component; and CBT-based interventions aimed at developing and enhancing positive coping skills, without a trauma-focused component. These latter interventions are offered on both an individual and a group basis.

psychological therapy including a trauma-focused component

We were only able to identify individual-based studies of psychological therapies including a trauma-focused component. All trauma-focused interventions were delivered alongside intervention aimed at treating SUD, or participants were recruited from SUD services. We found evidence of a small benefit for individual-based psychological therapies that included a trauma-focused component when compared against usual care or minimal intervention conditions for PTSD at the end of treatment and at 3 to 4 and 5 to 7 months after treatment. We found evidence of a small reduction in drug/alcohol use at 5 to 7 months after treatment, but not at earlier time points. There was evidence of lower rates of treatment completion in those receiving trauma-focused intervention compared to treatment as usual/minimal intervention, when considered against study-defined criteria for a treatment completer. There were no differences in PTSD- or SUD-related outcomes when individual-based trauma-focused psychological therapy was compared with an active psychological therapy for SUD only. However, data were only available from one trial, which was not well powered.

Non-trauma-focused interventions

Individual-based psychological therapy without a trauma-focused component

We identified one study that evaluated an individual-based psychological therapy without a trauma-focused component against a usual care or minimal intervention condition (Mueser 2008). We obtained outcome data for a small cohort of individuals with SUD; this study did not include any SUD intervention. We identified only one study that evaluated individual-based psychological therapy and included both PTSD- and SUD-related components (Najavits 2006a). We were not able to use data from this study. We could not identify any benefits for individual-based psychological therapy that did not offer a trauma-focused component when compared against a usual care condition or another active psychological therapy. These findings were also based on data from two small trials.

Group-based psychological therapy without a trauma-focused component

The majority of the group-based studies evaluating non-trauma-focused interventions were of Seeking Safety (Najavits 2002b). We found no improvement for PTSD severity at any time point when these interventions were compared against usual care/minimal intervention or against another active psychological therapy. We also found no benefits in terms of reduction in drug/alcohol use across studies, but did find a moderate reduction in drug/alcohol use for full-dose Seeking Safety through post-hoc analyses, when compared against treatment as usual/minimal intervention. This effect was not sustained at later follow-up points. Non-trauma-focused group-based interventions maintained a level of retention similar to control conditions for individual- and group-based interventions.

Treatment completion and drop-out

The level of drop-out was high across all studies. Study criteria for defining a treatment completer were often modest. Of those studies reporting treatment completers, only one achieved retention of over 70% (Sannibale 2013). Rates of completion in most other studies were between 50% and 70%, with one large study reporting a completion rate of 28% for those in the active intervention group (Frisman 2008). However, studies (including Frisman 2008) were often more successful at retaining participants in follow-up for research purposes. One study, Hien 2009, did investigate the reasons for drop-out in a follow-up study (Pinto 2011). Pinto 2011 found that participants with more education, higher attendance at 12-step meetings, and strong therapeutic alliance with their therapists had better retention rates. This multisite trial also found some site differences, with retention being highest in a site that offered childcare and had the lowest overall intake.

Adverse events

In contrast to Bisson 2013, 5 of the 14 included studies noted information about adverse events, with 3 studies reporting on adverse events in some detail (Foa 2013; Hien 2009; Mills 2012). There was no evidence of differences in adverse events for these studies (for details see Analysis 1.9 and Analysis 3.12).

Overall completeness and applicability of evidence

The objective of this review was to determine the efficacy of psychological therapies aimed at treating traumatic stress symptoms, substance misuse symptoms, or both in people with comorbid PTSD and SUD. In terms of applicability of findings, the studies included in this review were mainly conducted in veterans groups and amongst groups who had experienced significant abuse and interpersonal violence, and evaluated males only, females only, and both genders together. Studies took place in high-income, English-speaking countries, but participants were largely of low income and often living in relatively deprived settings. A strength of this review is that samples were ethnically diverse in the majority of studies. However, the results of this review may not be generalisable to other settings or participant groups. We only identified one study involving adolescents and no studies involving younger children. Most studies did not include people with comorbid psychiatric diagnoses or with cognitive impairment, who are arguably more difficult to treat. Generalising the results to more complex presentations is therefore problematic.

In addition to high drop-out rates, recruitment appears to have been a significant problem for some studies. Some studies ended before reaching recruitment targets (for example Boden 2012; Mills 2012; Norman unpublished; Sannibale 2013). One study took eight years to reach its recruitment target, with a large number of individuals who met inclusion criteria refusing to participate in the study (Foa 2013).

We outlined earlier that there is little consensus about the process of interventions in terms of treatment pathways. We had hoped

this review would help to address this issue. It has to a degree, but in practice, most studies recruited participants from substance misuse services, so many participants had received some level of substance use intervention prior to recruitment, and in most instances it is likely that substance or alcohol use, or both was stabilised to some extent prior to study intervention, often with the aid of pharmacological intervention. It is possible that the efficacy of psychological therapies is stronger than suggested by the data, as in several studies the usual care group were able to access a significant amount of clinician contact and would have been of the understanding that they were being treated, which may have been experienced as therapeutic. The review does include studies that evaluated combined intervention and integrated interventions, but we did not identify any studies where interventions were tested and delivered sequentially. The review also includes studies of some of the most well-known models for treating comorbidity, such as Seeking Safety, COPE, and programmes based around CBT. Most studies attempted to evaluate follow-up beyond the immediate completion of treatment, and several of the larger studies reported follow-up between 6 and 12 months after treatment was completed.

Some studies reported data on medium- to long-term follow-up. However, follow-up rates tended to be low, and whilst many studies used intention-to-treat (ITT) analyses, true follow-up effects relied heavily on estimation and may be too conservative or too optimistic of true effects. It should also be noted that whilst the majority of studies undertook ITT analyses, several studies based their ITT sample only on participants who attended at least one treatment session. This can be a legitimate approach when ineligible people are mistakenly randomised into a trial and if a potential participant is prematurely randomised as long as allocation to treatment arm cannot influence the likelihood that people receive the intervention (Fergusson 2002). However, the fact that some studies did this and others did not probably means that some studies included more participants who were likely to be ambivalent about engaging in treatment. We should note further that Coffey 2006, McGovern 2011, and Zlotnick 2009 only reported data for participants who were available to follow-up, and in some analyses this data was used in conjunction with ITT data from other studies. We undertook several sensitivity analyses excluding these studies. These analyses made no difference to our findings.

Quality of the evidence

We assessed the results for primary outcomes using GRADE protocols; see Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; Summary of findings 4. We found the quality of evidence for each comparison to be low or very low.

Risk of bias was a factor in downgrading GRADE judgements in all comparisons. As with the vast majority of trials of psychological therapy, participants and providers in the included studies were unblinded to allocation. We therefore judged all studies as being at high risk in terms of performance bias. More recent studies tended to be rated more favourably. In a number of studies, the information provided by the published report was insufficient to determine the risk of bias associated with key methodological indicators. We judged three studies as being at high risk on at least one other aspect of study design and four studies as at high risk on two other aspects of design. 'Other bias' was the most common aspect of design to be judged as high risk. Negative judgements on this aspect were made for a number of different reasons, and there was no particular common reason for this (see Characteristics of included studies). Lack of blinding of outcome assessors and selective reporting were the other main reasons for judgements of high risk.

We also downgraded GRADE judgements on the basis of unexplained statistical and clinical heterogeneity. Clinical populations were diverse in terms of type of trauma exposure, nature of substance misuse, and severity of substance abuse and dependence, with some studies only including participants with dependence, and one study excluding individuals with substance dependence (Mueser 2008). Mueser 2008 also differed from other studies in that all participants also had comorbidity for a serious mental illness. We attempted to group studies together in a way that was logical and clinically meaningful. It is, however, important for us to acknowledge that there is significant clinical heterogeneity within comparisons. The first of our main comparisons was of individual-based interventions with a trauma-focused component versus treatment as usual/minimal intervention (Analysis 1.1 to Analysis 1.12). Whilst all active interventions in this comparison included a trauma-focused component, the nature of delivery of trauma-focused intervention and the number of sessions of trauma-focused intervention differed, as did session length, the number of treatment sessions available, and the nature of additional substance use intervention. There was also significant clinical heterogeneity in the control conditions. The majority of studies included in these comparisons offered what would be considered combined PTSD/ SUD intervention. However, in some studies, SUD intervention was integral to the active intervention (for example through COPE, Mills 2012), whereas in other studies, participants in the active intervention received their SUD intervention from a separate source. Treatment-as-usual conditions in the studies in this comparison depended on what was available through local service delivery and therefore varied across studies. Not surprisingly, there was notable statistical heterogeneity in many of the analyses undertaken in this comparison, but the small number of studies limited the additional analyses we were able to undertake. There were also some differences in the interventions in the comparison of non-trauma-focused individual- and group-based interventions against treatment as usual/minimal intervention (Analysis 3.1 to Analysis 3.19; Analysis 4.1 to Analysis 4.9). Most group-based studies evaluated Seeking Safety. One study offered only 12 core sessions, rather than 25 sessions (Hien 2009); another incorporated some other cognitive intervention (Norman unpublished), and in a third participants received intervention whilst in a prison (Zlotnick 2009). Treatment as usual and minimal interventions also varied in this comparison, although statistical heterogeneity tended to be absent or smaller. In attempting to group studies and identify meaningful comparison, we tried to draw a distinction between control interventions evaluating an active psychological therapy from treatment as usual/minimal intervention. However, it is notable that "treatment as usual" interventions were often quite active and in most cases were likely to have contained some form of established or non-specific psychological therapy. We were only able to undertake limited investigation of factors potentially contributing to statistical heterogeneity because the number of studies included in each comparison was small.

Two of the comparisons used in this review were mostly moderately well powered. We downgraded the GRADE judgements of the

other two comparisons (see Summary of findings 2; Summary of findings 4) for reasons of imprecision of results, as the numbers of participants contributing to these comparisons were small. Evidence was collected by direct means for most outcomes used in meta analysis in this review.

Potential biases in the review process

The review followed guidelines set out by The Cochrane Collaboration (Higgins 2011). Two review authors independently read all the candidate studies and assessed them for inclusion. Three review authors rated all included studies for risk of bias and independently extracted data from them. In case of disagreements we consulted a fourth review author. This will have minimised potential bias.

Several unavoidable issues remain. For example, we were unable to undertake an assessment of publication bias. We searched numerous online databases systematically, scrutinised reference lists, contacted experts in the field, and handsearched relevant additional sources. We were able to identify a number of unpublished studies from conference abstracts and attempted to contact study authors where possible. We were able to include data from one unpublished study (Norman unpublished). It is, of course, possible that there are other unpublished studies that we have missed. We mainly contacted research groups who were known to us, in English-speaking countries (particularly the USA) and elsewhere in Europe, and a significant number of authors did not respond. We were not able to identify any relevant research groups outside of these areas of the world. We also included data from one study (Mueser 2008) that did not specifically provide interventions to treat PTSD/SUD comorbidity but included a significant minority of participants who met diagnosis. We included this study on the basis that it may provide evidence on how individuals with PTSD/SUD comorbidity respond to such non-specific intervention. We attempted to identify other similar studies by reviewing studies included in other relevant Cochrane reviews undertaken by the Cochrane Drugs and Alcohol Group and those reported in Bisson 2013. Some of the reviews that we searched were published several years ago, and it is therefore possible that we missed other relevant studies. We did also approach authors of several other studies, but we were not able to obtain subset data.

Although most studies reported data on an ITT basis, several studies reported incomplete data. We contacted authors to obtain missing results where possible. Some comparisons therefore included data from those participants available to follow-up, alongside ITT data. As we have outlined above, there was a great deal of clinical heterogeneity between trials included within comparisons within the review. There was also considerable statistical heterogeneity evident in many of the comparisons. In circumstances where we thought statistical heterogeneity to be an issue, we used a random-effects model, and reported this. The majority of studies that we identified compared an active psychological therapy against treatment-as-usual or minimal-intervention conditions. The studies comparing active psychological therapy against other psychological therapy tended to be small; this may mean that we were unable to identify effects that might be more apparent in studies that are better powered.

We reported some significant findings for treatment completion/drop-out. These findings were based on study definitions of what constituted a treatment completer. These definitions varied greatly across studies. It was not possible to compile data around more unified definitions, but it is possible that our finding in relation to treatment completion may not have occurred if the studies included were more consistent about their definitions of treatment completers.

Agreements and disagreements with other studies or reviews

This is the first systematic review of psychological therapies for PTSD and SUD that we are aware of to be based only on randomised controlled trials. Other reviews have based their conclusions on findings from both controlled and non-controlled studies (Berenz 2012; Najavits 2013; Torchalla 2012; van Dam 2012). To our knowledge, this is also the first review to undertake a detailed 'Risk of bias' assessment of included studies using the Cochrane 'Risk of bias' criteria (Higgins 2011), although other reviews have also commented upon methodological concerns (for example Najavits 2013; Torchalla 2012; van Dam 2012). In common with Berenz 2012 and van Dam 2012, we found that the most promising outcome data thus far are for psychological therapies that incorporate trauma-focused intervention alongside intervention for SUD. However, these treatment effects were small. This finding is consistent with the findings from a recent meta-analysis that compared treatment effects of studies for people with PTSD who had complex versus non-complex presentations (Gerger 2014). Gerger 2014 also found that the benefits of specific interventions were small in studies with participants with more complex clinical problems. Our findings are not consistent with the conclusions of Najavits 2013, in that the data we included found little evidence to support the use of non-trauma-focused interventions, although our findings were somewhat consistent with this review in that PTSD tended to improve (with some interventions) more than SUD. We also found that fewer participants assigned to trauma-focused intervention completed treatment than participants assigned to the comparable control condition. This finding is consistent with findings from the recently updated Cochrane review of psychological therapies for PTSD (Bisson 2013), suggesting that such interventions may not always be well tolerated.

AUTHORS' CONCLUSIONS

Implications for practice

We found evidence to suggest that psychological therapy that includes a trauma-focused component alongside intervention for SUD can help reduce PTSD symptom severity for people with PTSD and comorbid SUD. There is evidence to suggest that treatment effects may be sustained in the medium term. These results need to be interpreted with caution. Treatment effects were small and mostly for PTSD. We also found evidence to suggest that participants allocated to receive trauma-focused intervention were less likely to complete treatment than those who did not receive trauma-focused intervention. This suggests that there may be problems with tolerability of trauma-focused intervention for some people with this comorbidity. Clinicians and patients may want to consider this when making decisions about treatment. Participants in the studies included in this review are likely to have received a range of other stabilising interventions alongside trauma-focused treatment, and we found no evidence to support the delivery of trauma-focused interventions alone.

We found little evidence to support the use of non-trauma-focused interventions, delivered individually or through a group, although individual-based interventions have not been widely evaluated. Treatment drop-out was high across all included studies, regardless of intervention type; this is clearly a problem area in trying to help individuals with PTSD and comorbid SUD (Foa 2010; Schäfer 2007).

Clinical heterogeneity was a prominent feature of this review, which included studies across a number of populations, using a number of different forms of intervention, which we grouped in terms of similarity. Positive treatment effects for trauma-focused intervention alongside SUD interventions were small, and clinicians will want to exercise caution in deciding whether to provide the interventions identified in this review (Cloitre 2011; Najavits 2013). People with more severe and complex presentations (such as those with other serious mental illness, with cognitive impairment, and who are suicidal) were excluded from most studies in this review, and it would be inappropriate to generalise our findings to such individuals. Our conclusions are compromised by methodological issues evident in some studies and the high level of heterogeneity we found. Some studies were underpowered, and there were limited follow-up data, which limit conclusions regarding the long-term effects of psychological therapy. The follow-up period for most studies was short, limiting the conclusions that can be drawn about long-term effects. Only Frisman 2008 and Hien 2009 followed participants up to 12 months. PTSD and SUD are both cyclical and relapsing disorders, and longer-term follow-ups are important to demonstrating whether change is sustained over time (Bradley 2005). We assessed most of the evidence for each of the comparisons made in this review as being of low to very low quality, and findings may be liable to change as further evidence is accumulated.

Implications for research

We found few well-controlled studies of psychological therapies for PTSD and comorbid substance use. Further well-designed trials are clearly required, incorporating appropriate methods of randomisation, blinding of assessors, long-term follow-up, and appropriate training of therapists and monitoring of treatment adherence. The results of this review suggest that there are small benefits from interventions including a trauma-focused component alongside or following intervention treating symptoms of SUD, when compared against treatment as usual/minimal intervention. However, there is a need to replicate these findings over longer follow-up periods and to identify optimal modes of intervention delivery and new interventions that are more effective and can successfully retain participants in treatment. Future studies could investigate mediators and moderators of treatment compliance by evaluating factors that interfere with treatment retention (Ouimette 2003c; Pinto 2011). Non-trauma-focused interventions delivered on an individual basis have not been widely studied and should be evaluated further. Further comparison studies of one type of psychological therapy against another are required. As evidence accumulates, there will also be a need to differentiate effective interventions with different subgroups and different complexities of clinical presentation. Most of the studies in this review recruited participants from substance misuse services and/or provided supplementary SUD-related intervention, which was equivalent across treatment arms. There is little evidence about treatment effects when SUD-related intervention is minimal. Future studies should examine whether this is an essential component of treatment. There is some evidence to suggest that outcomes may be improved when psychological therapy is delivered in combination with pharmacological intervention for this patient group (Foa 2013); this should also be examined further. Finally, people with PTSD and comorbid SUD often require interventions from different services, and there is a need to evaluate different intervention combinations in order to identify optimal treatment pathways. Although non-trauma-focused interventions such as Seeking Safety have not shown significant evidence of effectiveness in this review, it may be that such programs, or components of them, have a role in enabling those seeking treatment to develop coping skills that may help them to tolerate trauma-focused intervention more easily. This should be investigated further.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Boden 2012

Methods	**Design:** Randomised effectiveness trial
Participants	**Setting:** Participants were military veterans recruited from a VA outpatient substance use disorder clinic. Treatment was delivered on an outpatient basis. **Inclusion criteria:** male veteran status and VA health care eligibility; a diagnosis of any current alcohol or drug use disorder; completion of an intake for outpatient SUD treatment at the participating mental health clinic; and meeting partial (i.e. defined as meeting criteria for 2 out of 3 PTSD symptom clusters, or at least 1 symptom in each symptom cluster) or full PTSD in clinical evaluation using CAPS.

Boden 2012 *(Continued)*

	Exclusion criteria: current participation in other day or inpatient mental health treatment; any contraindications communicated by the person's primary clinician; and acute psychosis, mania, dementia, or suicidal intent. **Sample size:** 125 individuals were assessed for eligibility; 117 were randomised; 8 participants were withdrawn after randomisation because they were found to meet 1 or more exclusion criteria; 98 attended at least 1 treatment session and were included in the analyses. **PTSD diagnosis:** 90.8**%** participants met full diagnosis for PTSD as measured by the CAPS; 9.8% met subthreshold diagnosis for PTSD. **SUD type and diagnosis:** All participants met diagnosis for SUD. Participants were polydrug users. **Mean age:** Seeking safety 55.1 (SD = 9.2) years; treatment as usual 52.9 (SD = 10.0) **Gender:** 100% male **Ethnicity:** 60.2% African American; 19.4% white; 7.1% Hispanic; 2% Native American; 5.1% other. **Country:** USA
Interventions	**Group 1: Group-based Seeking Safety plus treatment as usual:** n = 54. Seeking Safety is a present-focused, manualised, cognitive behavioural integrated treatment for PTSD and SUD, designed for both genders. Its primary goal is to reduce both PTSD and SUD by focusing on safe coping skills addressed through cognitive, behavioural, interpersonal, and case management domains. Participants were also able to access the treatment-as-usual interventions (described below). However, participants in this arm substituted SS groups and case management for the clinic's core substance use-focused group therapy and case management sessions. Groups were held twice weekly. Case management was based on the SS manual. **Group 2: Group-based treatment as usual:** n = 55. Treatment as usual involved participants entering twice-weekly "recovery" groups, focusing on building abstinence and, after approximately 90 days of therapy, on maintaining abstinence. Participants attended additional groups on smoking cessation, sobriety support, cocaine recovery, alcohol recovery, dual-diagnosis recovery, family therapy, anger management, cognitive behavioural therapy, fitness, relaxation, health education, hepatitis education, and developing outside activities as needed. All participants were assigned a case manager, and case management and individual therapy were available as deemed appropriate. Participants made use of clinic services as indicated by their treating clinician or as desired. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** IES-R **SUD:** ASI drug and alcohol composite scores for the previous 30 days. **Treatment acceptability:** Data are reported for the mean number of treatment sessions attended; participant satisfaction at 3-month assessment based on the Client Satisfaction Questionnaire. **Other:** Coping Responses Inventory **Follow-up:** End of treatment and at 3 months.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random allocation sequences were generated by the study statistician and implemented by use of sequentially numbered containers

Boden 2012 *(Continued)*

Allocation concealment (selection bias)	Low risk	Random allocation sequences were generated by the study statistician and implemented by use of sequentially numbered containers
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Research staff who enrolled participants and conducted outcomes assessment were blind to treatment assignment. To maintain blinding, staff conducting outcomes assessment were password-restricted from accessing data with information regarding treatment assignment, and participants were warned not to divulge information that might compromise blinding during interviews
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Treatment dropouts and withdrawals were clearly reported. Analysis of treatment outcomes was based on those participants available to follow-up
Selective reporting (reporting bias)	Low risk	Primary outcomes are specified in the protocol registered with ClinicalTrials.gov
Other bias	Unclear risk	Insufficient information available to be able to assess

Coffey 2006

Methods	**Design:** RCT - described as a laboratory-based experiment. The authors tested the hypothesis that alcohol craving elicited by a trauma cue might be attenuated if trauma-elicited negative emotion was reduced following trauma-focused imaginal exposure
Participants	**Setting:** Participants were recruited from 2 outpatient substance use treatment programmes. **Inclusion criteria:** Participants needed to meet current diagnosis for alcohol dependence and PTSD. All participants were involved in alcohol treatment. **Exclusion criteria:** Individuals were excluded if they met current diagnostic criteria for a psychotic disorder or were currently experiencing a manic episode. Although current major depression was not an exclusion criterion, severe major depression was. Individuals were also excluded if their PTSD diagnosis stemmed from combat or if they were currently or had ever engaged in exposure-based PTSD treatment. **Sample size:** The number of individuals assessed for eligibility is not reported. 43 individuals were invited to take part in the study and were randomised and 31 (who attended at least 1 treatment session) were included in the analyses. **PTSD diagnosis:** 43 (100%) of participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** 43 (100%) of participants met diagnosis for alcohol dependence. **Mean age:** 37.5 (SD = 8.0) years **Gender:** 29 (67%) female **Ethnicity:** 65% African American; 28% white; 5% Native American; 2% other **Country:** USA
Interventions	**Group 1: Individual imaginal exposure:** n= 16. Participants assigned to the exposure condition took part in six 60-min sessions of imaginal exposure targeting an index traumatic event. Participants were instructed to tell the story of their trauma by describing the event in the present tense from the first-

Coffey 2006 *(Continued)*

	person perspective. Participants were encouraged to include emotions and cognitions in their verbal description of the event. Participants described their trauma repeatedly and continuously over the course of the six 60-min clinical sessions. SUDS ratings were collected approximately every 5 min during each session. Each session was audiotaped, and participants were instructed to listen to the tape daily. **Group 2: Imagery-based relaxation:** n= 15. Participants assigned to the relaxation condition listened to an imagery-based relaxation audiotape for the 60-min session. As in the exposure condition, SUDS ratings were collected approximately every 5 min during each session. Participants were instructed to listen to the relaxation tape daily. **Experimental intervention modality:** Concurrent
Outcomes	**PTSD:** IES-R **SUD:** A cue reactivity paradigm was used to assess alcohol craving prior to, and after completion of, the 6 clinical sessions. **Treatment acceptability:** Attendance of 1, at least 4, and all 6 clinical sessions is described. **Other:** The PANAS; emotional distress as measured by SUDS **Follow-up:** End of treatment.
Notes	43 participants were assessed and randomised. Outcome data is reported for 17 responders of 31 participants who attended 1 or more intervention session

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The research assistant who conducted the assessment session and both laboratory sessions was unaware of the experimental condition to which participants had been randomly assigned. The research staff involved in the clinical sessions did not participate in the assessment session or either laboratory session
Incomplete outcome data (attrition bias) All outcomes	High risk	Outcome data is reported for 17 responders of 31 participants who attended 1 or more intervention session
Selective reporting (reporting bias)	High risk	Data related to craving response was based on a subset of 12 participants who reported a craving response to the cues at the first or the second laboratory session. This appears to have been based on a post-hoc decision
Other bias	Unclear risk	High attrition rates

Coffey submitted

Methods	**Design:** RCT
Participants	**Setting:** Participants were recruited from an unlocked residential SUD treatment facility. **Inclusion criteria:** DSM-IV diagnosis of both PTSD related to a non-combat trauma and alcohol dependence; 1 heavy drinking day in the past 60 days, as defined by consumption of 4 standard drinks for women and 5 standard drinks for men; and age between 18 and 60. **Exclusion criteria:** The presence of an acute psychotic disorder, bipolar disorder with an active manic episode (but not the presence of bipolar disorder, per se), imminent risk for suicide, prescription of craving-reducing medications (e.g. naltrexone) or medications to reduce alcohol use (e.g. disulphiram), self reported use, or urine drug screen indicating use, of a benzodiazapine, judged to have a medical condition that might limit co-operation or compromise the integrity of the data (e.g. organic brain syndrome, dementia, head injury, neuropathy, etc.), illiteracy in English, and being in an ongoing abusive relationship that resulted in a PTSD Criterion A event (but not a history of intimate partner violence, per se). **Sample size:** 222 individuals were assessed for eligibility; 148 were randomised, but 28 were subsequently excluded. Reasons for exclusion included cognitive impairment, psychosis, medical issues, drug screening, moved away, refusal to participate, and in one case for unknown reasons. The remaining 120 participants attended at least 1 treatment session and were included in analyses. **PTSD diagnosis:** All participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** All participants met diagnosis for alcohol dependence and 98.3% met criteria for other drug dependence, as measured by the CDIS-IV. **Mean age:** 33.72 (SD = 10.25) years **Gender:** 64 (53.3%) male; 56 (46.7%) female **Ethnicity:** 18.3% African American; 80.0% white; 0.8% other **Country:** USA
Interventions	**Group 1: Trauma-focused exposure therapy (EXP) + TAU:** n = 82. EXP is a well-described cognitive behavioural therapy that utilises imaginal and in vivo exposure techniques, either singly or in combination, to reduce the symptoms of PTSD resulting from a range of traumas. In addition to imaginal and in vivo exposure techniques, in the current study participants were provided psycho-education about PTSD, a rationale for EXP, and were taught breathing retraining as a method to manage arousal associated with PTSD. The imaginal exposures were audiotaped, and participants were instructed to listen to the tapes daily. 9 sessions of exposure were offered initially; if PTSD symptom severity did not decrease by at least 70%, an additional 3 sessions of EXP were offered. A number of adaptations were made to conventional exposure. Traditionally, exposure sessions are 90 minutes. The current study utilised 60-min EXP sessions. Additionally, protocol contained added psycho-education about the relationship between trauma and SUD symptoms and weekly check-ins about SUD treatment progress. Finally, the protocol provides integration of care at the team level, rather than the individual provider level. All participants received standard TAU for substance abuse. TAU consisted of daily group therapy for approximately 3 hours each day, daily recreation therapy, AA and NA meetings, individual drug counselling sessions, and completion of drug counselling homework. The 6-week TAU was provided by drug and alcohol counsellors unaffiliated with the current study. **Group 2: Healthy Lifestyles Sessions (HLS) + TAU:** n = 38. HLS is a structured 9- to 12-session intervention that provides education about a variety of health-related topics. HLS was designed to involve a similar amount of therapist contact and between-session homework as exposure. Topics covered included an introduction to treatment; sleep hygiene; progressive muscle relaxation; starting/maintaining an exercise programme; personal role identification; healthy eating and nutrition (2 sessions); diabetes (prevention or diabetes treatment adherence, depending on diabetes status); monitoring goals and values; cancer (a focus on breast cancer for women and colon cancer for men); HIV (reducing HIV risk or adhering to HIV treatment, depending on HIV status); and a final review session. Sessions included the provision of information, discussing participants' understanding of information, and answering questions about the information provided.

Coffey submitted *(Continued)*

	Experimental intervention modality: Combined
Outcomes	**PTSD:** CAPS; IES-R **SUD:** TLFB, the primary outcome was per cent days abstinent; ACQ-Now **Treatment acceptability:** Number completing at least 8 treatment sessions **Other:** BDI; BAI **Follow-up:** End of treatment; 3 and 6 months post-treatment
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence generation was undertaken by urn randomisation
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessors were blind to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Treatment dropouts and withdrawals were clearly reported. An ITT approach was used to analyse data based on participants who attended at least 1 treatment session. A number of other participants were also excluded from the study postrandomisation, and it was unclear if some of these exclusions might have been due to intervention-related factors
Selective reporting (reporting bias)	Unclear risk	All outcomes that were described were reported, but we were not able to identify a previously published protocol
Other bias	Unclear risk	28 individuals who were randomised were removed from the study. It is unclear whether this may have caused additional bias. Approximately half of the participants receiving the experimental intervention were also provided a session of motivational enhancement therapy for PTSD prior to beginning intervention. The other half of the experimental group and all of the HLS participants were provided a 60-minute relaxation session prior to the first scheduled treatment session. No significant differences were found between the 2 experimental groups, and they were therefore collapsed into a single experimental condition

Foa 2013

Methods	**Design:** RCT

Foa 2013 *(Continued)*

Participants	**Setting:** Treatment-seeking individuals were recruited through advertisements and professional referrals and treated on an outpatient basis. **Inclusion criteria:** Current PTSD and alcohol dependence according to DSM-IV; clinically significant trauma-related symptoms, as indicated by a score of at least 15 on the PSS-I; and heavy drinking in the past 30 days, defined as an average of more than 12 standard alcohol drinks per week with at least 1 day of 4 or more drinks determined by the TFBI. **Exclusion criteria:** Current substance dependence other than nicotine or cannabis; current psychotic disorder (e.g. schizophrenia, bipolar disorder); clinically significant suicidal or homicidal ideation; opiate use in the month prior to study entry; medical illnesses that could interfere with treatment (e.g. AIDS, active hepatitis); or pregnancy or nursing. **Sample size:** 657 individuals were assessed for eligibility; 165 were randomised, and all were included in the analyses. **PTSD diagnosis:** All participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** All participants met full diagnosis for alcohol dependence. **Mean age:** prolonged exposure + naltrexone 40.1 (95% CI 36.7 to 43.5); prolonged exposure + placebo 44.7 (95% CI 41.8 to 47.7); supportive counselling + naltrexone 44.9 (95% CI 41.8 to 47.9); supportive counselling + placebo 41.2 (95% CI 38.6 to 43.9) **Gender:** 108 (65.5%) male; 57 (34.5%) female **Ethnicity:** 63% African American; 30% white; 4.2% Hispanic; 0.6% other **Country:** USA
Interventions	Before randomisation to treatment, participants completed outpatient medical detoxification (at least 3 consecutive days of alcohol abstinence) with oxazepam as required to manage alcohol withdrawal symptoms. **Group 1: Prolonged exposure + naltrexone + supportive counselling:** n = 40. Prolonged exposure therapy consisted of 12 weekly 90-minute sessions followed by 6 biweekly sessions and included repeated imaginal exposure (i.e. revisiting and recounting traumatic memories) and processing the memory (i.e. discussing thoughts and feelings related to revisiting the memory). The target dose of naltrexone was 100 mg/d, starting with 50 mg/d for a minimum of 3 days and titrating up within 1 week. Supportive counselling was available as described below. **Group 2: Prolonged exposure + placebo + supportive counselling:** n = 40. Participants received PE as described above. Supportive counselling was available as described below. **Group 3: Supportive counselling + naltrexone:** n = 42. Supportive counselling was based on the BRENDA model, which combines medication management with compliance enhancement techniques based on motivational interviewing. Supportive counselling sessions were administered by a study nurse and lasted 30 to 45 minutes. Input included dispensing medication, monitoring compliance, assessing and providing education about alcoholism, and offering support and advice concerning drinking. Visits were weekly during the first 3 months and biweekly during the remaining 3 months. **Group 4: Supportive counselling + placebo:** n = 43. Supportive counselling was as described above. **Experimental intervention modality:** Combined
Outcomes	**PTSD:** PSS-I **SUD:** TLFB; PACS **Treatment acceptability:** Reported in terms of the mean number of sessions attended for PE. **Other:** -

Foa 2013 *(Continued)*

	Follow-up: End of treatment and 6 months' post-treatment
Notes	For the purpose of the review, we were interested in the comparison between prolonged exposure plus supportive counselling and supportive counselling

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not be blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Evaluators were blind to treatment group assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Treatment dropouts and withdrawals were clearly reported. An ITT approach was employed using hierarchical linear and non-linear modelling, which took into account dropouts and missing data
Selective reporting (reporting bias)	Low risk	Key outcomes are as specified in the protocol registered with ClinicalTrials.gov
Other bias	Low risk	There was no significant difference between the treatment groups on any demographic or baseline diagnostic characteristics. We identified no other potential biases

Frisman 2008

Methods	**Design:** RCT
Participants	**Setting:** Participants were recruited from amongst outpatients at 3 participating substance use disorder clinics. **Inclusion criteria:** (a) a history of trauma that fulfilled the conditions for DSM-IV PTSD criterion A, (b) a substance use disorder, and (c) DSM criteria for one of the following: PTSD, DESNOS plus at least 1 or more DSM-IV Axis I disorders, or a diagnosis of major depressive disorder, dysthymic disorder, or dissociative disorder. **Exclusion criteria:** Not specified. **Sample size:** 274 individuals were assessed for eligibility; 213 were randomised **PTSD diagnosis:** 202 (94.8%) of participants met full diagnosis for PTSD as measured by the CAPS. Of these, 72 (33.8%) met criteria for PTSD with DESNOS. 7 (3.3%) met criteria for DESNOS without PTSD, and 4 (1.9%) met criteria for other disorders, such as dissociative disorder and major depression. **SUD type and diagnosis:** Participants met diagnosis for substance abuse and substance dependence. Participants were polydrug users.

Frisman 2008 *(Continued)*

	Mean age: Intervention group: 37.84 (SD = 8.42) years; control group: 36.85 (SD = 8.44) years **Gender:** 130 (61%) female **Ethnicity:** 24.4% African American; 56.3% white; 10.3% Hispanic; 8.92% other **Country:** USA
Interventions	**Group 1: Group-based trauma-sensitive usual care plus Trauma Adaptive Recovery Group Education and Therapy (TARGET):** n = 141 Participants randomised to TARGET treatment were offered 8 or 9 weeks of manualised group treatment. TARGET provided psycho-education about the impact of traumatic exposure and PTSD on the body's stress response system and the brain using the strength-based concept of an adaptive psychobiological "alarm reaction". Participants were taught 7 core skills: focusing, recognising stress triggers, emotion identification, evaluating cognitions, defining personal goals, making choices with options grounded in personal strengths, and making a contribution to restore a sense of hope, faith, and purpose in the wake of trauma and PTSD. Experiential exercises were used to teach, model, role-play, and integrate skills and to use them to develop a coherent memory narrative of the client's life that incorporates a range of experiences including but not limited to traumatic stress. To enhance retention in the groups, small incentives that also reinforced aspects of the TARGET model (e.g. pens, key chains) were handed out on 3 occasions during the group. **Group 2: Trauma-sensitive usual care:** n = 72 Participants received regular substance abuse treatment sessions. Counsellors providing this intervention received training on trauma-sensitive care. Training workshops included information about the effect of traumatic events and disorders that trauma may cause or exacerbate. The counsellors also learned about the typical problems of trauma survivors and some of the ways in which past trauma can interfere with substance abuse recovery. Counsellors received literature about trauma, post-traumatic stress, and substance abuse recovery that could be shared with clients. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** GAIN-traumatic stress symptoms; PTCI **SUD:** GAIN subscales for substance use frequency, per cent drinking to intoxication, per cent using any drugs, and per cent abusing drugs or alcohol were used to assess changes in substance use and abuse. **Treatment acceptability:** Mean number of sessions attended for the active intervention group and mean number of standard-care sessions attended for both groups. **Other:** GAIN for depressive symptoms, anxiety symptoms, and self efficacy **Follow-up:** 6 and 12 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	By cohort using a random number program
Allocation concealment (selection bias)	Unclear risk	Insufficient information to be able to assess
Blinding of participants and personnel (performance bias)	High risk	Participants and personnel were not blinded to allocation

Frisman 2008 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	A trained research assistant conducted face-to-face interviews. No further information was available
Incomplete outcome data (attrition bias) All outcomes	Low risk	Attrition and drop-out are well described. Hierarchical linear modelling was used to enable estimation where data were unavailable
Selective reporting (reporting bias)	Unclear risk	Traumatic stress symptoms as indexed by GAIN were described in the methodology as a primary outcome, along with a number of other outcomes. However, this outcome is not reported, although other prespecified outcomes are reported
Other bias	High risk	The process of allocation was modified partway through the study, as delays in starting groups early on "meant that many participants received an insufficient dose". It was unclear as to why the number of participants randomised to the active intervention group was nearly double the number randomised to the control group. There was a high drop-out rate. Counsellors to participants in the control condition could not be prevented from formally referring to the FREEDOM steps or using the handouts or other tangible materials from TARGET in non-TARGET groups. This led study authors to conclude that there was "contamination of the comparison group treatment with TARGET principles and techniques".

Hien 2004

Methods	**Design:** Partial RCT described as a "quasi-experimental clinical trial"
Participants	**Setting:** Participants were recruited through advertisements and referred through substance use treatment programmes. Participants were treated on an outpatient basis. **Inclusion criteria:** Current or subthreshold PTSD (defined as DSM-IV criteria A, B, and E and the presence of either C or D) and current DSM-IV substance dependence; if they reported using substances at least 3 times a week on the Substance Use Inventory; Mini-Mental State Examination score greater than 21; age 18 to 55 years; female; and English-speaking. **Exclusion criteria:** Advanced-stage medical disease (e.g. AIDS, tuberculosis) as indicated by global physical deterioration and incapacitation, organic mental syndrome (associated with chronic drug abuse), and psychiatric exclusions (current active suicidality; current Axis I diagnoses other than atypical bipolar, depressive, or anxiety disorders; and history of psychosis). **Sample size:** 207 individuals were assessed for eligibility; 128 met full study eligibility criteria, 115 agreed to participate, and 96 of these were randomised. 32 of the 128 women became a non-randomised community care comparison group. 75 of the 96 women who were randomised attended at least 1 treatment session and were included in the ITT analyses. **PTSD diagnosis:** 88% of women met full diagnosis for PTSD as measured by the CAPS. The other 12% met criteria for subthreshold PTSD. **SUD type and diagnosis:** Women were included on the basis that they met criteria for substance dependence. Women were polydrug users. **Mean age:** 38.2 (SD = 9.1) for Seeking Safety; 33.8 (SD = 8.3) for relapse prevention. The difference in age was statistically significant. **Gender:** 128 (100%) female

Hien 2004 *(Continued)*

	Ethnicity: 42.7% African American; 36% white; 20% Hispanic; 13.3% multiracial; 1.3% other **Country:** USA
Interventions	**Group 1: Individual-based Seeking Safety plus standard care:** n = 41. The intervention is not fully described but is introduced as a short-term, manualised cognitive behavioural treatment that simultaneously addresses trauma and substance abuse. Women were offered two 1-hour treatment sessions weekly over 12 weeks. **Group 2: Individual-based relapse prevention plus standard care:** n = 34. The intervention is not fully described but is introduced as an empirically validated cognitive behavioural therapy focusing on the identification of triggers and coping strategies for managing substance cravings and relapse. **Group 3: Standard community treatment:** n = 32. The intervention is not described. Women in this arm were not randomised. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** The primary PTSD outcome was a composite score from scores on the CAPS, IES-R, and CGI Scale. **SUD:** The primary SUD outcome was a composite score from scores on the Substance Use Inventory and CGI Scale. **Treatment acceptability:** Data are reported for number of participants attending at least 25% of treatment sessions. **Other:** Items from CGI Scale were used to assess global severity of psychiatric symptoms; Global Assessment Scale and the HDRS were also used. **Follow-up:** 3, 6, and 9 months postbaseline
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information to be able to assess
Allocation concealment (selection bias)	Unclear risk	Insufficient information to be able to assess
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information to be able to assess
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Treatment dropouts and withdrawals were clearly reported. An ITT approach was used, using last observation carried forward. However, ITT was based on participants attending at least 1 treatment session. It was unclear if those who were randomised but who did not attend any sessions were aware of their allocation (Fergusson 2002)
Selective reporting (reporting bias)	Unclear risk	Composite outcome scores for both PTSD and SUD were used as primary outcomes. The authors state that this was done to reduce the possibility of Type

Hien 2004 *(Continued)*

		I error. It is unclear how composite scores were generated. Raw scores are reported for PTSD measures but not for SUD measures
Other bias	Unclear risk	Insufficient information to be able to assess

Hien 2009

Methods	**Design:** RCT
Participants	**Setting:** Participants were enrolled in 7 community-based substance abuse treatment programs (CTPs) across the USA. **Inclusion criteria:** To be eligible, individuals needed to have had at least 1 traumatic event in their lifetime and to meet DSM–IV–TR criteria for either full or subthreshold PTSD (where they did not meet criteria for either category C (avoidance and numbing symptoms) or category D (symptoms of increased arousal) but met all other criteria). Other inclusion criteria were between 18 and 65 years of age, had used alcohol or an illicit substance within the past 6 months, had a current diagnosis of drug or alcohol abuse or dependence, and were capable of giving informed consent. **Exclusion criteria:** Individuals were excluded if they had an advanced stage medical disease as indicated by global physical deterioration, impaired cognition, significant risk of suicidal/homicidal intent or behaviour, a history of schizophrenia-spectrum diagnosis, a history of active (past 2 months) psychosis, or involvement in litigation related to PTSD. Individuals were also excluded if they did not speak English or if they refused to be video- or audiotaped. **Sample size:** 1963 individuals were assessed for eligibility; 353 were randomised, and all were included in the analyses. **PTSD diagnosis:** 80.4% of women met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** Women met diagnosis for substance abuse and substance dependence. Women were polydrug users. **Mean age:** 39.2 (SD = 9.2) years **Gender:** 353 (100%) female **Ethnicity:** 34% African American; 45.6% white; 6.5% Latina; 13.3% multiracial; 0.6% other **Country:** USA
Interventions	**Group 1: Group-based Seeking Safety plus treatment as usual:** n = 176. Seeking Safety is a structured cognitive behavioural treatment with both safety/trauma and substance use components integrated into each session. All sessions have the same structure: (a) check-in, including reports of any unsafe behaviours and use of coping skills, (b) session quotation, a brief point of inspiration to affectively engage women and link to the session topic, (c) relating the material to the women's lives, in which handouts are used to facilitate discussion and structured skill practice, and (d) check-out, including a commitment to specific between-session skills practice. Each session covered a different topic as follows: safety, taking back power from PTSD, when substances are in control, honesty, setting boundaries in relationships, compassion, healing from anger, creating meaning, integrating the split self, taking good care of oneself, red and green flags, and detaching from emotional pain (grounding). Seeking Safety treatment was abbreviated from 25 to 12 core sessions (75 to 90 minutes) delivered over 6 weeks to fit within a feasible time frame for community-based outpatient treatment programs. However, because 2 women needed to be present to conduct the group, many women took longer than 6 weeks to complete the interventions. All study participants were enrolled in 1 of the participating community treatment programs and were asked to attend treatment as usual at the program during the 6-week treatment phase of the study. Treatment as usual was not kept constant across sites but was allowed to vary. Outpatient treatment differed across sites in frequency and length of sessions per week, although most offered intensive outpatient services of 3 days per week or more. The treatment orientation of the

Hien 2009 *(Continued)*

	programs also varied, but none of the programs provided trauma-focused treatment to women during the study. **Group 2: Group-based Women's Health Education plus treatment as usual:** n = 177. Women's Health Education (WHE) was intended to control for therapeutic time and attention. WHE is a psycho-educational, manualised health curriculum focused on topics such as understanding the female body, human sexual behaviour, pregnancy and childbirth, sexually transmitted diseases, HIV, and AIDS. WHE was designed to provide equivalent therapeutic attention, expectancy of benefit, and an issue-oriented focus, but without theory-driven techniques (i.e. those of Seeking Safety) or any explicit focus on or psycho-education specific to substance abuse or trauma. All WHE sessions followed a common format: (a) introduction of topic, (b) review of group rules and between-session assignment, (c) topic presentation, (d) a video, storytelling, and/or text readings, and (e) topic exercises in a variety of formats to facilitate group discussion and application of session materials, and (f) setting between-session goals. Treatment as usual for the WHE group was as described above. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** CAPS total score; PSS-SR total score **SUD:** Substance use diagnosis as measured by the Composite International Diagnostic Interview for DSM–IV; quantity and frequency of substance use as measured by the Substance Use Inventory; biologically confirmed abstinence from drugs of abuse was obtained by use of the SureStep urine drug screen card; recent alcohol use was tested with the Alco Screen-Saliva Alcohol Test. **Treatment acceptability:** Data are reported for number of women attending at least 1 group treatment session and number attending at least 6 treatment sessions. **Other:** None **Follow-up:** 1 week, 3, 6, and 12 months. The PSS-SR and SUI were administered weekly during the treatment phase as well as at all other time points.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A statistician generated 1 blocked randomisation list (block size known only to the statistician) for the entire study
Allocation concealment (selection bias)	Low risk	Each participating community-based substance abuse treatment program received sets of 60 sealed, tamper evident security envelopes, containing 1 randomisation number and the corresponding treatment assignment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Independent assessors who remained unaware of randomisation assignment performed all baseline and post-treatment assessments
Incomplete outcome data (attrition bias) All outcomes	Low risk	Treatment dropouts and withdrawals were clearly reported. An ITT approach was employed using generalised estimating equations
Selective reporting (reporting bias)	Unclear risk	Follow-up outcomes were obtained at 1 week and 3, 6, and 12 months. The summary of outcomes table reports average outcome scores for the follow-up period of 3 to 12 months. Use of averaged outcome scores was not specified in

Hien 2009 *(Continued)*

		the methodology. It is unclear how data from these time points were used in analyses. Some analyses are reported for the 12-month follow-up point. It is unclear if data were reported in this way at the request of the publishing journal or by decision of the research group
Other bias	Low risk	There was no significant difference between the 2 treatment groups on any demographic or baseline diagnostic characteristics. We identified no other potential biases

McGovern 2011

Methods	**Design:** RCT
Participants	**Setting:** Participants were new admissions to a community addiction treatment program and recruited from 1 of 7 participating community intensive outpatient or methadone maintenance programs. **Inclusion criteria:** Participants were at least 18 years of age, were actively enrolled in outpatient addiction services, and met criteria for any substance use disorder. Participants were also required to have a diagnosis of PTSD verified by the CAPS with total symptom score equal to or greater than 44. **Exclusion criteria:** Acute psychotic symptoms (people with a psychotic disorder were eligible if their symptoms were stable and they were receiving appropriate mental health services); psychiatric hospitalisation or suicide attempt in the past month, unless the hospitalisation or attempt was directly related to substance intoxication or detoxification and the person was currently stable; or unstable medical and legal situations such that ability to participate in the full duration of the study seemed unlikely. **Sample size:** 77 individuals were assessed for eligibility; 53 were randomised, and 36 attended at least 1 treatment session. 53 were included in the analyses. **PTSD diagnosis:** All participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** All participants met diagnosis for a substance use disorder. Type of substance use and the number meeting substance dependence were not specified. **Mean age:** Integrated CBT plus standard care group: 39.09 (SD = 11.32) years; individual addiction counselling plus standard care group: 35.48 (SD = 9.44) years **Gender:** 23 (43.4%) male; 30 (56.6%) female **Ethnicity:** 90.6% white; other ethnicities were not described **Country:** USA
Interventions	**Group 1: Integrated cognitive behavioural therapy (ICBT) plus standard care:** n = 32. ICBT is a manual-guided individual-based therapy focusing on PTSD symptoms and substance use. It was designed for integration into routine community addiction treatment programming. Participants were required to be active in either intensive outpatient or methadone maintenance services. ICBT consisted of 8 modules: introduction to treatment, crisis and relapse prevention planning, breathing retraining, psycho-education about PTSD primary symptoms, psycho-education about additional associated symptoms, two cognitive restructuring modules, and generalisation training. ICBT was delivered in an individual format, within a weekly 45- to 50-minute session, over approximately 12 to 14 sessions. A client workbook was to be used in conjunction with the therapist manual with practice handout items for homework in between treatment sessions. Standard care occurred in either methadone maintenance or intensive outpatient clinics. 2 of the 7 recruiting programs were methadone maintenance, and 5 were intensive outpatient programs. **Group 2: Individual addiction counselling (IAC) plus standard care:** n = 21. IAC is a manual-guided individual-based therapy designed to be integrated into an addiction treatment or methadone maintenance program. IAC targeted substance use only and was considered complementary to a typical community addiction treatment program. IAC consisted of 5 modules: treatment initiation, early ab-

McGovern 2011 *(Continued)*

	stinence, maintaining abstinence, recovery, and termination. IAC was delivered in 10 to 12 weekly sessions. As with ICBT, individual addiction counselling had participant practice handouts for homework in between treatment sessions. Standard care was as described above. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** CAPS **SUD:** ASI alcohol and drug composites; toxicology: recent alcohol intake and drug metabolites for amphetamine, benzodiazepines, cannabis, cocaine, methamphetamine, and opiates were screened for using urine and breath samples gathered at each assessment period. **Treatment acceptability:** This was described in terms of initiation (number of participants attending at least 1 treatment session), engagement (number completing at least 2 sessions), and completion (number attending at least 75% of sessions). **Other:** BDI **Follow-up:** 3 and 6 months postbaseline
Notes	It is unclear as to why there is such sizeable difference between the numbers of participants randomised to the 2 conditions

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported. It is reported that research interviewers were blinded to treatment assignment at randomisation, but other information about the randomisation process is not provided
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Research interviewers were not blinded to treatment assignment at the follow-up assessments
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Analysis was undertaken using generalised estimating equations analyses, which allowed analyses without excluding participants based on missing data points or drop-out. However, the study only achieved a follow-up rate of 53%, and as the authors acknowledge, this "reduces the power and the ability to detect differences between treatment conditions".
Selective reporting (reporting bias)	Low risk	Primary outcomes are specified in the protocol registered with ClinicalTrials.gov
Other bias	High risk	There were a number of minor differences between the 2 groups at baseline (e.g. PTSD severity). The effects of these differences are unclear. The number of treatment sessions provided to the intervention (12 to 14) was longer than that provided to the control intervention (10 to 12)

Mills 2012

Methods	**Design:** RCT
Participants	**Setting:** Participants were seen on an outpatient basis and were recruited from substance use treatment services, media advertisements, and practitioner referrals. **Inclusion criteria:** Past-month DSM-IV-TR diagnoses of PTSD and substance dependence, age 18 years or older, and fluency in English. **Exclusion criteria:** Individuals were excluded from participating if they were currently suicidal (expressed suicidal ideation accompanied by a plan and intent), had a recent history of self harm (past 6 months), had current active symptoms of psychosis, or experienced cognitive impairment severe enough to impede treatment. **PTSD diagnosis:** All participants met full diagnosis for PTSD as measured by the CAPS. **Sample size:** 334 individuals were assessed for eligibility; 103 were randomised, and all were included in the analyses. **SUD type and diagnosis:** All participants were reported to be substance dependent. Participants were polydrug users and had used a mean of 4 drug classes in the previous month. **Mean age:** 33.7 (SD = 7.9) years **Gender:** 64 (62.1%) female **Ethnicity:** Australian born: 87 (84.5%); 6 (5.8%) Aboriginal or Torres Strait Islander **Country:** Australia
Interventions	**Group 1: Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE):** n = 55. COPE is a modified version of Concurrent Treatment of PTSD and Cocaine Dependence. The model represents an integration of existing evidence-based manualised CBT interventions for PTSD and substance dependence. Intervention consists of 13 individual-based 90-minute sessions (i.e. 19.5 hours) delivered by a clinical psychologist. Although designed to be delivered weekly, flexibility was permitted. Treatment components include motivational enhancement and CBT for substance use; psycho-education relating to both disorders and their interaction; in vivo exposure; imaginal exposure; and cognitive therapy for PTSD. The final session was dedicated to providing a review of the treatment, devising an aftercare plan, and termination of therapy. **Group 2: Usual treatment:** n = 48. Both the treatment and the control group were able to engage in usual treatment for substance dependence. As such, participants could access any type of substance use treatment currently available in the community, including outpatient counselling, inpatient or outpatient detoxification, residential rehabilitation, and pharmacotherapies (e.g. methadone, buprenorphine, buprenorphine plus naloxone, naltrexone). **Experimental intervention modality:** Combined
Outcomes	**PTSD:** CAPS **SUD:** CIDI **Treatment acceptability:** Data are reported for number of participants attending at least 1 treatment session; number attending at least 1 imaginal exposure session; and number attending all sessions. **Other:** BDI, STAI, IPDE **Follow-up:** 6 weeks, 3 and 9 months postbaseline
Notes	The study concluded with a lower sample size than planned due to a low recruitment rate. It is unclear why there is such sizeable difference between the numbers of participants randomised to the 2 conditions

Mills 2012 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Block randomization was conducted in groups of 10, stratified according to sex ... "
Allocation concealment (selection bias)	Low risk	" ... by a person independent of the research."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Interviews were administered by 2 trained research officers blinded to group allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Outcome data were analysed on an ITT basis. Missing data were imputed using multiple imputation
Selective reporting (reporting bias)	Low risk	Key outcomes are as specified in the protocol registered with the World Health Organization's trials portal
Other bias	High risk	Participants in the control group were more likely to have reported a history of childhood sexual abuse. This was controlled for in analyses. There was considerable variability in the time taken to complete treatment, with some participants continuing treatment well beyond the planned treatment period of 13 weeks and at least 1 receiving treatment around the final follow-up point

Mueser 2008

Methods	**Design:** RCT
Participants	**Setting:** Individuals with severe mental illness were recruited from community mental health centres. **Inclusion criteria:** Minimum age 18 years; designation by the states of New Hampshire or Vermont as having a severe mental illness, defined as a DSM–IV Axis I disorder and persistent impairment in the areas of work, school, or ability to care for oneself; DSM–IV diagnosis of major depression, bipolar disorder, schizoaffective disorder, or schizophrenia; current DSM–IV diagnosis of PTSD; and legal ability and willingness to provide informed consent to participate in the study. **Exclusion criteria:** Psychiatric hospitalisation or suicide attempt within the past 3 months; current DSM–IV substance dependence. **Sample size:** 270 individuals were assessed for eligibility; 108 were randomised, and all were included in the analyses. **PTSD diagnosis:** All participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** Nature of substance abuse was not specified. 44 (40.7%) of participants met diagnosis for substance use disorder. Outcome data are available for this subgroup. **Mean age:** 44.21 (SD = 10.64) years **Gender:** 35/44 (79.5%) female

Mueser 2008 *(Continued)*

	Ethnicity: 38 (86.4%) white; (4.5%) African American; (4.5%) American Indian/Alaska Native; (2.3%) Hispanic; (2.3%) Asian-Pacific Islander **Country:** USA
Interventions	**Group 1: Individual CBT for PTSD:** n = 17. Sessions included an introduction to the programme; crisis plan review; psycho-education on core and associated symptoms of PTSD; cognitive restructuring; generalisation training; and termination. Participants were offered 12 to 16 sessions over 4 to 6 months. **Group 2: Treatment as usual:** n = 27. Participants assigned to TAU continued to receive the usual services they had been receiving before enrolment in the program. None of the mental health centres offered either cognitive restructuring or exposure therapy treatments for PTSD, although supportive counselling for trauma-related problems was available. **Experimental intervention modality:** Treatment of PTSD only
Outcomes	**PTSD:** CAPS **SUD: -** **Treatment acceptability:** Data are reported for number of participants in the experimental condition attending at least 6 treatment sessions. **Other:** PTCI; PTSD Knowledge Test; Brief Psychiatric Rating Scale; BDI-II; BAI; 12-Item Short Form Health Survey; client version of the Working Alliance Inventory **Follow-up:** End of treatment and at 3 and 6 months' post-treatment
Notes	This study did not specifically aim to treat individuals meeting diagnosis for SUD. A subset of participants met SUD diagnosis, and study authors provided data for these individuals. These participants only met criteria for substance abuse; individuals meeting diagnosis for substance dependence were excluded

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was conducted by a computer-based randomisation program
Allocation concealment (selection bias)	Low risk	Randomisation was conducted at a central location in a research centre. Assignments were not known in advance by either clinical or research staff
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Assessments were conducted by blinded interviewers at all assessment points. Participants were instructed at the beginning of interviews not to talk about any treatments for trauma-related problems they may have received. Interviewers were requested to inform the project co-ordinator if the client broke the blind during an interview. Interviewers were not asked to guess clients' treatment assignments, to avoid directly encouraging them to formulate hypotheses about how treatment may have affected clients' symptoms, which could have influenced subsequent ratings. No specific instances of blind breaking were noted in the study
Incomplete outcome data (attrition bias)	Low risk	Withdrawals are thoroughly described. ITT analysis was conducted to determine the effects of primary outcomes

Mueser 2008 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	Outcomes were reported as specified in the methodology section, but we were not able to identify a previously published protocol
Other bias	Low risk	There were no differences between the groups on any demographic, diagnostic, or baseline measures or in the rates of follow-up assessments

Najavits 2006a

Methods	**Design:** RCT
Participants	**Setting:** Participants were adolescent girls who were treated on an outpatient basis and were recruited through posted fliers and active recruitment from local clinics, hospitals, schools, and clinicians. **Inclusion criteria:** Participants met current DSM-IV criteria for both PTSD and SUD. They also had to report active substance use within the past 60 days. **Exclusion criteria:** Potential participants were excluded if they had a history of bipolar I disorder (mania), psychotic disorder, were mandated to treatment, or had characteristics that would interfere with treatment completion (mental retardation, homelessness, impending incarceration, or a life-threatening illness). **Sample size:** The number of individuals assessed for eligibility was not specified; 33 were randomised, and all were included in the analyses. **PTSD diagnosis:** All participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** Most participants (n = 31, 93.9%) met diagnosis for substance dependence. Participants were polydrug users. **Mean age:** 16.06 (1.22) **Gender:** 100% female **Ethnicity:** 78.8% white; 12.8% Asian-Pacific Islander; 3% Hispanic; 3% African American; 3% multiethnic **Country:** USA
Interventions	**Group 1: Individual-adapted Seeking Safety plus treatment as usual:** n = 18. This coping skills therapy targets current PTSD and SUD. The treatment manual has 25 topics representing cognitive, behavioural, and interpersonal domains. Each topic offers a safe coping skill relevant to both disorders, such as Asking for Help, Compassion, Setting Boundaries in Relationships, and Honesty. The treatment has five principles: (1) safety as the priority; (2) integrated treatment of both disorders; (3) a focus on ideals; (4) four content areas: cognitive, behavioural, interpersonal, and case management; and (5) attention to therapist processes. The original manual was modified to take account of the developmental level of adolescents. Participants were offered 25 50-minute sessions over 3 months. **Group 2: Treatment as usual:** n = 15. All participants were allowed to attend any concurrent treatments they naturalistically sought (e.g. Alcoholics Anonymous, psychotropic medication, and other individual and group psychotherapies). **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** Trauma Symptom Checklist for Children **SUD:** Personal Experiences Inventory

Najavits 2006a *(Continued)*

	Treatment acceptability: For the Seeking Safety group, the mean number of all treatment sessions attended and the number of Seeking Safety sessions attended were reported. Data were also reported for client satisfaction (see below). **Other:** Beliefs About Substance Use; World Assumptions Scale; Adolescent Psychopathology Scale; CSQ; HAQ; Teen Treatment Services Review interview **Follow-up:** End of treatment and at 3 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Information about sequence generation and allocation concealment were provided by the lead study author. A statistician independent of the study generated the randomisation list prior to the first randomisation using a random number generator
Allocation concealment (selection bias)	Low risk	The list was administered "lock-step", and the principal investigator and therapists were unable to influence randomisation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	The process of outcome assessment was not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Dropouts were well reported. Authors employed a full intent-to-treat analysis using a random effects model to analyse data
Selective reporting (reporting bias)	High risk	The Personal Experiences Inventory was identified as the primary measure. This measure was described as having 2 subsections (chemical involvement problem severity and psychosocial problems), each with multiple subscales. More specific information about whether a total score, subsection score, or subscale score was the primary outcome was not given. Other outcome measures also had multiple subscales. Outcomes were not clearly reported. A table describing outcomes at intake, end of treatment, and 3 months' follow-up only shows data for outcomes that were significant
Other bias	High risk	The TAU group had a higher level of psychopathology as measured at baseline. There was no attempt to control for this. The study describes a number of outcome measures, with a large number of subscales. We estimated 40 outcomes. It appears there were no attempts to correct for the use of multiple statistical testing

Norman unpublished

Methods	**Design:** RCT
Participants	**Setting:** Participants were female victims of interpersonal violence. They were recruited through flyers posted in community agencies that serve IPV victims and in primary care and psychiatry clinics.

Norman unpublished *(Continued)*

	Inclusion criteria: Female interpersonal violence victims over the age of 18, with at least 1 month out of the abusive relationship, met DSM-IV criteria for PTSD and an alcohol use disorder, literate in English, had not changed psychotropic medications or dosages within the previous 2 months and agreed not to during the active phase (first 12 weeks) of the intervention, and had an identified primary care physician. **Exclusion criteria:** Moderate or severe cognitive impairment as measured by a Mini-Mental State Examination score less than or equal to 18, history of psychosis (women with histories of psychosis or mania were only included if their symptoms had been well managed by pharmacotherapy for the most recent 6-month period). **Sample size:** 78 individuals were assessed for eligibility, 35 were randomised, and 29 received at least 1 session of treatment or remained in contact with the research group and were included in analysis. **PTSD diagnosis:** 25 (86.2%) of women met full diagnosis for PTSD as measured by the CAPS; other women met subthreshold diagnosis for PTSD. **SUD type and diagnosis:** All women met diagnosis for alcohol use disorder. **Mean age:** Seeking Safety: 45.27 (SD = 8.44); facilitated 12-step: 37.38 (SD = 9.13) **Gender:** 100% female **Ethnicity:** 65.5% white; 6.9% African American; 24.1% Hispanic; 3.4% American Indian **Country:** USA
Interventions	**Group 1: Adapted group-based Seeking Safety plus treatment as usual:** n = 20. Seeking Safety plus Cognitive Trauma Therapy for Battered Women with PTSD (CTT-BW) (Kubany 2004).The intervention was a 24-session group treatment protocol delivered over 12 weeks, incorporating the following interventions: psycho-education regarding PTSD and alcohol use disorders, skills to reduce self harm behaviours, behavioural activation, exposure to trauma, identifying and managing triggers, building social support, coping skills, assertive communication, managing affect, problem solving, grounding, and cognitive restructuring. **Group 2: 12-step supportive group:** n = 9. Therapist-led supportive group using a 12-step model where women were encouraged to discuss issues related to domestic violence and abstinence from alcohol. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** CAPS, PCL-C **SUD:** TLFB, Conceptual Cues/Coping Questionnaire **Treatment acceptability: -** **Other:** Adult Attachment Interview, Motivation/Self Esteem Scale, Anxiety Sensitivity Index, BDI, CD-RISC-10, Negative Mood Regulation Expectancies Scale, Self Compassion Scale, Coping Skills **Follow-up:** End of treatment and at 3 and 6 months' post-treatment
Notes	This study had originally intended to recruit 100 individuals but were unable to achieve this within the period that the study was funded. Investigators had great difficulty gathering data after the initial follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation was computer generated

Norman unpublished *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Allocation was handled by the study co-ordinator
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	High risk	Assessors were not blind to allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	ITT analysis was performed on women who attended at least 1 treatment session. Women who were randomised but did not attend any intervention sessions were unaware of their allocation (Fergusson 2002)
Selective reporting (reporting bias)	Low risk	Key outcomes are as specified in the protocol registered with ClinicalTrials.gov
Other bias	High risk	There was a significant difference in the average age of the two groups. It is unclear why there is such sizeable difference in the numbers of women randomised to the 2 conditions. There was also a sizeable, though non-significant, difference in alcohol consumption at baseline, and notable differences in ethnic makeup between the 2 groups

Sannibale 2013

Methods	**Design:** RCT
Participants	**Setting:** Participants were recruited from a range of services in metropolitan Sydney, Australia and seen on an outpatient basis. **Inclusion criteria:** Individuals were eligible if they were 18 years of age or older, consumed alcohol at hazardous levels (men 29 or more and women 15 or more 10 g ethanol drinks per week) and met DSM-IV diagnostic criteria for PTSD, determined by the CAPS. AUD diagnosis was determined by the Structured Clinical Interview for DSM-IV. Individuals on stable doses (for 2 months or longer) of pharmacotherapy for depression or alcohol dependence were eligible, as were individuals who needed and completed alcohol withdrawal. **Exclusion criteria:** People were excluded if they were 17 years or younger, had current psychosis, severe suicide risk, significant cognitive impairment, limited English comprehension, or severe substance dependence. **Sample size:** 154 individuals were screened and 90 assessed for eligibility; 62 were randomised, and all were included in the analyses. **PTSD diagnosis:** 58 (94%) of participants met full diagnosis for PTSD as measured by the CAPS. **SUD type and diagnosis:** All participants met criteria for AUD. **Mean age:** 41.18 (SD = 11.91) years **Gender:** 33 (53%) female **Ethnicity:** Not reported **Country:** Australia

Sannibale 2013 *(Continued)*

Interventions	**Group 1: Integrated CBT for PTSD and AUD:** n = 33. Participants in both conditions received the same treatment targeting AUD. This consisted of motivational interviewing, intervention focused on coping with cravings, cognitive intervention related to drinking and management of negative moods. Participants in this arm also received cognitive behavioural intervention for PTSD, based on a prolonged exposure model with cognitive restructuring. Treatment in both the experimental and control condition was manualised, and consisted of 12, once-weekly 90-minute individual sessions with structured daily homework tasks. **Group 2: CBT for AUD and supportive counselling:** n = 29. In addition to the shared components described above, this group also received supportive counselling. Treatment in this arm targeted AUD symptoms only, not PTSD symptoms. **Experimental intervention modality:** Combined
Outcomes	**PTSD:** CAPS, PDS **SUD:** TLFB, SADQ **Treatment acceptability:** Median sessions attended, number attending 1 or more sessions, 6 or more sessions, 9 or more sessions. **Other:** Short Inventory of Problems, BDI, STAI **Follow-up:** Post-treatment and 5 and 9 months' post-treatment
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"Randomisation was conducted according to a random number system by a person independent of the study ... "
Allocation concealment (selection bias)	Low risk	" ... and treatment was concealed."
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Follow-up assessments were conducted by independent clinicians who were unaware of the participants' treatment condition and did not have access to participant clinical or supervision notes or treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	All analyses were based on intent-to-treat, including all participants who entered the trial
Selective reporting (reporting bias)	Low risk	Outcomes were reported as specified in the methodology section
Other bias	Low risk	There were no differences between the groups on any demographic, diagnostic, or baseline measures or in the rates of follow-up assessments

Zlotnick 2009

Methods	**Design:** RCT
Participants	**Setting:** Treatment was conducted on the minimum-security wing of a female prison. Participants were recruited from a voluntary residential substance abuse treatment program for women requesting intensive substance abuse treatment. **Inclusion criteria:** DSM-IV criteria for current PTSD or subthreshold PTSD (i.e. had at least 1 symptom from all 3 clusters that were associated with impairment/distress) within the previous month as determined by the CAPS; and DSM-IV criteria for substance dependence 1 month prior to entering prison as determined by the Structured Clinical Interview for DSM-IV. **Exclusion criteria:** Women were excluded if they were actively psychotic at the time of recruitment, did not know English well enough to be able to understand the consent form or measures, or were diagnosed with organic brain impairment. **Sample size:** 92 women were assessed for eligibility; 49 were randomised, and 44 were included in the analyses. **PTSD diagnosis:** 83.5% of women met full diagnosis for PTSD as measured by the CAPS, and 16.5% met the subthreshold definition. **SUD type and diagnosis:** Women were polydrug users. 87.8% met criteria for alcohol dependence prior to imprisonment, with another 4.1% meeting criteria for lifetime alcohol abuse. The percentages of women who had ever used a single substance at a level typically indicating dependence (10 or more times in 1 month) were 93.9% for cocaine, 75.5% for cannabis, 59.2% for heroin or other opioids, 38.8% for sedatives/hypnotics/anxiolytics, 30.6% for hallucinogens/PCP, and 26.5% for stimulants. **Mean age:** 34.6 (SD = 7.4) years **Gender:** 100% female **Ethnicity:** 23 (46.9%) white; 16 (32.7%) African American; 7 (14.2%) Hispanic; and 3 (6.1%) other races/ethnicities **Country:** USA
Interventions	**Group 1: Group-based Seeking Safety plus treatment as usual:** n = 27. Seeking Safety is a present-focused therapy to help people attain safety from trauma/PTSD and substance abuse. The treatment was designed for flexible use. SS is based on a number of key principles: safety, integrated treatment of both PTSD and substance abuse at the same time, a focus on ideals, and attention to clinician processes. Interventions are in the domain of cognitive, behavioural, interpersonal, and case management. Seeking Safety consists of 25 topics that can be conducted in any order: Introduction/Case Management, Safety, PTSD: Taking Back Your Power, When Substances Control You, Honesty, Asking for Help, Setting Boundaries in Relationships, Getting Others to Support Your Recovery, Healthy Relationships, Community Resources, Compassion, Creating Meaning, Discovery, Integrating the Split Self, Recovery Thinking, Taking Good Care of Yourself, Commitment, Respecting Your Time, Coping with Triggers, Self-Nurturing, Red and Green Flags, Detaching from Emotional Pain (Grounding), Life Choices, and Termination. SS was conducted in group modality for 90 min, typically 3 times a week for 6 to 8 weeks while the women were in prison, with 3 to 5 women per group. After release from prison, each woman in SS was offered weekly individual 60-min “booster” sessions for 12 weeks to reinforce material from the group sessions. **Group 2: Treatment as usual:** n = 22. All women in this study were enrolled in a 28-bed residential substance use treatment program in the minimum-security wing (approximately 30 hours per week). Women typically attend this program for 3 to 6 months, depending on the length of their sentences. Substance use treatment was abstinence-oriented, focused on the 12-step model, and took place in a psycho-educational large-group format, with weekly individual case management and drug counselling. Psycho-educational groups included attention to women's health, domestic violence, affect management, relapse prevention, career exploration, anger management, and parenting, conduct-

Zlotnick 2009 *(Continued)*

	ed by the same clinicians who conducted the SS treatment. This program did not offer any treatment specifically for trauma. Prior to prison release, the women received case management services, although this discontinued once the women were released from prison. All women leaving prison were referred for further substance use treatment. **Experimental intervention modality:** Integrated
Outcomes	**PTSD:** CAPS; Trauma Symptom Checklist 40 **SUD:** ASI; TLFB **Treatment acceptability:** Treatment utilisation; CSQ; mean number of sessions attended **Other:** Brief Symptom Inventory; legal composite score of the ASI (for criminal activity) **Follow-up:** 12 weeks after the start of the program and 3 and 6 months following release from prison
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not reported
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants and personnel were not blinded to allocation
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study included data only from those who were available to follow-up. The number of women who did not provide data at follow-up was fairly small but slightly disproportionate to the SS group. We did not feel this difference was sufficient to have a clinically relevant impact on observed effect sizes
Selective reporting (reporting bias)	Unclear risk	Outcomes were reported as specified in the methodology section, but we were not able to identify a previously published protocol
Other bias	High risk	The authors acknowledge potential contamination of treatment and control conditions in the closed communal setting of a prison wing. Postrelease follow-up dose was not equivalent. Women in the SS group were offered up to 12 booster sessions on release from prison. Women in the control group were referred for further substance use treatment

AA: Alcoholics Anonymous
ACQ-Now: Alcohol Craving Questionnaire-Now
ASI: Addiction Severity Index
AUD: alcohol use disorder
BAI: Beck Anxiety Inventory
BDI: Beck Depression Inventory
CAPS: Clinician Administered PTSD Scale

CBT: cognitive behavioural therapy
CDIS-IV: Computerized Diagnostic Interview Schedule
CD-RISC-10: 10-item Connor-Davidson Resilience Scale
CGI: Clinical Global Impressions
CI: confidence interval
CIDI: Composite International Diagnostic Interview
CSQ: Client Satisfaction Questionnaire
DESNOS: Disorders of Extreme Stress Not Otherwise Specified
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition Text Revision
FREEDOM: self-regulation via Focusing (SOS: Slow down, Orient, Self-check); processing current traumatic stress reactions via Recognizing current triggers, Emotions, and cognitive Evaluations, and, strength-based reintegration by Defining core goals, identifying currently effective responses (Options), and affirming core values by Making positive contributions
GAIN: Global Appraisal of Individual Needs
HAQ: Helping Alliance Questionnaire
HDRS: Hamilton Depression Rating Scale
HLS: Healthy Lifestyles Sessions
IES-R: Impact of Events Scale-Revised
IPDE: International Personality Disorder Examination
IPV: interpersonal violence
ITT: intention-to-treat
HIV: human immunodeficiency virus
NA: Narcotics Anonymous
PACS: Penn Alcohol Craving Scale
PANAS: Positive and Negative Affect Schedule
PCL-C: PTSD Checklist-Civilian Version
PDS: Post-traumatic Stress Diagnostic Scale
PE: prolonged exposure
PSS-I: PTSD Symptom Scale-Interview
PSS-SR: PTSD Symptom Scale–Self-Report
PTCI: Post-traumatic Cognitions Inventory
PTSD: post-traumatic stress disorder
RCT: randomised controlled trial
SADQ: Severity of Alcohol Dependence Questionnaire
SD: standard deviation
SS: Seeking Safety
STAI: State-Trait Anxiety Inventory
SUD: substance use disorder
SUDS: Subjective Units of Distress
SUI: Substance Use Inventory
TAU: treatment as usual
TLFB: Timeline Followback Interview
VA: Veterans Affairs

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Brief 2013	Types of assessment: PTSD was not established through a formal and reliable means but through use of a self report instrument
Cucciare 2013	Types of assessment: PTSD was not established through a formal and reliable means but through use of a self report instrument
Forbes 2012	Types of participants: Less than 80% had SUD at baseline. We did obtain outcome data for a subgroup of participants in this study but decided that we could not include the study as participants who were identified as having an alcohol use disorder were not diagnosed through a clinician-administered assessment

Study	Reason for exclusion
Ford 2007	Types of assessment: PTSD was not established through a formal and reliable means but through use of a self report instrument
Ford 2011	Types of assessment: PTSD was not established through a formal and reliable means but through use of a self report instrument
Ghee 2009	Types of assessment: PTSD was not established through a formal and reliable means but through use of a self report instrument
Glasner-Edwards 2013	Types of assessment: PTSD was established in a subset of participants at 3 years' follow-up. PTSD was not established at baseline
Hien 2015	Type of intervention: The experimental intervention was pharmacological
Lynch 2012	Types of studies: Not a randomised controlled trial
McDevitt-Murphy 2014	Types of participants: Participants were included on the basis of screening for hazardous drinking. Alcohol use disorder was not diagnosed through a clinician-administered assessment
Meshberg-Cohen 2010	Types of participants: Less than 80% had PTSD at baseline. We were unable to obtain outcome data for the subset who did have PTSD
Perez-Dandieu 2014	Types of assessment: PTSD was not established through a formal and reliable means but through use of a self report instrument
Rosen 2013	Type of intervention: Not a psychological therapy
Saladin 1995	Types of studies: Not a randomised controlled trial
Triffleman 2000	Types of participants: Less than 80% had PTSD at baseline. We were unable to obtain outcome data for the subset who did have PTSD
Triffleman 2001	A full report of this study is not yet available
van Dam 2013	Types of participants: Less than 80% of participants were diagnosed as having PTSD/SUD at baseline, and we were unable to obtain subset data

PTSD: post-traumatic stress disorder
SUD: substance use disorder

Characteristics of studies awaiting assessment *[ordered by study ID]*

Barrett 2015

Methods	Randomised controlled trial
Participants	Male prisoners with PTSD and comorbid substance use
Interventions	(Seeking Safety + TAU) vs TAU (alone)
Outcomes	SUDs, PTSD (acceptability, feasibility, and preliminary efficacy of Seeking Safety among male Australian prisoners)

Barrett 2015 *(Continued)*

Notes	Does not meet 80% PTSD threshold but does meet other criteria. I will approach the author for subset data

McGovern 2015

Methods	Randomised controlled trial
Participants	Outpatients in addiction services with PTSD and SUDs
Interventions	Cognitive behavioural therapy vs individual addiction counselling vs TAU
Outcomes	Primary outcomes: PTSD symptom severity (CAPS score); Drug and alcohol symptom severity (ASI-Self Administered); Frequency of substance use (TLFB Interview); Positive toxicology screens (urine drug screen and breathalyser).
Notes	Study reports not retrieved in March 2015 search results (first added to CCDANCTR 29 July 2015, via an OVID PsycINFO alert)

Park 2012

Methods	Randomised controlled trial
Participants	A subset of 204 participants with PTSD were included in a cohort of 553 randomised participants with co-occurring addiction and mental disorder
Interventions	Integrated chronic disease management vs primary care intervention
Outcomes	Abstinence, depression, anxiety
Notes	Conference abstract only (full study report not retrieved in March 2015 search results, added to CCDANCTR 13 April 2015, via PsycINFO OVID alert)

Perez-Dandieu 2015

Methods	Randomised controlled trial
Participants	Treatment of SUD in 7 women with SUD and PTSD comorbidity
Interventions	Effects of EMDR associated with ST 3-phase protocol: 1. Eight EMDR sessions focused on reprocessing traumatic memory; 2. Eight EMDR sessions (traumatic memory) associated with ST (traumatic attachment)

Perez-Dandieu 2015 *(Continued)*

	3. Eight EMDR sessions (addictive memory) associated with ST
Outcomes	PTSD, SUDs, and attachment disorder
Notes	Conference abstract only, full study report not yet available

Simpson 2011

Methods	Randomised controlled trial
Participants	84 individuals with current PTSD and alcohol dependence were randomised
Interventions	Experiential acceptance vs cognitive restructuring vs attention placebo
Outcomes	71 participants completed the study (84.5%); 13 of the 84 were lost to follow-up. PTSD and alcohol-related outcomes were not reported in the conference abstract.
Notes	Report of primary outcomes identified later (Stappenbeck 2015), added to CCDANCTR 13 April 2015, via a PsycINFO OVID alert dated 25 March 2015) Contact with trialists Tracey Simpson and Cindy Stappenbeck, confirmed this was the same trial as NCT00760994

Skidmore 2013

Methods	Randomised controlled trial
Participants	145 individuals with co-occurring alcohol or substance dependence, depression, and trauma exposure were randomised
Interventions	Integrated cognitive behavioural therapy (ICBT) for co-occurring depression and addiction plus cognitive processing therapy vs ICBT for co-occurring depression and addiction plus continuation of ICBT
Outcomes	Group assignment (ICBT vs CPT) was not related to attendance. PTSD and alcohol-related outcomes were not reported in abstract
Notes	Conference abstract, full study report not yet available

Wolf 2015

Methods	Randomised and non-randomised participants
Participants	Incarcerated men with PTSD and SUDs, housed at a high-security prison operated by the Pennsylvania Department of Corrections
Interventions	Integrated group therapy: Seeking Safety vs Men's Trauma Recovery and Empowerment Model vs wait-list control
Outcomes	Primary outcomes:

Wolf 2015 *(Continued)*

	PTSD Checklist-Civilian Version, CAPS, Global Severity Index, Brief Symptom Inventory
Notes	This study meets most of our inclusion criteria. However, it includes both randomised and non-randomised participants. We would need to determine whether we could obtain data for randomised participants only

ASI: Addiction Severity Index
CAPS: Clinician Administered PTSD Scale
EMDR: eye movement desensitisation and reprocessing
PTSD: post-traumatic stress disorder
ST: schema therapy
SUD: substance use disorder
TAU: treatment as usual
TLFB: Timeline Followback Interview

Characteristics of ongoing studies *[ordered by study ID]*

DRKS00004288

Trial name or title	Cognitive-behavioral treatment for female patients with PTSD and SUD
Methods	Multicentre randomised controlled trial
Participants	342 females with PTSD and SUD
Interventions	Seeking Safety (14 sessions) vs structured relapse prevention vs TAU
Outcomes	PTSD symptoms, substance use
Starting date	October 2012
Contact information	Ingo Schäfer: ischafer@uke.de
Notes	

NCT00946322

Trial name or title	Couple-based treatment for alcohol use disorders and post-traumatic stress disorder (CTAP)
Methods	Randomised controlled trial
Participants	Veterans meeting current DSM-IV diagnosis for alcohol abuse or dependence and PTSD
Interventions	TAU vs couple-based treatment for alcohol use disorders and PTSD
Outcomes	Number of days drinking or using drugs; problems related to drinking or using drugs; PTSD; couple relationship adjustment; number of days of heavy drinking or using drugs (outcome measures not specified)
Starting date	August 2010
Contact information	Jeremiah A Schumm: Jeremiah.Schumm@va.gov
Notes	

NCT01029197

Trial name or title	Multicomponent cognitive behavioral therapy (CBT) for posttraumatic stress disorder (PTSD) and substance abuse (PTSD/SUD)
Methods	Pilot randomised controlled trial
Participants	Participants will be 50 volunteer adults with PTSD, SUD, and serious mental illness who are receiving services at the Freedom House Recovery Center, served through the Orange Person Chatham Area Program
Interventions	Group and individual CBT and exposure therapy for PTSD
Outcomes	Clinician Administered PTSD Scale, Addiction Severity Index
Starting date	August 2009
Contact information	Karen Cusack: Karen.cusack@va.gov
Notes	

NCT01186315

Trial name or title	Post-traumatic stress disorder (PTSD), addiction, and virtual reality
Methods	Randomised controlled trial
Participants	Military veterans, National Guardsmen, and reservists with PTSD and problems with addiction
Interventions	Prolonged exposure vs prolonged exposure plus virtual reality-based exposure to cues for marijuana, cocaine, heroin, cigarette, and/or alcohol use, and phone-based reminders of learning (extinction reminders) to virtual reality exposure
Outcomes	Acceptibility, change in PTSD symptoms, change in substance use
Starting date	December 2008
Contact information	Zachary Rosenthal, Duke University
Notes	

NCT01211106

Trial name or title	Integrated vs sequential treatment for PTSD and addiction among OEF/OIF veterans
Methods	Randomised controlled trial
Participants	Male or female Persian Gulf-era veterans (18 to 65 years old). Current diagnosis of PTSD (symptom duration > 3 months) with clinically significant trauma-related symptoms, as indicated by a score of at least 50 on the PTSD Checklist.

NCT01211106 *(Continued)*

	Current abuse or dependence on alcohol, stimulants such as cocaine, opioids, including prescription opioids or benzodiazepines.
Interventions	Prolonged exposure vs motivational enhancement therapy
Outcomes	Substance use and PTSD symptoms
Starting date	February 2011
Contact information	David W. Oslin: oslin@upenn.edu
Notes	

NCT01274741

Trial name or title	Pilot study of an integrated exposure-based model for posttraumatic stress disorder and substance use disorder
Methods	Randomised controlled trial
Participants	Individuals meeting DSM-IV criteria for current PTSD and current SUD
Interventions	Integrated psychotherapy for PTSD/SUD ("Creating Change") vs modified TAU
Outcomes	Change in substance use from baseline to 3 months' post-treatment measured via urine drug screens and the Addiction Severity Index composite scores; change in PTSD symptoms from baseline to 3 months' post-treatment assessed using the PTSD Checklist and the Clinician Administered PTSD Scale
Starting date	January 2011
Contact information	Lisa Najavits: Lnajavits@hms.harvard.edu
Notes	

NCT01338506

Trial name or title	Integrated treatment of Operation Enduring Freedom/Operation Iraqi Freedom veterans with posttraumatic stress disorder and substance use disorders
Methods	Randomised controlled trial
Participants	Adult male and female active-duty Operation Iraqi Freedom (OIF)/Operation Enduring Freedom (OEF) military personnel and separated OIF/OEF veterans aged 18 to 65 years
Interventions	Concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE) vs TAU
Outcomes	Clinician Administered PTSD Scale; reduction of substance use or abstinence
Starting date	April 2011
Contact information	Sudie E. Back: backs@musc.edu

NCT01338506 *(Continued)*

Notes	

NCT01357577

Trial name or title	Cognitive behavioral therapy (CBT) for PTSD in veterans with co-occurring SUDs
Methods	Randomised controlled trial
Participants	Veterans with a current SUD diagnosis, scoring at least 45 on the Clinician Administered PTSD Scale
Interventions	CBT plus TAU vs TAU
Outcomes	PTSD symptom severity will be measured by the Clinician Administered PTSD Scale. Other measures not provided
Starting date	October 2012
Contact information	Liz Forshay: elizabeth.forshay@va.gov
Notes	

NCT01365247

Trial name or title	Concurrent treatment for substance dependent individuals with post-traumatic stress disorder (PTSD)
Methods	Randomised controlled trial
Participants	Participants must meet DSM-IV criteria for current or past substance dependence and current PTSD
Interventions	Concurrent treatment of PTSD and substance use disorders using prolonged exposure (COPE) and relapse prevention therapy vs a delayed-treatment control group
Outcomes	PTSD symptom severity, substance use severity, global psychiatric symptom severity, treatment retention and compliance
Starting date	September 2008
Contact information	Teresa Lopez-Castro: lopezcastro.phd.ccny@gmail.com; Lesia Ruglass: lmr2146@columbia.edu
Notes	

NCT01457404

Trial name or title	Integrated cognitive behavioral therapy for co-occurring PTSD and substance use disorders
Methods	Randomised controlled trial

NCT01457404 *(Continued)*

Participants	OEF/OIF/OND Veteran status with a diagnosis of PTSD (confirmed by the Clinician Administered PTSD Scale with a total symptom score of 44 or more) and a diagnosis of a SUD (abuse or dependence) (confirmed by the Structured Clinical Interview for DSM-IV Section E)
Interventions	Integrated cognitive behavioural therapy vs TAU
Outcomes	Decrease from baseline in Clinician Administered PTSD Scale score (PTSD symptom severity) at 3 and 6 months. Reduction from baseline in substance use severity (Addiction Severity Index) at 3 and 6 months.
Starting date	February 2011
Contact information	Mark McGovern: mark.p.mcgovern@dartmouth.edu
Notes	

NCT01597856

Trial name or title	Evaluation and treatment of substance abuse in veterans with PTSD disability claims
Methods	Randomised controlled trial
Participants	Veteran of OEF or OIF enrolling for compensation and pension for PTSD
Interventions	Screening, brief intervention, and referral to treatment (SBIRT) vs no additional treatment
Outcomes	Treatment attendance, substance use, days of alcohol use, PTSD
Starting date	March 2013
Contact information	Marc Rosen: marc.rosen@va.gov
Notes	

NCT01663337

Trial name or title	Sequence of symptom change during AUD (alcohol use or dependence) or PTSD (posttraumatic stress disorder) treatment for comorbid PTSD/AUD
Methods	Randomised controlled trial
Participants	Adults ≥ 18 years of age with a current DSM-V diagnosis of alcohol abuse/dependence and PTSD
Interventions	Cognitive processing therapy vs relapse prevention therapy vs assessment only
Outcomes	Primary outcomes: Reduction in PTSD symptom severity (Clinician Administered PTSD Scale) Reduction in alcohol consumption (Form 90 (Alcohol Consumption))
Starting date	March 2013

NCT01663337 *(Continued)*

Contact information	Debra Kaysen: dkaysen@u.washington.edu
Notes	

NCT01693978

Trial name or title	Contingency outcomes in prolonged exposure (COPE)
Methods	Randomised controlled trial
Participants	Participants must meet DSM-IV criteria for SUD and current PTSD
Interventions	Prolonged exposure with contingency management vs prolonged exposure
Outcomes	Prolonged exposure attendance, PTSD symptoms, drug use
Starting date	September 2012
Contact information	Jessica Peirce, Johns Hopkins University
Notes	

NCT01849029

Trial name or title	Cognitive processing intervention for HIV/STI and substance use among native women
Methods	Randomised controlled trial
Participants	Sexually active women with current substance use and PTSD (score 30 or hire on the PTSD Check-list)
Interventions	Cognitive processing therapy vs wait-list control
Outcomes	Primary outcome: PTSD Symptom Scale-Interview
Starting date	October 2013
Contact information	Cynthia Pearson: pearsonc@u.washington.edu
Notes	

NCT02081417

Trial name or title	Patient-centered trauma treatment (PaCTT)
Methods	Randomised controlled trial
Participants	Meet DSM-IV diagnostic criteria for lifetime and current full or subthreshold PTSD and DSM-IV diagnostic criteria for current substance abuse or dependence

NCT02081417 *(Continued)*

Interventions	Peer-led Seeking Safety group vs clinician-led Seeking Safety group
Outcomes	PTSD severity as indexed by the PTSD Checklist, change in substance use as indexed by the Addiction Severity Index
Starting date	October 2013
Contact information	Annette Crisanti: acrsanti@salud.unm.edu
Notes	

NCT02335125

Trial name or title	A policy relevant US trauma care system pragmatic trial for PTSD and comorbidity pilot (TSOS 6)
Methods	Randomised controlled trial
Participants	Inclusion criteria: Inpatient/emergency admission for traumatic injury (The goal of this pilot study is to develop and implement a larger-scale, multisite, stepped collaborative care trial that targets injured patients with presentations of PTSD and related comorbidity)
Interventions	The intervention aims to prevent the development of chronic PTSD and depressive symptoms, alcohol use problems, and enduring physical disability in survivors of both traumatic brain and non-traumatic brain injuries
Outcomes	Primary outcomes: PTSD Checklist-Civilian Version at 1 month; Alcohol Use Disorders Identification Test at 1 month; Patient Health Questionnaire 9-item Depression Scale at 1 month
Starting date	February 2015
Contact information	Douglas Zatzick: dzatzick@u.washington.edu
Notes	

NTR3084

Trial name or title	A study on the effectiveness of the cognitive behavioral therapy "Seeking Safety" in reducing trauma and addiction related symptoms in a Dutch substance-use disorder population
Methods	Randomised controlled trial
Participants	Outpatients from substance misuse services with active symptoms of PTSD in the past 6 months
Interventions	Seeking Safety vs TAU
Outcomes	The primary outcome measure will be substance use severity. Secondary outcome measures are PTSD and trauma symptoms, coping skills, functioning, and cognitions
Starting date	January 2012
Contact information	Tim Kok: t.kok@tactus.nl

NTR3084 *(Continued)*

Notes

AUD: alcohol use disorder
CBT: cognitive behavioural therapy
DSM: Diagnostic and Statistical Manual of Mental Disorders
OEF/OIF/OND: Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn
PTSD: post-traumatic stress disorder
SUD: substance use disorder
TAU: treatment as usual

DATA AND ANALYSES

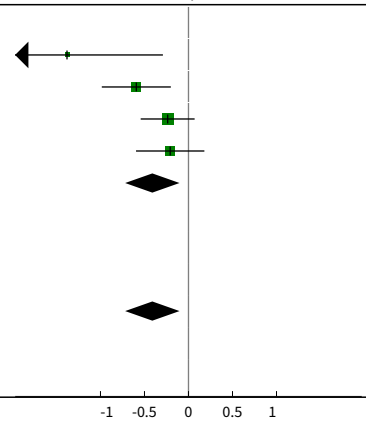
Comparison 1. Trauma-focused psychological therapy vs control therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD severity following treatment completion	4	405	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.72, -0.10]
1.1 Individual intervention	4	405	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.72, -0.10]
2 PTSD severity 3-4 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 PTSD severity 5-7 months following treatment completion	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.34 [-0.58, -0.10]
3.1 Individual intervention	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.34 [-0.58, -0.10]
4 Drug or alcohol use, or both following treatment completion	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.41, 0.15]
4.1 Individual intervention	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.13 [-0.41, 0.15]
5 Drug or alcohol use, or both 3-4 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Drug or alcohol use, or both 5-7 months following treatment completion	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.48, -0.07]
6.1 Individual intervention	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.28 [-0.48, -0.07]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Treatment completers	3	316	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.64, 0.96]
7.1 Individual intervention	3	316	Risk Ratio (M-H, Random, 95% CI)	0.78 [0.64, 0.96]
8 PTSD diagnosis following treatment completion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1 Individual intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Adverse events			Other data	No numeric data
9.1 Individual intervention			Other data	No numeric data
10 Adverse events	2	268	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.34, 1.90]
10.1 Individual intervention	2	268	Risk Ratio (M-H, Random, 95% CI)	0.81 [0.34, 1.90]
11 Mean number of sessions attended for intervention group			Other data	No numeric data
11.1 Studies including intervention for SUD			Other data	No numeric data
12 Sensitivity analysis: PTSD severity following treatment completion	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-0.56, -0.10]
12.1 Individual intervention	3	388	Std. Mean Difference (IV, Random, 95% CI)	-0.33 [-0.56, -0.10]

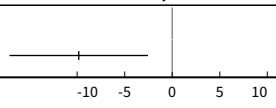
Analysis 1.1. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 1 PTSD severity following treatment completion.

Study or subgroup	Trauma focused int N	Trauma focused int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.1.1 Individual intervention							
Coffey 2006	8	24.1 (13.1)	9	45 (15.4)		7%	-1.38[-2.47,-0.29]
Coffey submitted	82	34 (22.3)	38	47 (20.5)		28.8%	-0.59[-0.98,-0.2]
Foa 2013	80	12.8 (12.4)	85	15.4 (9.9)		35.14%	-0.24[-0.54,0.07]
Mills 2012	55	67.9 (29.3)	48	73.4 (22.7)		29.06%	-0.21[-0.6,0.18]
Subtotal ***	**225**		**180**			**100%**	**-0.41[-0.72,-0.1]**
Heterogeneity: Tau^2=0.05; Chi^2=5.93, df=3(P=0.11); I^2=49.44%							
Test for overall effect: Z=2.61(P=0.01)							
Total ***	**225**		**180**			**100%**	**-0.41[-0.72,-0.1]**
Heterogeneity: Tau^2=0.05; Chi^2=5.93, df=3(P=0.11); I^2=49.44%							
Test for overall effect: Z=2.61(P=0.01)							



Analysis 1.2. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 2 PTSD severity 3-4 months following treatment completion.

Study or subgroup	Trauma focused int N	Mean(SD)	Control int N	Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.2.1 Individual intervention						
Coffey submitted	82	15.6 (19.6)	38	25.4 (18.6)		-9.83[-17.11,-2.55]



Analysis 1.3. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 3 PTSD severity 5-7 months following treatment completion.

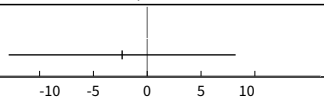
Study or subgroup	Trauma focused int N	Mean(SD)	Control int N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.3.1 Individual intervention							
Coffey submitted	82	15.6 (19.6)	38	25.4 (18.6)		29.3%	-0.51[-0.9,-0.12]
Foa 2013	80	9.4 (13)	85	11 (10.7)		41.66%	-0.14[-0.44,0.17]
Mills 2012	55	52.9 (33.9)	48	67.2 (27.6)		29.04%	-0.46[-0.85,-0.06]
Subtotal ***	**217**		**171**			**100%**	**-0.34[-0.58,-0.1]**
Heterogeneity: Tau^2=0.01; Chi^2=2.7, df=2(P=0.26); I^2=26.01%							
Test for overall effect: Z=2.76(P=0.01)							
Total ***	**217**		**171**			**100%**	**-0.34[-0.58,-0.1]**
Heterogeneity: Tau^2=0.01; Chi^2=2.7, df=2(P=0.26); I^2=26.01%							
Test for overall effect: Z=2.76(P=0.01)							

Analysis 1.4. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 4 Drug or alcohol use, or both following treatment completion.

Study or subgroup	Trauma focused int N	Mean(SD)	Control int N	Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.4.1 Individual intervention							
Coffey submitted	82	104.5 (58.1)	38	117.2 (54.1)		30.62%	-0.22[-0.61,0.16]
Foa 2013	80	10.4 (21.1)	85	8.4 (16.3)		39.17%	0.1[-0.2,0.41]
Mills 2012	55	2.5 (2.7)	48	3.4 (2.5)		30.2%	-0.35[-0.74,0.04]
Subtotal ***	**217**		**171**			**100%**	**-0.13[-0.41,0.15]**
Heterogeneity: Tau^2=0.03; Chi^2=3.63, df=2(P=0.16); I^2=44.95%							
Test for overall effect: Z=0.94(P=0.35)							
Total ***	**217**		**171**			**100%**	**-0.13[-0.41,0.15]**
Heterogeneity: Tau^2=0.03; Chi^2=3.63, df=2(P=0.16); I^2=44.95%							
Test for overall effect: Z=0.94(P=0.35)							

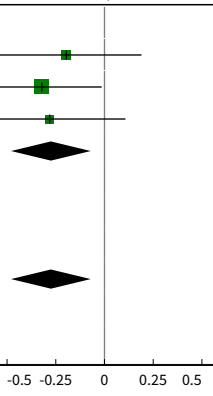
Analysis 1.5. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 5 Drug or alcohol use, or both 3-4 months following treatment completion.

Study or subgroup	Trauma focused int N	Trauma focused int Mean(SD)	Control int N	Control int Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
1.5.1 Individual intervention						
Coffey submitted	82	95.4 (28.5)	38	97.7 (26.9)		-2.33[-12.87,8.21]



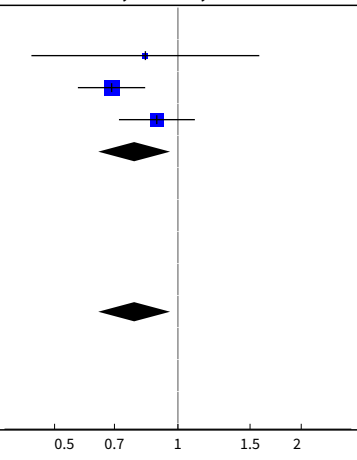
Analysis 1.6. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 6 Drug or alcohol use, or both 5-7 months following treatment completion.

Study or subgroup	Trauma focused int N	Trauma focused int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.6.1 Individual intervention							
Coffey submitted	82	89.5 (27.1)	38	94.8 (26.5)		28.13%	-0.2[-0.58,0.19]
Foa 2013	80	13.9 (25.9)	85	24.4 (38.1)		44.26%	-0.32[-0.63,-0.01]
Mills 2012	55	2.3 (2.6)	48	3 (2.5)		27.61%	-0.28[-0.67,0.11]
Subtotal ***	**217**		**171**			**100%**	**-0.28[-0.48,-0.07]**
Heterogeneity: Tau^2=0; Chi^2=0.25, df=2(P=0.88); I^2=0%							
Test for overall effect: Z=2.64(P=0.01)							
Total ***	**217**		**171**			**100%**	**-0.28[-0.48,-0.07]**
Heterogeneity: Tau^2=0; Chi^2=0.25, df=2(P=0.88); I^2=0%							
Test for overall effect: Z=2.64(P=0.01)							



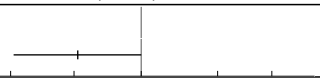
Analysis 1.7. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 7 Treatment completers.

Study or subgroup	Control int n/N	Trauma focused int n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.7.1 Individual intervention					
Coffey 2006	8/16	9/15		8.89%	0.83[0.44,1.58]
Coffey submitted	52/82	35/38		47.93%	0.69[0.57,0.83]
Foa 2013	51/80	61/85		43.18%	0.89[0.72,1.1]
Subtotal (95% CI)	**178**	**138**		**100%**	**0.78[0.64,0.96]**
Total events: 111 (Control int), 105 (Trauma focused int)					
Heterogeneity: Tau^2=0.01; Chi^2=3.41, df=2(P=0.18); I^2=41.26%					
Test for overall effect: Z=2.39(P=0.02)					
Total (95% CI)	**178**	**138**		**100%**	**0.78[0.64,0.96]**
Total events: 111 (Control int), 105 (Trauma focused int)					
Heterogeneity: Tau^2=0.01; Chi^2=3.41, df=2(P=0.18); I^2=41.26%					
Test for overall effect: Z=2.39(P=0.02)					



Analysis 1.8. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 8 PTSD diagnosis following treatment completion.

Study or subgroup	Trauma focused int n/N	Control int n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.8.1 Individual intervention				
Coffey submitted	37/82	24/38		0.71[0.51,1]

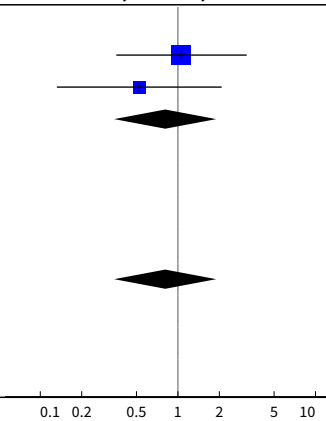


Analysis 1.9. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 9 Adverse events.

Study	Adverse events
Individual intervention	
Coffey 2006	Not reported
Coffey submitted	Not reported
Foa 2013	Twelve participants were removed from the study because of serious adverse events (serious suicidal ideation, n = 7; serious medical illness, n = 3; psychotic symptoms, n = 1; death, n = 1; however, none of these events was determined to be related to the study).
Mills 2012	Two participants from the treatment group (3.6%) and 5 participants from the control group (10.4%) attempted suicide during the study (OR, 0.32 [95% CI, 0.06-1.76]). Although it is possible that these attempts were related to participation in the study, all 7 individuals reported that this was not the case and elected to remain involved with the study. Additionally, 1 participant from the treatment group (1.8%) died as a result of a preexisting medical condition.

Analysis 1.10. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 10 Adverse events.

Study or subgroup	Trauma focused int n/N	Control int n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.10.1 Individual intervention					
Foa 2013	6/80	6/85		61.53%	1.06[0.36,3.16]
Mills 2012	3/55	5/48		38.47%	0.52[0.13,2.08]
Subtotal (95% CI)	**135**	**133**		**100%**	**0.81[0.34,1.9]**
Total events: 9 (Trauma focused int), 11 (Control int)					
Heterogeneity: Tau^2=0; Chi^2=0.62, df=1(P=0.43); I^2=0%					
Test for overall effect: Z=0.49(P=0.63)					
Total (95% CI)	**135**	**133**		**100%**	**0.81[0.34,1.9]**
Total events: 9 (Trauma focused int), 11 (Control int)					
Heterogeneity: Tau^2=0; Chi^2=0.62, df=1(P=0.43); I^2=0%					
Test for overall effect: Z=0.49(P=0.63)					



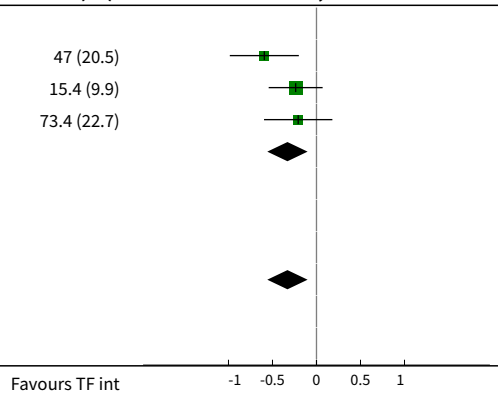
Analysis 1.11. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 11 Mean number of sessions attended for intervention group.

Study	Mean number of sessions attended for intervention group: Mean number sessions attended by intervention group (& SD)	Number sessions available	Percentage attended
Studies including intervention for SUD			

Study	Mean number of sessions attended for intervention group: Mean number sessions attended by intervention group (& SD)	Number sessions available	Percentage attended
Coffey submitted	8.16 (3.26) approximated	12	68.0%
Foa 2013	6.33 (5.31)	18	35.2%
Mills 2012	5.83 (4.94)	13	44.9%

Analysis 1.12. Comparison 1 Trauma-focused psychological therapy vs control therapy, Outcome 12 Sensitivity analysis: PTSD severity following treatment completion.

Study or subgroup	Trauma focused int N	Trauma focused int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1.12.1 Individual intervention							
Coffey submitted	82	34 (22.3)	38	47 (20.5)		28.57%	-0.59[-0.98,-0.2]
Foa 2013	80	12.8 (12.4)	85	15.4 (9.9)		42.39%	-0.24[-0.54,0.07]
Mills 2012	55	67.9 (29.3)	48	73.4 (22.7)		29.05%	-0.21[-0.6,0.18]
Subtotal ***	**217**		**171**			**100%**	**-0.33[-0.56,-0.1]**
Heterogeneity: Tau^2=0.01; Chi^2=2.46, df=2(P=0.29); I^2=18.7%							
Test for overall effect: Z=2.82(P=0)							
Total ***	**217**		**171**			**100%**	**-0.33[-0.56,-0.1]**
Heterogeneity: Tau^2=0.01; Chi^2=2.46, df=2(P=0.29); I^2=18.7%							
Test for overall effect: Z=2.82(P=0)							



Comparison 2. Trauma-focused psychological therapy vs active psychological therapy for SUD only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD severity following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
1.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
2 PTSD severity 5-7 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
2.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
3 PTSD severity 8-10 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Drug or alcohol use, or both following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
4.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 Drug or alcohol use, or both 5-7 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
6 Drug or alcohol use, or both 8-10 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
6.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
7 Treatment completers	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
7.1 Individual intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
8 PTSD diagnosis following treatment completion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1 Individual intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 SUD diagnosis following treatment completion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
9.1 Individual intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 2.1. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 1 PTSD severity following treatment completion.

Study or subgroup	Trauma focused int		Intervention for SUD only		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.1.1 Individual intervention						
Sannibale 2013	24	42.8 (26.5)	22	46.7 (26.3)		-3.91[-19.16,11.34]
				Favours TF int	-20 -10 0 10 20	Favours SUD only int

Analysis 2.2. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 2 PTSD severity 5-7 months following treatment completion.

Study or subgroup	Trauma focused int		Intervention for SUD only		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.2.1 Individual intervention						
Sannibale 2013	24	40.4 (23.5)	21	49.7 (22.9)		-9.32[-22.89,4.25]
				Favours TF int	-20 -10 0 10 20	Favours SUD only int

Analysis 2.3. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 3 PTSD severity 8-10 months following treatment completion.

Study or subgroup	Trauma focused int		Intervention for SUD only		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.3.1 Individual intervention						
Sannibale 2013	26	43.3 (28.3)	21	41.2 (34.2)		2.11[-16.1,20.32]
				Favours TF int	-50 -25 0 25 50	Favours SUD only int

Analysis 2.4. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 4 Drug or alcohol use, or both following treatment completion.

Study or subgroup	Trauma focused int		Intervention for SUD only		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.4.1 Individual intervention						
Sannibale 2013	24	7.5 (5.2)	22	8.7 (9.5)		-1.27[-5.76,3.22]
				Favours TF int	-20 -10 0 10 20	Favours SUD only int

Analysis 2.5. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 5 Drug or alcohol use, or both 5-7 months following treatment completion.

Study or subgroup	Trauma focused int		Intervention for SUD only		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.5.1 Individual intervention						
Sannibale 2013	24	8.8 (5.9)	21	6.9 (6.2)		1.9[-1.65,5.45]
				Favours TF int	-20 -10 0 10 20	Favours SUD only int

Analysis 2.6. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 6 Drug or alcohol use, or both 8-10 months following treatment completion.

Study or subgroup	Trauma focused int		Intervention for SUD only		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
2.6.1 Individual intervention						
Sannibale 2013	26	7 (4.2)	21	7.9 (6.2)		-0.93[-4.04,2.18]
				Favours TF int	-20 -10 0 10 20	Favours SUD only int

Analysis 2.7. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 7 Treatment completers.

Study or subgroup	Trauma focused int	Intervention for SUD only	Risk Ratio	Risk Ratio
	n/N	n/N	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
2.7.1 Individual intervention				
Sannibale 2013	24/33	21/29		1[0.74,1.36]
		Favours SUD only int	1	Favours TF int

Analysis 2.8. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 8 PTSD diagnosis following treatment completion.

Study or subgroup	Trauma focused int n/N	Intervention for SUD only n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
2.8.1 Individual intervention				
Sannibale 2013	19/33	16/29		1.04[0.67,1.62]
		Favours TF int	0.5 0.7 1 1.5 2	Favours SUD only int

Analysis 2.9. Comparison 2 Trauma-focused psychological therapy vs active psychological therapy for SUD only, Outcome 9 SUD diagnosis following treatment completion.

Study or subgroup	Trauma focused int n/N	Intervention for SUD only n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
2.9.1 Individual intervention				
Sannibale 2013	25/33	19/29		1.16[0.83,1.6]
		Favours TF int	1	Favours SUD only int

Comparison 3. Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy

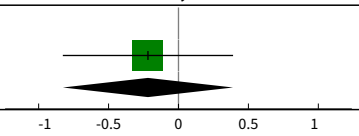
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD severity following treatment completion	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1 Individual intervention	1	44	Std. Mean Difference (IV, Random, 95% CI)	-0.22 [-0.83, 0.39]
1.2 Group intervention	4	513	Std. Mean Difference (IV, Random, 95% CI)	-0.02 [-0.19, 0.16]
2 PTSD severity 3-4 months following treatment completion	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 Individual intervention	1	44	Std. Mean Difference (IV, Random, 95% CI)	-0.25 [-0.86, 0.36]
2.2 Group intervention	4	499	Std. Mean Difference (IV, Random, 95% CI)	0.00 [-0.17, 0.18]
3 PTSD severity 5-7 months following treatment completion	5		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 Individual intervention	1	44	Std. Mean Difference (IV, Random, 95% CI)	-0.20 [-0.81, 0.41]
3.2 Group intervention	4	566	Std. Mean Difference (IV, Random, 95% CI)	-0.14 [-0.31, 0.03]

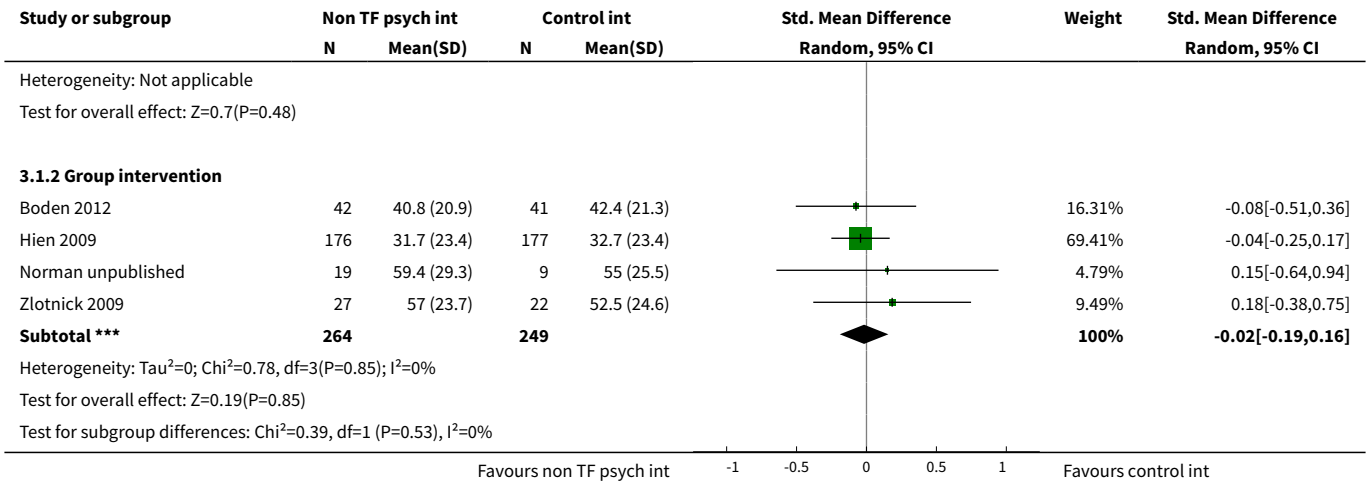
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 PTSD severity 12 months following treatment completion	2	518	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.25, 0.10]
4.1 Group intervention	2	518	Std. Mean Difference (IV, Random, 95% CI)	-0.07 [-0.25, 0.10]
5 Drug or alcohol use, or both following treatment completion	3	464	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.97, 0.14]
5.1 Group intervention	3	464	Std. Mean Difference (IV, Random, 95% CI)	-0.41 [-0.97, 0.14]
6 Drug or alcohol use, or both 3-4 months following treatment completion	4	499	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.40, 0.23]
6.1 Group intervention	4	499	Std. Mean Difference (IV, Random, 95% CI)	-0.08 [-0.40, 0.23]
7 Drug or alcohol use, or both 5-7 months following treatment completion	4	572	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.23, 0.11]
7.1 Group intervention	4	572	Std. Mean Difference (IV, Random, 95% CI)	-0.06 [-0.23, 0.11]
8 Drug or alcohol use, or both 12 months following treatment completion	2	528	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.15, 0.20]
8.1 Group intervention	2	528	Std. Mean Difference (IV, Random, 95% CI)	0.02 [-0.15, 0.20]
9 Treatment completers			Other data	No numeric data
9.1 Individual intervention			Other data	No numeric data
9.2 Group intervention			Other data	No numeric data
10 Treatment completers	2	381	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.88, 1.45]
10.1 Group intervention	2	381	Risk Ratio (M-H, Random, 95% CI)	1.13 [0.88, 1.45]
11 PTSD diagnosis following treatment completion	2	77	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.66, 1.54]
11.1 Group intervention	2	77	Risk Ratio (M-H, Random, 95% CI)	1.01 [0.66, 1.54]
12 Adverse events			Other data	No numeric data
12.1 Group intervention			Other data	No numeric data

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13 Study-related adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
13.1 Group intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
14 Mean number of sessions attended for intervention group			Other data	No numeric data
14.1 Group intervention			Other data	No numeric data
15 Mean number of sessions attended	2	381	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.59, 0.79]
15.1 Group intervention	2	381	Std. Mean Difference (IV, Random, 95% CI)	0.10 [-0.59, 0.79]
16 Sensitivity analysis: PTSD severity 5-7 months following treatment completion	3		Std. Mean Difference (IV, Random, 95% CI)	Subtotals only
16.1 Group intervention	3	425	Std. Mean Difference (IV, Random, 95% CI)	-0.12 [-0.34, 0.10]
17 Sensitivity analysis: PTSD severity 12 months following treatment completion	1	353	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.25, 0.17]
17.1 Group intervention	1	353	Std. Mean Difference (IV, Random, 95% CI)	-0.04 [-0.25, 0.17]
18 Sensitivity analysis: drug or alcohol use, or both 5-7 months following treatment completion	3	425	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.30, 0.08]
18.1 Group intervention	3	425	Std. Mean Difference (IV, Random, 95% CI)	-0.11 [-0.30, 0.08]
19 Sensitivity analysis: drug or alcohol use, or both 12 months following treatment completion	1	353	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.21, 0.21]
19.1 Group intervention	1	353	Std. Mean Difference (IV, Random, 95% CI)	0.0 [-0.21, 0.21]

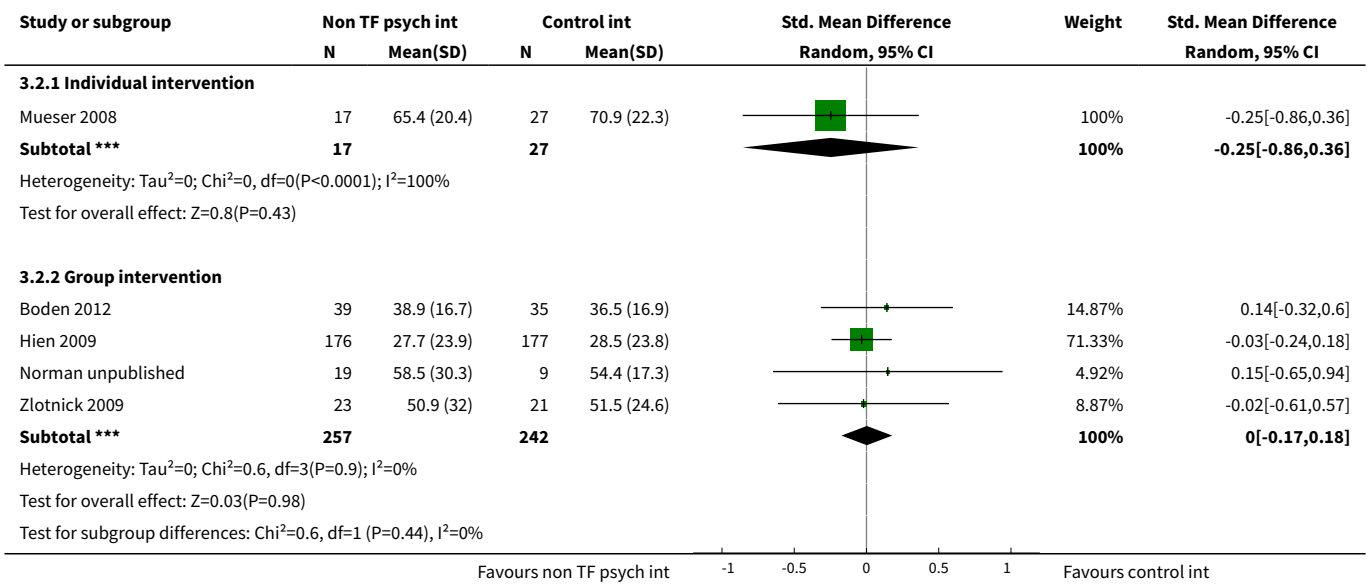
Analysis 3.1. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 1 PTSD severity following treatment completion.

Study or subgroup	Non TF psych int		Control int		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
3.1.1 Individual intervention							
Mueser 2008	17	68.1 (18.9)	27	72.4 (19.9)		100%	-0.22[-0.83,0.39]
Subtotal ***	**17**		**27**			**100%**	**-0.22[-0.83,0.39]**

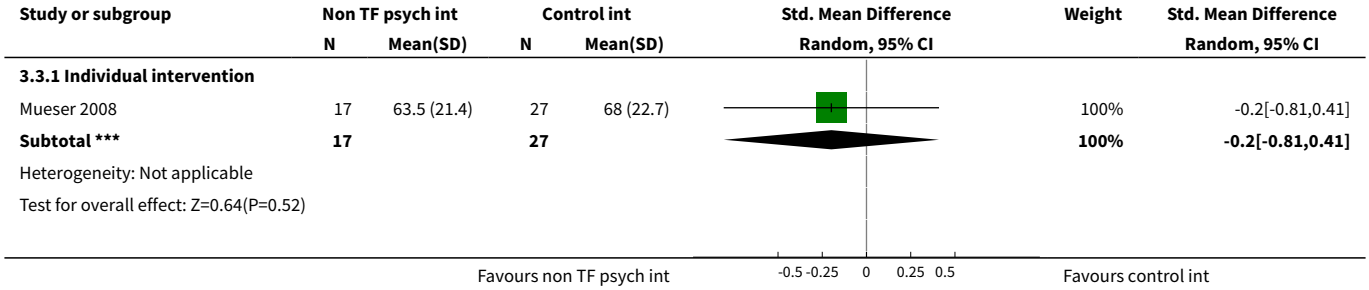


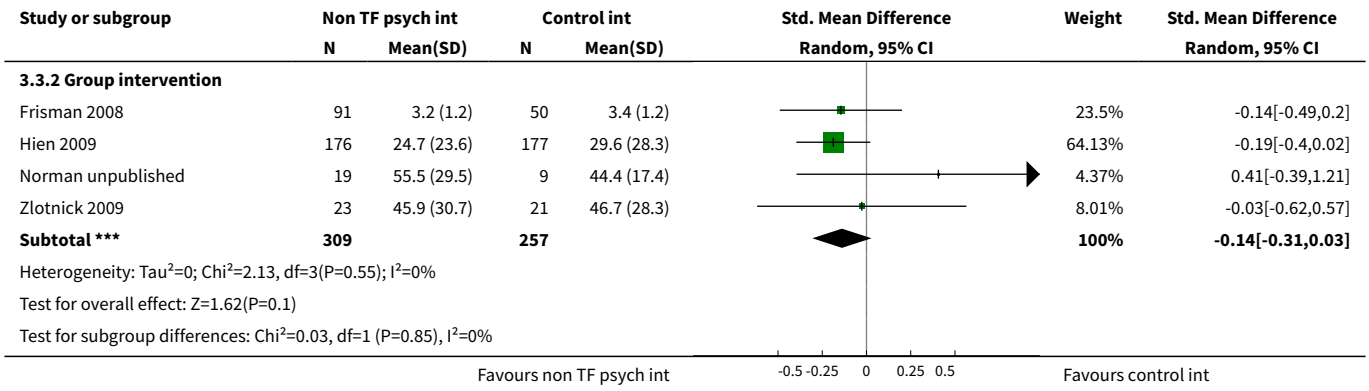


Analysis 3.2. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 2 PTSD severity 3-4 months following treatment completion.

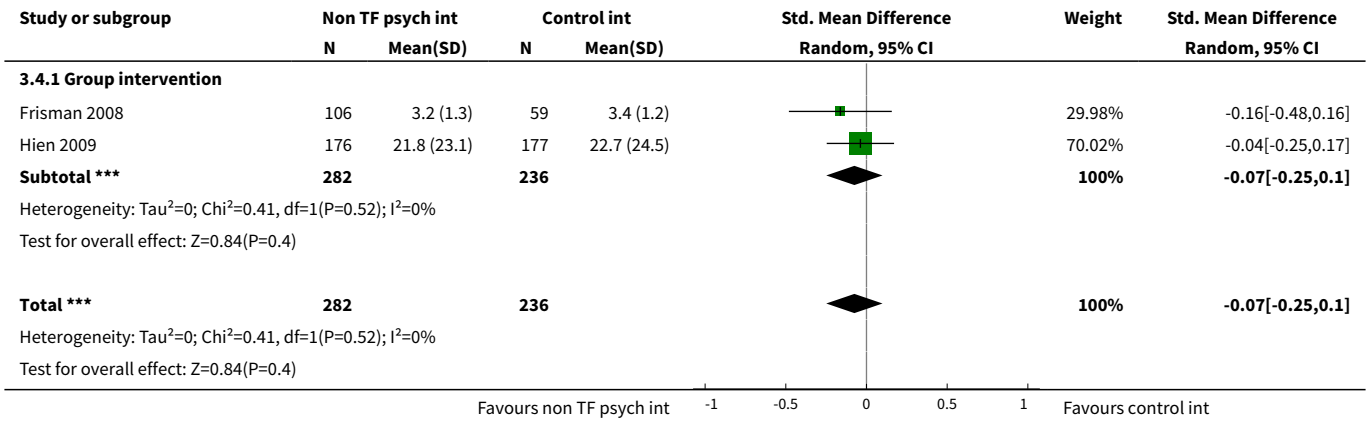


Analysis 3.3. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 3 PTSD severity 5-7 months following treatment completion.

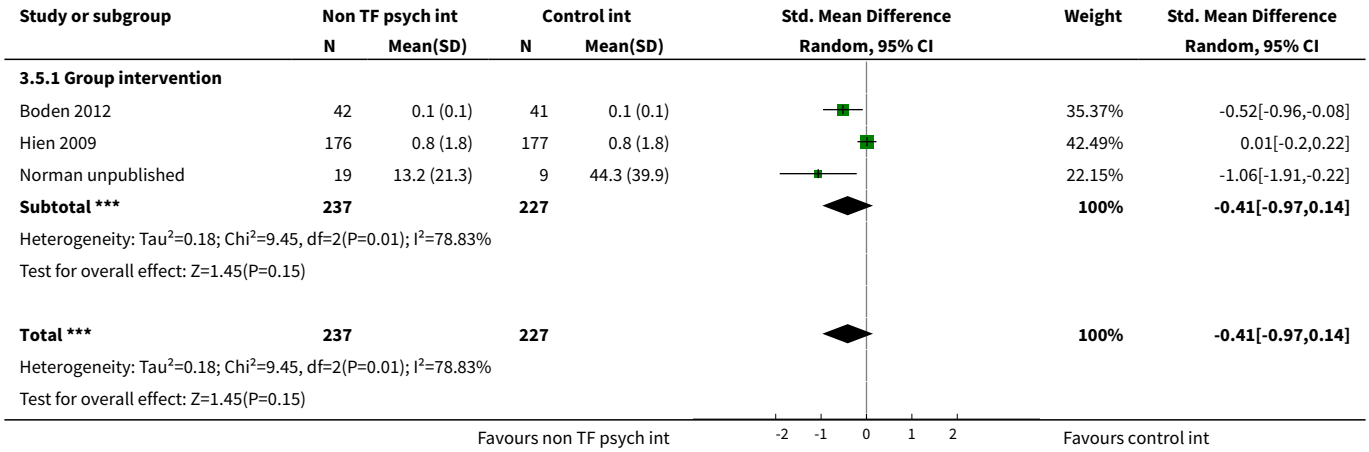




Analysis 3.4. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 4 PTSD severity 12 months following treatment completion.

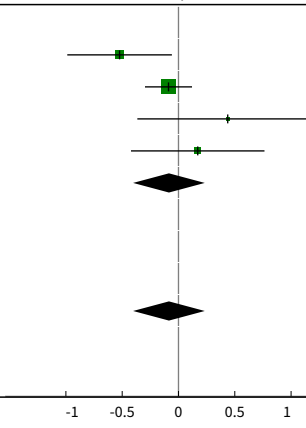


Analysis 3.5. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 5 Drug or alcohol use, or both following treatment completion.



Analysis 3.6. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 6 Drug or alcohol use, or both 3-4 months following treatment completion.

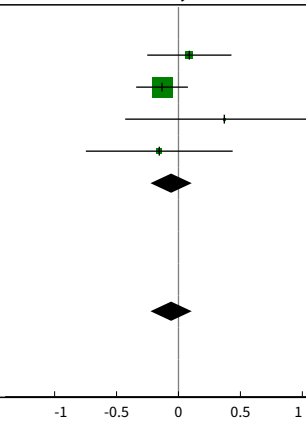
Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.6.1 Group intervention							
Boden 2012	39	0.1 (0.1)	35	0.1 (0.1)		25.14%	-0.52[-0.99,-0.06]
Hien 2009	176	1.1 (2.2)	177	1.3 (2.3)		43.86%	-0.09[-0.3,0.12]
Norman unpublished	19	44.8 (27.9)	9	31.4 (33.3)		12.19%	0.44[-0.37,1.24]
Zlotnick 2009	23	0.2 (0.1)	21	0.2 (0.1)		18.81%	0.17[-0.42,0.76]
Subtotal ***	**257**		**242**			**100%**	**-0.08[-0.4,0.23]**
Heterogeneity: Tau^2=0.05; Chi^2=5.72, df=3(P=0.13); I^2=47.57%							
Test for overall effect: Z=0.52(P=0.6)							
Total ***	**257**		**242**			**100%**	**-0.08[-0.4,0.23]**
Heterogeneity: Tau^2=0.05; Chi^2=5.72, df=3(P=0.13); I^2=47.57%							
Test for overall effect: Z=0.52(P=0.6)							



Favours non TF psych int — Favours control int

Analysis 3.7. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 7 Drug or alcohol use, or both 5-7 months following treatment completion.

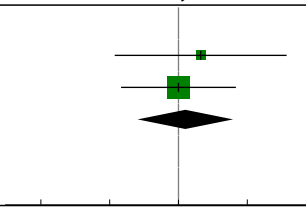
Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.7.1 Group intervention							
Frisman 2008	96	0.1 (0.1)	51	0 (0.1)		24.07%	0.09[-0.25,0.43]
Hien 2009	176	1.2 (2.1)	177	1.5 (2.4)		63.68%	-0.13[-0.34,0.08]
Norman unpublished	19	40.2 (28.8)	9	28.6 (34)		4.34%	0.37[-0.43,1.17]
Zlotnick 2009	23	0.2 (0.1)	21	0.2 (0.1)		7.91%	-0.16[-0.75,0.44]
Subtotal ***	**314**		**258**			**100%**	**-0.06[-0.23,0.11]**
Heterogeneity: Tau^2=0; Chi^2=2.4, df=3(P=0.49); I^2=0%							
Test for overall effect: Z=0.7(P=0.48)							
Total ***	**314**		**258**			**100%**	**-0.06[-0.23,0.11]**
Heterogeneity: Tau^2=0; Chi^2=2.4, df=3(P=0.49); I^2=0%							
Test for overall effect: Z=0.7(P=0.48)							



Favours non TF psych int — Favours control int

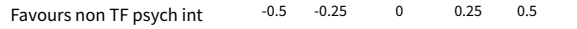
Analysis 3.8. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 8 Drug or alcohol use, or both 12 months following treatment completion.

Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.8.1 Group intervention							
Frisman 2008	115	0.1 (0.1)	60	0.1 (0.1)		30.87%	0.08[-0.23,0.39]
Hien 2009	176	1.7 (2.5)	177	1.7 (2.6)		69.13%	0[-0.21,0.21]
Subtotal ***	**291**		**237**			**100%**	**0.02[-0.15,0.2]**
Heterogeneity: Tau^2=0; Chi^2=0.18, df=1(P=0.67); I^2=0%							
Test for overall effect: Z=0.28(P=0.78)							



Favours non TF psych int — Favours control int

Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
Total * **	**291**		**237**			**100%**	**0.02[-0.15,0.2]**
Heterogeneity: Tau²=0; Chi²=0.18, df=1(P=0.67); I²=0%							
Test for overall effect: Z=0.28(P=0.78)							

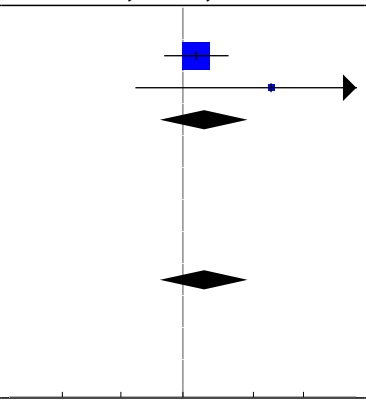


Analysis 3.9. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 9 Treatment completers.

Study	Treatment completers
Individual intervention	
Mueser 2008	12/16 (70.6%)
Group intervention	
Frisman 2008	39/141 (28%)

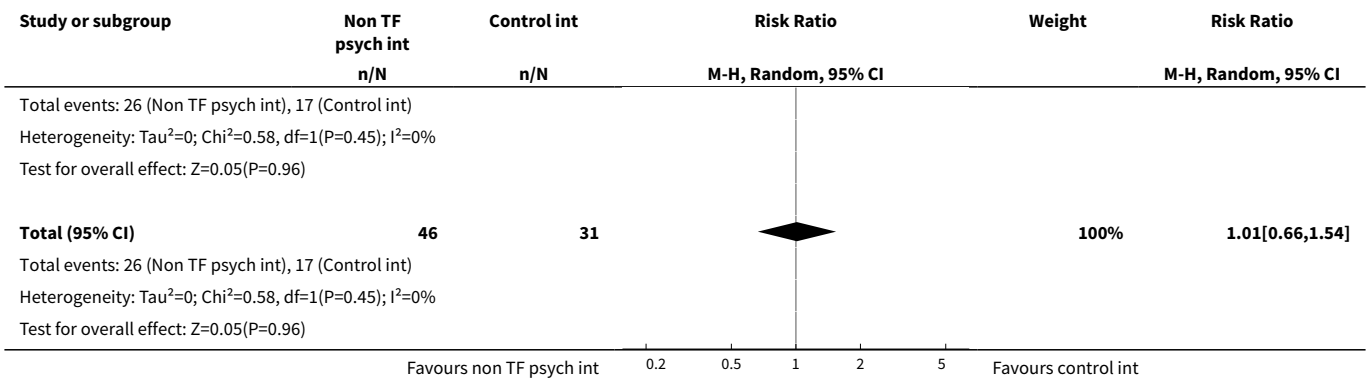
Analysis 3.10. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 10 Treatment completers.

Study or subgroup	Non TF psych int n/N	Control int n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
3.10.1 Group intervention					
Hien 2009	103/176	96/177		90.21%	1.08[0.9,1.3]
Norman unpublished	14/19	4/9		9.79%	1.66[0.76,3.61]
Subtotal (95% CI)	**195**	**186**		**100%**	**1.13[0.88,1.45]**
Total events: 117 (Non TF psych int), 100 (Control int)					
Heterogeneity: Tau²=0.01; Chi²=1.11, df=1(P=0.29); I²=10.07%					
Test for overall effect: Z=0.92(P=0.36)					
Total (95% CI)	**195**	**186**		**100%**	**1.13[0.88,1.45]**
Total events: 117 (Non TF psych int), 100 (Control int)					
Heterogeneity: Tau²=0.01; Chi²=1.11, df=1(P=0.29); I²=10.07%					
Test for overall effect: Z=0.92(P=0.36)					



Analysis 3.11. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 11 PTSD diagnosis following treatment completion.

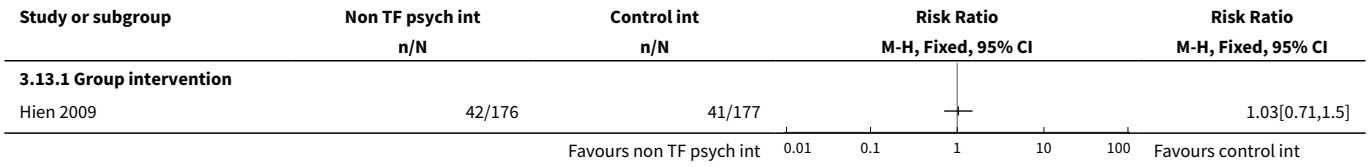
Study or subgroup	Non TF psych int n/N	Control int n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
3.11.1 Group intervention					
Norman unpublished	13/19	5/9		40.73%	1.23[0.64,2.38]
Zlotnick 2009	13/27	12/22		59.27%	0.88[0.51,1.52]
Subtotal (95% CI)	**46**	**31**		**100%**	**1.01[0.66,1.54]**



Analysis 3.12. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 12 Adverse events.

Study	Adverse events
Group intervention	
Boden 2012	No harmful or unintended effects were observed during the trial.
Frisman 2008	Not reported
Hien 2009	83 study related adverse events were identified (Killeen 2008). Of these 61 were rated as moderate to severe: 28 for the experimental condition; 33 for the control condition.
Najavits 2006a	Not reported
Norman unpublished	No adverse events occurred during the study.
Zlotnick 2009	Not reported

Analysis 3.13. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 13 Study-related adverse events.



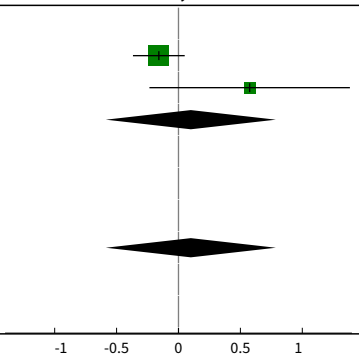
Analysis 3.14. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 14 Mean number of sessions attended for intervention group.

Study	Mean number of sessions attended for intervention group				
	Mean number treatment condition sessions attended by intervention group (& SD)	Number sessions available	Percentage active intervention sessions attended	Mean number sessions attended by control group (& SD)	Percentage attended
Group intervention					
Boden 2012	Not reported			Not reported	
Frisman 2008	**3.41 (3.38)** active intervention sessions + 30.67 (37.38) TAU sessions	9 active intervention sessions plus TAU sessions	37.9%	39.0 (69.62) TAU sessions	
Hien 2009	6.2 (4.5)	12	51.7%	6.9 (4.3)	57.5%

Study	Mean number sessions attended for intervention group: Mean number treatment condition sessions attended by intervention group (& SD)	Number sessions available	Percentage active intervention sessions attended	Mean number sessions attended by control group (& SD)	Percentage attended
Najavits 2006a	**9.67(5.05)** active intervention session (11.78 (6.25) active intervention +TAU sessions)	25 active intervention sessions plus TAU sessions	38.7%	Not reported	
Norman unpublished	12.5 (8.77)	24	52.1%	7.78 (5.78)	32.4%
Zlotnick 2009	15.6 (6.2)	25	62.4%	Not reported	

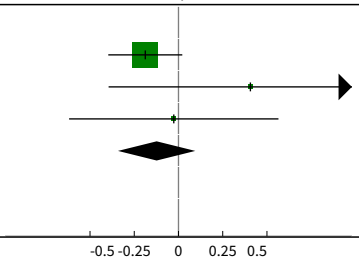
Analysis 3.15. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 15 Mean number of sessions attended.

Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.15.1 Group intervention							
Hien 2009	176	6.2 (4.5)	177	6.9 (4.3)		64.79%	-0.16[-0.37,0.05]
Norman unpublished	19	12.5 (8.8)	9	7.8 (5.8)		35.21%	0.57[-0.23,1.38]
Subtotal ***	**195**		**186**			**100%**	**0.1[-0.59,0.79]**
Heterogeneity: Tau^2=0.18; Chi^2=2.96, df=1(P=0.09); I^2=66.19%							
Test for overall effect: Z=0.28(P=0.78)							
Total ***	**195**		**186**			**100%**	**0.1[-0.59,0.79]**
Heterogeneity: Tau^2=0.18; Chi^2=2.96, df=1(P=0.09); I^2=66.19%							
Test for overall effect: Z=0.28(P=0.78)							



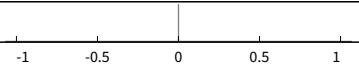
Analysis 3.16. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 16 Sensitivity analysis: PTSD severity 5-7 months following treatment completion.

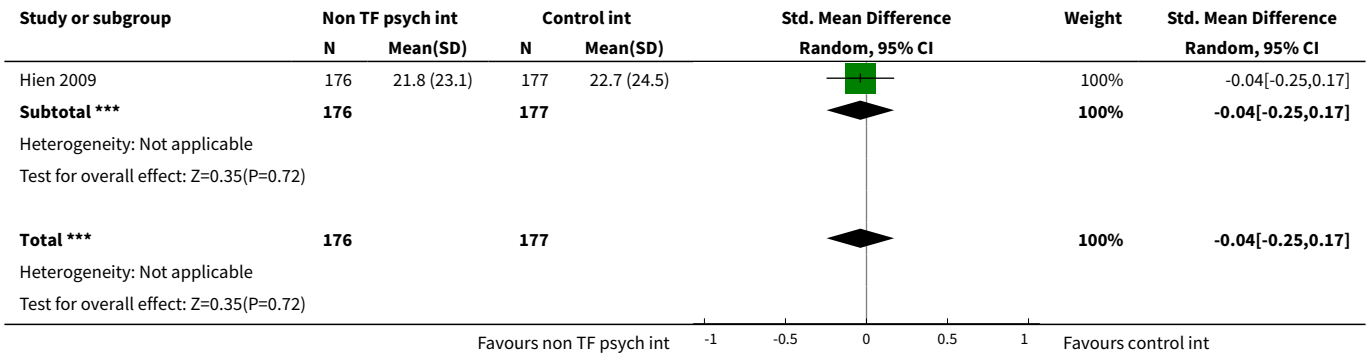
Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.16.1 Group intervention							
Hien 2009	176	24.7 (23.6)	177	29.6 (28.3)		79.7%	-0.19[-0.4,0.02]
Norman unpublished	19	55.5 (29.5)	9	44.4 (17.4)		7.26%	0.41[-0.39,1.21]
Zlotnick 2009	23	45.9 (30.7)	21	46.7 (28.3)		13.05%	-0.03[-0.62,0.57]
Subtotal ***	**218**		**207**			**100%**	**-0.12[-0.34,0.1]**
Heterogeneity: Tau^2=0; Chi^2=2.13, df=2(P=0.35); I^2=5.9%							
Test for overall effect: Z=1.11(P=0.27)							



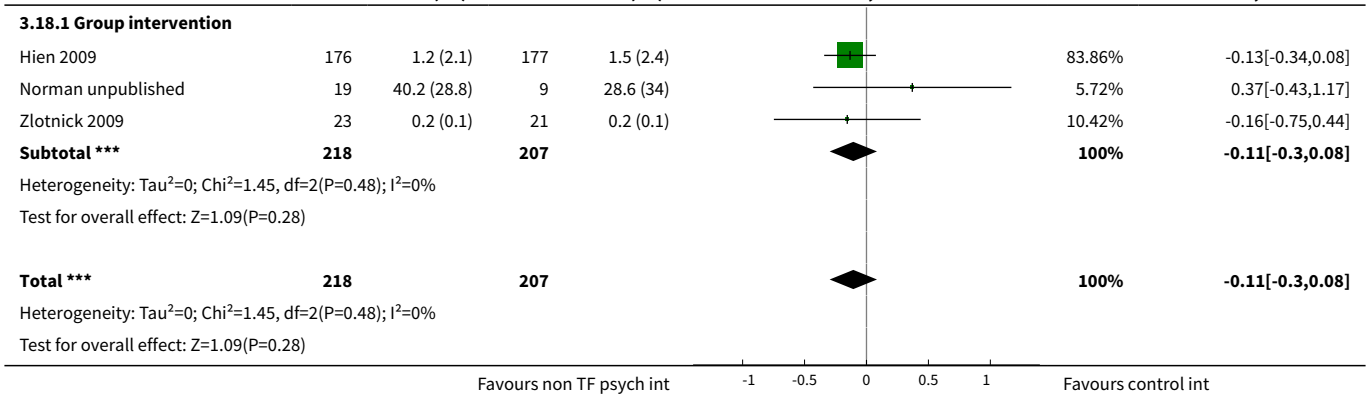
Analysis 3.17. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 17 Sensitivity analysis: PTSD severity 12 months following treatment completion.

Study or subgroup	Non TF psych int N	Non TF psych int Mean(SD)	Control int N	Control int Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
3.17.1 Group intervention							

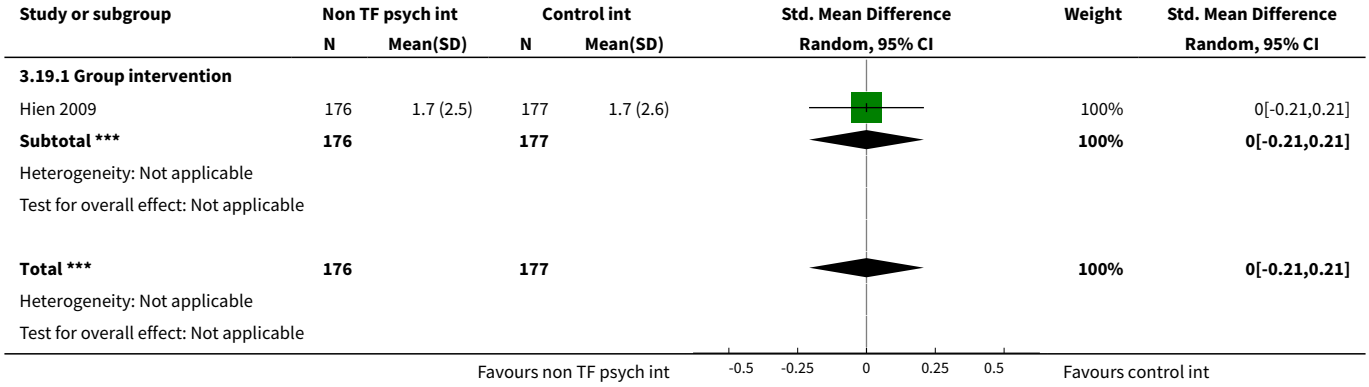




Analysis 3.18. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 18 Sensitivity analysis: drug or alcohol use, or both 5-7 months following treatment completion.



Analysis 3.19. Comparison 3 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs control therapy, Outcome 19 Sensitivity analysis: drug or alcohol use, or both 12 months following treatment completion.



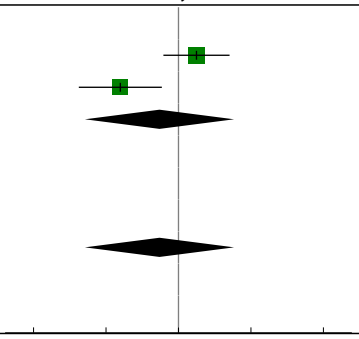
Comparison 4. Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD severity following treatment completion	2	128	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-1.29, 0.77]
1.1 Individual intervention	2	128	Std. Mean Difference (IV, Random, 95% CI)	-0.26 [-1.29, 0.77]
2 PTSD severity 3-4 months following treatment completion	2	128	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.31, 0.55]
2.1 Individual intervention	2	128	Std. Mean Difference (IV, Random, 95% CI)	0.12 [-0.31, 0.55]
3 PTSD severity 5-7 months following treatment completion	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
3.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]
4 Drug or alcohol use, or both following treatment completion	2	128	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.13, 0.57]
4.1 Individual intervention	2	128	Std. Mean Difference (IV, Random, 95% CI)	0.22 [-0.13, 0.57]
5 Drug or alcohol use, or both 3-4 months following treatment completion	2	128	Std. Mean Difference (IV, Random, 95% CI)	0.18 [-0.18, 0.53]
5.1 Individual intervention	2	128	Std. Mean Difference (IV, Random, 95% CI)	0.18 [-0.18, 0.53]
6 Drug or alcohol use, or both 5-7 months following treatment completion	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
6.1 Individual intervention	1		Mean Difference (IV, Random, 95% CI)	0.0 [0.0, 0.0]
7 Treatment completers	2	128	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.68, 1.20]
7.1 Individual intervention	2	128	Risk Ratio (M-H, Random, 95% CI)	0.91 [0.68, 1.20]
8 PTSD diagnosis following treatment completion	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected
8.1 Individual intervention	1		Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Mean number of sessions attended	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Individual intervention	1		Mean Difference (IV, Fixed, 95% CI)	0.0 [0.0, 0.0]

Analysis 4.1. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 1 PTSD severity following treatment completion.

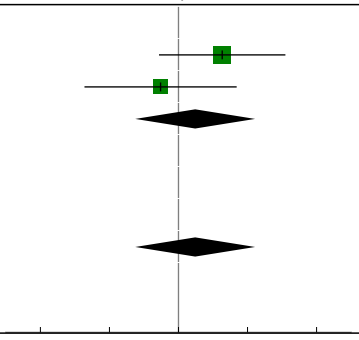
Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
4.1.1 Individual intervention							
Hien 2004	41	57.2 (22.3)	34	51.2 (25.2)		51.41%	0.25[-0.21,0.7]
McGovern 2011	32	36.1 (19.2)	21	52.6 (21.9)		48.59%	-0.8[-1.38,-0.23]
Subtotal ***	**73**		**55**			**100%**	**-0.26[-1.29,0.77]**
Heterogeneity: Tau^2=0.48; Chi^2=7.91, df=1(P=0); I^2=87.35%							
Test for overall effect: Z=0.5(P=0.62)							
Total ***	**73**		**55**			**100%**	**-0.26[-1.29,0.77]**
Heterogeneity: Tau^2=0.48; Chi^2=7.91, df=1(P=0); I^2=87.35%							
Test for overall effect: Z=0.5(P=0.62)							



Favours non-TF int | Favours int SUD only

Analysis 4.2. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 2 PTSD severity 3-4 months following treatment completion.

Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
4.2.1 Individual intervention							
Hien 2004	41	59.9 (21.1)	34	52.7 (24.1)		56.16%	0.32[-0.14,0.77]
McGovern 2011	32	46.5 (21.8)	21	49.8 (28.6)		43.84%	-0.13[-0.68,0.42]
Subtotal ***	**73**		**55**			**100%**	**0.12[-0.31,0.55]**
Heterogeneity: Tau^2=0.03; Chi^2=1.49, df=1(P=0.22); I^2=32.96%							
Test for overall effect: Z=0.55(P=0.59)							
Total ***	**73**		**55**			**100%**	**0.12[-0.31,0.55]**
Heterogeneity: Tau^2=0.03; Chi^2=1.49, df=1(P=0.22); I^2=32.96%							
Test for overall effect: Z=0.55(P=0.59)							



Favours non-TF int | Favours int SUD only

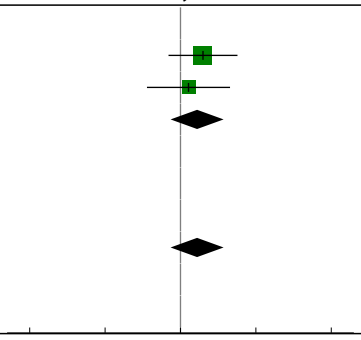
Analysis 4.3. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 3 PTSD severity 5-7 months following treatment completion.

Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
4.3.1 Individual intervention						
Hien 2004	41	55.3 (20.9)	34	47.8 (27.7)		7.52[-3.78,18.82]

Favours non-TF int — Favours int SUD only

Analysis 4.4. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 4 Drug or alcohol use, or both following treatment completion.

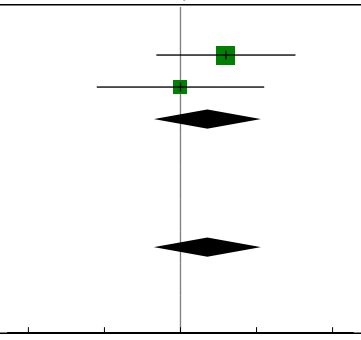
Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
4.4.1 Individual intervention							
Hien 2004	41	-0.1 (0.6)	34	-0.3 (0.6)		59.2%	0.3[-0.16,0.76]
McGovern 2011	32	0.1 (0.1)	21	0.1 (0.1)		40.8%	0.11[-0.44,0.66]
Subtotal ***	**73**		**55**			**100%**	**0.22[-0.13,0.57]**
Heterogeneity: Tau^2=0; Chi^2=0.28, df=1(P=0.6); I^2=0%							
Test for overall effect: Z=1.23(P=0.22)							
Total ***	**73**		**55**			**100%**	**0.22[-0.13,0.57]**
Heterogeneity: Tau^2=0; Chi^2=0.28, df=1(P=0.6); I^2=0%							
Test for overall effect: Z=1.23(P=0.22)							



Favours non-TF int — Favours int SUD only

Analysis 4.5. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 5 Drug or alcohol use, or both 3-4 months following treatment completion.

Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
4.5.1 Individual intervention							
Hien 2004	41	-0.1 (0.6)	34	-0.3 (0.6)		59.17%	0.3[-0.16,0.76]
McGovern 2011	32	0.1 (0.1)	21	0.1 (0.1)		40.83%	0[-0.55,0.55]
Subtotal ***	**73**		**55**			**100%**	**0.18[-0.18,0.53]**
Heterogeneity: Tau^2=0; Chi^2=0.67, df=1(P=0.41); I^2=0%							
Test for overall effect: Z=0.98(P=0.32)							
Total ***	**73**		**55**			**100%**	**0.18[-0.18,0.53]**
Heterogeneity: Tau^2=0; Chi^2=0.67, df=1(P=0.41); I^2=0%							
Test for overall effect: Z=0.98(P=0.32)							



Favours non-TF int — Favours int SUD only

Analysis 4.6. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 6 Drug or alcohol use, or both 5-7 months following treatment completion.

Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Mean Difference Random, 95% CI	Mean Difference Random, 95% CI
4.6.1 Individual intervention						
Hien 2004	41	-0.1 (0.5)	34	-0.2 (0.8)		0.1[-0.2,0.4]

Favours non-TF int -0.5 -0.25 0 0.25 0.5 Favours int SUD only

Analysis 4.7. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 7 Treatment completers.

Study or subgroup	Non-TF int PTSD & SUD n/N	Intervention for SUD only n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
4.7.1 Individual intervention					
Hien 2004	25/41	24/34		75.01%	0.86[0.62,1.2]
McGovern 2011	16/32	10/21		24.99%	1.05[0.6,1.85]
Subtotal (95% CI)	**73**	**55**		**100%**	**0.91[0.68,1.2]**
Total events: 41 (Non-TF int PTSD & SUD), 34 (Intervention for SUD only)					
Heterogeneity: Tau^2=0; Chi^2=0.36, df=1(P=0.55); I^2=0%					
Test for overall effect: Z=0.68(P=0.5)					
Total (95% CI)	**73**	**55**		**100%**	**0.91[0.68,1.2]**
Total events: 41 (Non-TF int PTSD & SUD), 34 (Intervention for SUD only)					
Heterogeneity: Tau^2=0; Chi^2=0.36, df=1(P=0.55); I^2=0%					
Test for overall effect: Z=0.68(P=0.5)					

Favours int SUD only 0.5 0.7 1 1.5 2 Favours non-TF int

Analysis 4.8. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 8 PTSD diagnosis following treatment completion.

Study or subgroup	Non-TF int PTSD & SUD n/N	Intervention for SUD only n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
4.8.1 Individual intervention				
McGovern 2011	23/32	16/21		0.94[0.68,1.3]

Favours non-TF int 1 Favours int SUD only

Analysis 4.9. Comparison 4 Non-trauma-focused psychological therapy for PTSD and SUD or PTSD only vs active psychological therapy for SUD only, Outcome 9 Mean number of sessions attended.

Study or subgroup	Non-TF int PTSD & SUD N	Non-TF int PTSD & SUD Mean(SD)	Intervention for SUD only N	Intervention for SUD only Mean(SD)	Mean Difference Fixed, 95% CI	Mean Difference Fixed, 95% CI
4.9.1 Individual intervention						
Hien 2004	41	12 (6.7)	34	12.1 (9)		-0.1[-3.75,3.55]

Favours non-TF int -5 -2.5 0 2.5 5 Favours int SUD only

APPENDICES

Appendix 1. Cochrane Central Register of Controlled Trials (CENTRAL)

We will search CENTRAL using the following terms:

[Condition]

#1 MeSH descriptor STRESS DISORDERS, TRAUMATIC, explode all trees

#2 (trauma* NEXT stress*)

#3 (psycho* NEXT trauma*)

#4 (stress* NEXT (extreme or disorder*))

#5 DESNOS *[Disorders of Extreme Stress]*

#6 (posttrauma* or post-trauma* or (post NEXT trauma*) or PTSD)

#7 (#1 or #2 or #3 or #4 or #5 or #6)

[Population: comorbid substance abuse]

#8 MeSH descriptor SUBSTANCE-RELATED DISORDERS explode all trees

#9 (substance use disorder or SUD)

#10 drug NEXT abuse

#11 (abuser* or abusing or addict* or depend* or habit* or misuse or user*)

#12 ((abuse) not (child* or sex*))

[Common drugs of abuse]

#13 (adinazolam or aerosol* or alcohol* or alprazolam or amphetamin* or anthramycin or anxiolytic* or ativan or barbituat* or bentazepam or benzodiazepin* or bromazepan or brotizolam or buprenorphin* or camazepam or cannabi* or chlordiazepoxid* or cinolazepam or clobazam or clonazepam or clorazepam or clotiazepam or cloxazolam or cocaine* or codeine or crack or crystal or cyprazepam or depressant* or diacetylmorphin* or diazepam* or doxefazepam or ecstasy or estazolam or etizolam or fentanyl or flunitrazepam or flurazepam or flutazoram or flutoprazepam or fosazepam or gases or GHB or girisopam or halazepam or hallucinogen* or haloxazepam or heroin* or hydromorphone or hydroquinone or hypnotic* or inhalant* or ketamin* or ketazolam or librium or loflazepate or loprazolam or lorazepam or lormetazepam or LSD or marihuana* or marijuana* or MDMA or meclonazepam or medazepam or meperidine or mephedrone or mescalin* or metaclazepam or methadone or methamphetamin* or methaqualone or mexazolam or midazepam or midazolam or morphine* or narcotic* or nerisopam or nimetazepam or nitrazepam or nitrites or (nitrous NEXT oxide) or n-methyl-3,4-methylenedioxyamphetamine or nordazepam or opiate* or opiod* or opium or oxazepam or oxazolam or oxazypam or oxycodone or oxzepam or painkiller* or (pain NEXT killer*) or PCP or pethidin* or phencyclidin* or pinasepam or prazepam or propazepam or propoxyphene or psilocybin or psychedelic* or psychoactive* or psychostimulant* or quinazolinone or ripazepam or ritalin or sedative* or serazepin* or solvent* or steroid* or stimulant* or substance* or temazepam or tetrazepam or tofisopam or tramadol or triazolam or triflubazam or valium or vicodin)

#14 (drug* NEAR (recreational or street))

#15 (#8 or #9 or #10 or #11 or #12 or #13 or #14)

[Condition + Population]

#16 (#7 and #15)

Appendix 2. Researchers contacted through the search process

Sudie Back, Matthew Boden, Marcel Bonn Miller, Kathleen Brady, Pamela Brown, Karen Cusack, Marylene Cloitre, Scott Coffey, Mark Creamer, Colin Drummond, Edna Foa, David Forbes, Julian Ford, Elizabeth Forshay, Anna Cash Ghee, Benjamin Goldstein, Michael Hase, Denise Hien, Debra Kaysen, Daniel Kivlahan, Karen Krinsley, Mark McGovern, Sarah Meshberg-Cohen, Nena Messina, Katherine Mills, Kim

Mueser, Lisa Najavits, Sonya Norman, Paige Ouimette, Tae Woo Park, Barbera Rothbaum, Josef Ruzek, Elizabeth Santa Ana, Ingo Schäfer, Paula Schnurr, Jodie Trafton, Elisa Triffleman, Debora van Dam, Richard Velleman, Anka Vujanovic, Doug Zatzick, Caron Zlotnick.

Of these, Scott Coffey, David Forbes, Julian Ford, Denise Hien, Debra Kaysen, Katherine Mills, Kim Mueser, Lisa Najavits, Sonya Norman and Elizabeth Santa Ana responded with additional data.

CONTRIBUTIONS OF AUTHORS

NPR drafted the review.

PAR undertook screening of papers, evaluation of risk of bias, data extraction, and commented on the protocol and write-up of the review.

NJ undertook evaluation of risk of bias, data extraction, and commented on the write-up of the review.

JIB undertook supervision of the review, arbitrated over issues of contention, and commented on the protocol and write-up of the review.

DECLARATIONS OF INTEREST

NPR: None declared.

PAR: None declared.

NJ: None declared.

JIB: None declared.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We added a section explaining how we would approach meta-analysis under the heading 'Main planned comparisons' in Data extraction and management. We decided to include studies where less than 80% of participants met our diagnostic inclusion criteria if we were able to obtain study data on the subset that met diagnosis.

In the protocol we framed the section 'Experimental interventions' as a 'catch-all' list of the types of intervention that we thought might potentially have been investigated in this patient group. It was not our intention to necessarily group our comparisons on this basis. We have therefore revised this section in order to provide a more meaningful structure to the review. Specific treatment models such as COPE and Seeking Safety were subsumed into other types of approaches, as they provided specific examples of these approaches. The distinction between trauma-focused and non-trauma-focused approaches was consistent with that of the review undertaken by van Dam 2012. We also recognised that we needed to articulate that we would undertake separate analysis for group- and individual-based interventions. Group-based interventions are generally considered to show weaker effects than individual-based interventions (Najavits 2014 [personal communication]). This finding has been specifically in relation to PTSD (Bisson 2013). We have removed categories for other psychological approaches, stepped care and interventions aimed at enhancing positive well-being through physiotherapy, occupational therapy, or guided self help. We can say with hindsight that it is highly unlikely we would have found evaluations of these types of interventions in this specific population.

We included a fourth review author, NJ, in order to provide balance to the review author group's expertise in the fields of treatment of PTSD and SUD. NJ is an expert in the treatment of SUDs.

As a post hoc addition, we defined the time points of interest in the Types of outcome measures section. As a further post hoc addition, we described our approach to summarising comparison findings under the heading 'Summary of findings'.

INDEX TERMS

Medical Subject Headings (MeSH)

Alcoholism [diagnosis] [therapy]; Psychotherapy [*methods]; Randomized Controlled Trials as Topic; Stress Disorders, Post-Traumatic [diagnosis] [*therapy]; Substance-Related Disorders [diagnosis] [*therapy]

MeSH check words

Adult; Humans