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Psychological interventions for post-traumatic stress disorder (PTSD) in people with severe mental illness (Review)

Sin J, Spain D, Furuta M, Murrells T, Norman I

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[Intervention Review]

Psychological interventions for post-traumatic stress disorder (PTSD) in people with severe mental illness

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ABSTRACT

Background

Increasing evidence indicates that individuals who develop severe mental illness (SMI) are also vulnerable to developing post-traumatic stress disorder (PTSD), due to increased risk of exposure to traumatic events and social adversity. The effectiveness of trauma-focused psychological interventions (TFPIs) for PTSD in the general population is well-established. TFPIs involve identifying and changing unhelpful beliefs about traumatic experiences, processing of traumatic memories, and developing new ways of responding to cues associated with trauma. Little is known about the potential feasibility, acceptability and effectiveness of TFPIs for individuals who have a SMI and PTSD.

Objectives

To evaluate the effectiveness of psychological interventions for PTSD symptoms or other symptoms of psychological distress arising from trauma in people with SMI.

Search methods

We searched the Cochrane Schizophrenia Group's Trials Study-Based Register (up until March 10, 2016), screened reference lists of relevant reports and reviews, and contacted trial authors for unpublished and/or specific outcome data.

Selection criteria

We included all relevant randomised controlled trials (RCTs) which investigated TFPIs for people with SMI and PTSD, and reported useable data.

Data collection and analysis

Three review authors (DS, MF, IN) independently screened the titles and abstracts of all references identified, and read short-listed full text papers. We assessed risk of bias in each case. We calculated the risk ratio (RR) and 95% confidence interval (CI) for binary outcomes, and the mean difference (MD) and 95% CI for continuous data, on an intention-to-treat basis. We assessed quality of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) and created 'Summary of findings' tables.

Main results

Four trials involving a total of 300 adults with SMI and PTSD are included. These trials evaluated three active intervention therapies: trauma-focused cognitive behavioural therapy (TF-CBT), eye movement desensitisation and reprocessing (EMDR), and brief psychoeducation for PTSD, all delivered via individual sessions. Our main outcomes of interest were PTSD symptoms, quality of life/well-being, symptoms of co-morbid psychosis, anxiety symptoms, depressive symptoms, adverse events and health economic outcomes.

1. TF-CBT versus usual care/waiting list

Three trials provided data for this comparison, however, continuous outcome data available were more often found to be skewed than unskewed, leading to the necessity of conducting analyses separately for the two types of continuous data. Using the unskewed data only, results showed no significant differences between TF-CBT and usual care in reducing clinician-rated PTSD symptoms at short term (1 RCT, n =13, MD 13.15, 95% CI -4.09 to 30.39,*low-quality evidence*). Limited unskewed data showed equivocal results between groups in terms of general quality of life (1 RCT, n = 39, MD -0.60, 95% CI -4.47 to 3.27, *low-quality evidence*), symptoms of psychosis (1 RCT, n = 9, MD -6.93, 95% CI -34.17 to 20.31, *low-quality evidence*), and anxiety (1 RCT, n = 9, MD 12.57, 95% CI -5.54 to 30.68, *very low-quality evidence*), at medium term. The only available data on depression symptoms were skewed and were equivocal across groups at medium term (2 RCTs, n = 48, MD 3.26, 95% CI -3.66 to 10.18, *very low-quality evidence*). TF-CBT was not associated with more adverse events (1 RCT, n = 100, RR 0.44, 95% CI 0.09 to 2.31, *low-quality evidence*) at medium term. No data were available for health economic outcomes. Very limited data for PTSD and other symptoms were available over the long term.

2. EMDR versus waiting list

One trial provided data for this comparison. Favourable effects were found for EMDR in terms of PTSD symptom severity at medium term but data were skewed (1 RCT, n = 83, MD -12.31, 95% CI -22.72 to -1.90, *very low-quality evidence).* EMDR was not associated with more adverse events (1 RCT, n = 102, RR 0.21, 95% CI 0.02 to 1.85, *low-quality evidence*). No data were available for quality of life, symptoms of co-morbid psychosis, depression, anxiety and health economics.

3. *TF-CBT versus EMDR*

One trial compared TF-CBT with EMDR. PTSD symptom severity, based on skewed data (1 RCT, n = 88, MD -1.69, 95% CI -12.63 to 9.23, *very low-quality evidence*) was similar between treatment groups. No data were available for the other main outcomes.

4. *TF-CBT versus psychoeducation*

One trial compared TF-CBT with psychoeducation. Results were equivocal for PTSD symptom severity (1 RCT, n = 52, MD 0.23, 95% CI -14.66 to 15.12, *low-quality evidence*) and general quality of life (1 RCT, n = 49, MD 0.11, 95% CI -0.74 to 0.95, *low-quality evidence*) by medium term. No data were available for the other outcomes of interest.

Authors' conclusions

Very few trials have investigated TFPIs for individuals with SMI and PTSD. Results from trials of TF-CBT are limited and inconclusive regarding its effectiveness on PTSD, or on psychotic symptoms or other symptoms of psychological distress. Only one trial evaluated EMDR and provided limited preliminary evidence favouring EMDR compared to waiting list. Comparing TF-CBT head-to-head with EMDR and brief psychoeducation respectively, showed no clear effect for either therapy. Both TF-CBT and EMDR do not appear to cause more (or less) adverse effects, compared to waiting list or usual care; these findings however, are mostly based on *low to very low-quality* evidence. Further larger scale trials are now needed to provide high-quality evidence to confirm or refute these preliminary findings, and to establish which intervention modalities and techniques are associated with improved outcomes, especially in the long term.

PLAIN LANGUAGE SUMMARY

Psychological interventions for post-traumatic stress disorder (PTSD) in people with severe mental illness

Background

Post-traumatic stress disorder (PTSD) typically develops after a traumatic event is experienced or witnessed by an individual, or may develop when trauma is experienced by someone close to them. There is growing evidence that people with a severe mental illness (SMI) are vulnerable to developing PTSD due to increased risk of childhood and adulthood trauma. It is estimated that around a third of individuals with SMI also suffer from PTSD. A number of psychological interventions are available for the treatment of PTSD which are collectively known as 'trauma-focused psychological interventions' (TFPIs).

Searching for evidence

We searched the Cochrane Schizophrenia Group Trial's Register in January 2015 and March 2016 and found four relevant studies involving 300 adults diagnosed with both SMI and PTSD. The participants received treatments that included trauma-focused cognitive behavioural therapy (TF-CBT), eye movement desensitisation and reprocessing (EMDR), and brief psychoeducation. All of these therapies support individuals to work through and process the memories, emotions and behaviours associated with trauma.

Key results

When TF-CBT was compared to the care usually received, no effect for reducing PTSD, psychotic, depressive or anxiety symptoms or improving quality of life, was noted. There was some low-quality evidence from two studies that people with SMI and PTSD receiving TF-CBT were more likely to recover from PTSD, that is, having PTSD symptoms which are below diagnostic threshold. TF-CBT was not linked to an increase in side effects.

A comparison of people receiving EMDR against those awaiting treatment showed a favourable effect for reducing the symptoms of PTSD (very low-quality evidence). Again, there was no difference in side effects. No data were available for the effect of EMDR on quality of life, psychosis, depression or anxiety.

A comparison of TF-CBT with EMDR indicated no difference in reduction of PTSD symptom severity (very low-quality evidence).

Finally, when TF-CBT was compared with brief psychoeducation there was no evidence that either therapy was superior in treating a range of PTSD symptoms.

Quality of the evidence

The review identifies limited, low-quality evidence on TF-CBT and EMDR. The effects of these treatments in reducing the symptoms of PTSD remain unclear although they do not appear to cause any more side effects than waiting for treatment. However, many important outcomes of interest have not been reported on and more research into the benefits of trauma-focused psychological interventions for individuals with SMI and PTSD is required.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Individual TF-CBT compared to waiting list/usual care for PTSD and severe mental illness

Individual TF-CBT compared to waiting list/**usual care for PTSD and severe mental illness**

Patient or population: Adults with co-morbid PTSD and SMI
Settings: Community
Intervention: Individual TF-CBT
Comparison: Waiting list/usual care

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	Waiting list/usual care	Individual TF-CBT			
PTSD symptoms: Clinician-rated PTSD symptom severity - average endpoint CAPS total score (high = poor) - short term (6 months)		The mean clinician-rated PTSD symptom severity - average endpoint caps total score (high = poor) - short term - unskewed data in the intervention groups was **13.15 higher** (4.09 lower to 30.39 higher)	13 (1 study)	⊕⊕⊖⊖ **low** [1,2]	Other data available for this outcome were skewed.
Quality of life: 1. General quality of life - average endpoint QLS total score (high = good) - medium term		The average endpoint QLS total score - medium term (10-12 months) in the intervention groups was **0.60 lower** (4.47 lower to 3.27 higher)	39 (1 study)	⊕⊕⊖⊖ **low** [1,2]	
Symptoms of co-morbid psychosis: 1. Overall mental state - average endpoint BPRS total score (high = poor) - medium term		The mean overall mental state - average endpoint BPRS total score (high = poor) - medium term, in the intervention groups was **6.93 lower** (34.17 lower to 20.31 higher)	9 (1 study)	⊕⊕⊖⊖ **low** [1,2]	
Anxiety symptoms - average endpoint BAI total score (high = poor) - medium term (12 months)		The mean anxiety symptoms in the intervention groups was **12.57 higher** (5.54 lower to 30.68 higher)	9 (1 study)	⊕⊖⊖⊖ **very low** [1,2]	

Depressive symptoms - average endpoint BDI-II total (high = poor) - medium term (12 months) - skewed data		The mean depressive symptoms - average endpoint BDI-II total (high = poor) in the intervention groups was **3.26 higher** (3.66 lower to 10.18 higher)	48 (2 studies)	⊕⊖⊖⊖ **very low** [1,3]	No unskewed data available.
Adverse events - incidents of unspecified severe adverse events - medium term	**Study population**		100 (1 study) **RR (0.44) CI 0.09 to 2.31**	⊕⊕⊖⊖ **low** [2]	
	85 per 1000	**37 per 1000** (8 to 197)			
	Moderate				
	85 per 1000	**37 per 1000** (8 to 196)			
Health economics	-	-	-	-	No data available.

*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).
CI: Confidence interval; **RR:** risk ratio.

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] Indirectness: downgraded by one level to 'serious' - continuous measure with a wide score range used which may not reflect clinical significant change accurately.
[2] Imprecision: downgraded by one level to 'serious' - only one study with a small sample size (or subgroup sample size) provides data for this outcome.
[3] Imprecision: downgraded by one level to 'serious' - all available data from 2 studies were skewed.

Summary of findings 2. EMDR compared to waiting list/usual care for PTSD and severe mental illness

EMDR compared to waiting list/**usual care for PTSD and severe mental illness**

Patient or population: Adults with co-morbid PTSD and SMI
Settings: Community
Intervention: EMDR
Comparison: Waiting list

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

	Assumed risk	Corresponding risk		(GRADE)	
	Waiting list	**EMDR**			
PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - Medium term - skewed data		The mean clinician-rated PTSD symptom severity - average endpoint caps total score (high = poor) - medium term (7-9 months) - skewed data in the intervention groups was **12.31 lower** (22.72 to 1.90 lower)	83 (1 study)	⊕⊝⊝⊝ **very low** [1,2,3]	Only available data were skewed.
Quality of life: 1. General quality of life	-		-	-	No data available.
Symptoms of co-morbid psychosis: 1. Overall mental state	-	-	-	-	No data available.
Anxiety symptoms	-	-	-	-	No data available.
Depressive symptoms	-	-	-	-	No data available.
Adverse events - incidents of unspecified severe adverse events - medium term	**Study population**		102 (1 study)	⊕⊕⊝⊝ **low** [3]	
	85 per 1000	**18 per 1000** (2 to 157)			
	Moderate				
	85 per 1000	**18 per 1000** (2 to 157)			
Health economics	-	-	-	-	No data available.

*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).
CI: Confidence interval.

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] Only data available were skewed.
[2] Continuous measure with a wide score range used which may not reflect clinical significant change accurately.
[3] Only one study provided data on this outcome.

Summary of findings 3. Individual TF-CBT compared to EMDR for PTSD and severe mental illness

Individual TF-CBT compared to EMDR for PTSD and severe mental illness

Patient or population: Adults with co-morbid PTSD and SMI
Settings: Community
Intervention: TF-CBT
Comparison: EMDR

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	EMDR	TF-CBT			
PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - Medium term - skewed data		The mean clinician-rated PTSD symptom severity - average endpoint caps total score (high = poor) - medium term (7-9 months) - skewed data in the intervention groups was **1.69 lower** (12.61 lower to 9.23 higher)	88 (1 study)	⊕⊝⊝⊝ **very low** [1,2]	Only data available were skewed.
Quality of life: 1. General quality of life	-	-	-	-	No data available.
Symptoms of co-morbid psychosis: 1. Overall mental state	-	-	-	-	No data available.
Anxiety symptoms	-	-	-	-	No data available.
Depressive symptoms	-	-	-	-	No data available.
Adverse events - incidents of unspecified severe events - medium term	-	-	-	-	Secondary review outcomes not analysed in this comparison.
Health economics	-	-	-	-	No data available.

*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).
CI: Confidence interval.

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] Only one study provided data which were skewed.
[2] Continuous outcome measure with a wide score range was used, score changes may not reflect meaningful clinical changes.

Summary of findings 4. Individual TF-CBT compared to Brief PTSD psychoeducation for PTSD and severe mental illness

Individual TF-CBT compared to Brief PTSD psychoeducation for PTSD and severe mental illness

Patient or population: Adults with co-morbid PTSD and SMI
Settings: Community
Intervention: Individual TF-CBT versus brief PTSD psychoeducation
Comparison: Brief PTSD psychoeducation

Outcomes	Illustrative comparative risks* (95% CI)		No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk			
	Brief PTSD psychoeducation	Individual TF-CBT versus brief PTSD psychoeducation			
PTSD symptom severity: 1. Clinician-rated PTSD severity - average endpoint CAPS total score (high = poor) - Medium term		The mean clinician-rated PTSD symptom severity - average endpoint caps total score (high = poor) - medium term (10-12 months) - unskewed data in the intervention groups was **0.23 higher** (14.66 lower to 15.12 higher)	52 (1 study)	⊕⊕⊖⊖ **low** [1,2]	
Quality of life: 1. General quality of life - average endpoint QoLI total score (high = good) - Long term		The mean quality of life: (a) general quality of life - average endpoint QoLI total score (high = good) - long term (16-18 months) - unskewed data in the intervention groups was **0.11 higher**	49 (1 study)	⊕⊕⊖⊖ **low** [1,2]	

	(0.74 lower to 0.96 higher)				
Symptoms of co-morbid psychosis: 1. Overall mental state	-	-	-	-	Secondary review outcomes not analysed in this comparison.
Anxiety symptoms	-		-	-	Secondary review outcomes not analysed in this comparison.
Depressive symptoms	-		-	-	Secondary review outcomes not analysed in this comparison.
Adverse events - incidents of unspecified severe adverse events	-	-	-	-	No data available.
Health economics	-	-	-	-	No data available.

*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).
CI: Confidence interval.

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] Only data from one study with small subgroup sample available.
[2] Continuous measure used which may not reflect clinical significant change accurately.

BACKGROUND

Description of the condition

Severe mental illness (SMI) is defined according to three dimensions: 1) a non-organic psychotic disorder; 2) treatment duration lasting for two years or more; and 3) disability resulting in impairments in social and occupational functioning (Ruggeri 2000). Psychosis is manifested by delusions or hallucinations into which an individual has limited insight (APA 2013), and which subsequently causes disturbances in functioning and relationships, despite ongoing treatment and care. Psychosis is characterised by positive and negative symptoms, for example: delusions, hallucinations, thought disorder, perceptual disturbances, and blunting or incongruity of emotional responses. The cluster of schizophrenia and related disorders (e.g. schizoaffective disorder, schizophreniform disorder and delusional disorder) are considered to be the most common psychotic disorders (WHO 1992). Individuals living with 'early onset psychosis' or 'first episode psychosis' and those who are receiving treatment and support from early intervention services are also considered to meet criteria for SMI due to the similarities in their clinical presentation and the resultant impairment and disability (NICE 2014). Bipolar disorder (Type 1) diagnoses also fall within the remit of SMI. Bipolar disorder is primarily characterised by episodes of fluctuating mood: alternating between elevated mood and increased activity - that is often accompanied by psychotic symptoms, and decreased energy and activity (WHO 1992).

The onset of SMI tends to occur around late adolescence and early adulthood (NICE 2014). The prevalence of schizophrenia - based on a 2005 review of surveys undertaken in 46 countries - has been reported to be 0.4% for lifetime prevalence up to the point of assessment, and 0.3% in the 12-month period prior to assessment (Saha 2005). The 12-month prevalence rate of Type 1 bipolar disorder is estimated to be 0.72% and the lifetime prevalence rate is reported to be 0.8%, according to a 2004 review of previous surveys (Waraich 2004). It is well-established that people living with SMI often have co-morbid mental health problems, most commonly depression, anxiety disorders, and post-traumatic stress disorder (PTSD; NICE 2014; Read 2008).

The relationship between SMI and co-morbid PTSD is complex and poorly understood, but there is increasing evidence to suggest that the much higher prevalence of childhood sexual and physical abuse, and social adversity continuing into adulthood amongst people affected by SMI are likely to be risk mechanisms for PTSD (Bebbington 2011; Read 2008). It is estimated that around a third of individuals with SMI also suffer from PTSD (Brunet 2012; Kilcommons 2005; NICE 2014).

Post-traumatic stress disorder is a trauma and stress-related disorder. An individual may develop PTSD in response to directly experiencing or witnessing a traumatic event in person or vicariously, for example to a family member or close friend (APA 2013). The Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria highlights that a traumatic stressor usually involves a perceived threat to life (either one's own life or that of another person), or physical integrity (A1 - stressor criteria), and intense fear, helplessness or horror (A2 - specific subjective emotional reaction criteria; APA 2013; APA, 2000). DSM diagnostic criteria are considered to be more strict than the International Classification of Diseases-10 (ICD-10) diagnostic criteria; hence most randomised controlled trials (RCTs) of PTSD use DSM criteria (NICE 2005). DSM-5 outlines four distinct diagnostic clusters of PTSD symptoms (APA 2013), instead of the three clusters described in the previous version (APA, 2000), as follows: re-experiencing (e.g. intrusive thoughts/images related to the trauma), avoidance (e.g. sites or cues related to the trauma), arousal (e.g. 'fight or flight' reactions, or panic), and negative cognitions and low mood. PTSD is relatively common, with prevalence rates estimated as 0.4% and 3.5% in the general adult population (Bisson 2013; Darves-Bornoz 2008; Kessler 1995; NICE 2005). The symptoms of PTSD often cause intense distress, physiological reactions, and can significantly impair individuals' quality of life and functioning in multiple domains including interpersonal relationships (e.g. difficulties with trusting others, avoidance of intimacy; APA 2013; NICE 2005). PTSD is also commonly associated with other co-morbid conditions, such as substance use, depression, and/or ongoing physical health concerns such as pain and disability resulting from the traumatic event (NICE 2005; NICE 2013).

While the concept of PTSD has been conventionally applied to survivors of combat, accidents and disasters, and victims of violent crimes such as physical and sexual assaults, it has recently been suggested that the illness experience of SMI itself, for example, experiencing threatening or persecutory psychotic symptoms, can be traumatic (Jackson 2009; Kilcommons 2005). In about one-third of people with SMI, the experience of a recent onset of psychosis is an event of such severity that it can lead to PTSD or at least to PTSD symptoms (Brunet 2012; Morrison 2003; Mueser 2010), with the traumagenic elements of the psychotic experiences meeting the criteria for a traumatic event according to the DSM-IV-tr A1 and A2 criteria (APA, 2000).

Description of the intervention

Several psychological therapies have been found to be effective treatments for PTSD in the general population. These include several modes of exposure therapy, trauma-focused cognitive behavioural therapy (TF-CBT) and eye movement desensitisation and reprocessing (EMDR) (Bisson 2013; Bradley 2005; NICE 2005). All these therapies share some core elements that support individuals to work through and process their trauma memories, cognitions and attributions of traumatic events, and hence they are collectively known as 'trauma-focused psychological therapies' (Bisson 2013; Ehlers 2010; NICE 2005; NICE 2013; Schnyder 2015). Both TF-CBT and EMDR are recommended by the UK National Institute for Health and Care Excellence (NICE) guideline about the treatment of PTSD in child and adult populations; with a course of eight to 12 individual outpatient sessions of TF-CBT or EMDR being the most common form of treatment (NICE 2005; NICE 2013). Exposure therapy typically involves asking the person to relive the trauma, either in their imagination or by writing or audio-recording a trauma narrative to create a detailed account of the event. The individual is then asked repeatedly to listen to or read the narrative in order to become habituated to the anxiety symptoms that are generated. An alternative form of exposure therapy involves graded re-exposure to cues associated with the traumatic event, for example, using a hierarchy of cues (which are related to the trauma) (Creamer 2004; Schnyder 2015). Prolonged exposure (PE) therapy stipulates two such principal components: imaginal exposure (i.e. repeated revisiting and recounting of distressing trauma memories) followed by 15-20 minutes of processing in which the

imaginal exposure experience and other related emotions and perceptions are discussed, and, in vivo exposure (i.e. gradual approaching of avoided, safe trauma-related situations) (Foa 2007). TF-CBT primarily involves supporting individuals to identify, examine and change unhelpful thoughts about others (e.g. people are not trustworthy), themselves (e.g. it is my fault this happened, I am a failure), the world (e.g. the world is dangerous); or unhelpful behavioural responses that may perpetuate trauma symptoms or hamper functioning (e.g. avoiding using public transport in London following the 7 July 2005 (7/7) bombing; or drinking to excess in an attempt to promote sleep), or both (Ehlers 2005; Resick 2003). EMDR was discovered accidentally by Shapiro through her personal experience of rapid eye movements easing distress (Shapiro 1989). Shapiro further developed EMDR into a structured protocol-driven trauma-focused therapy to alleviate the distress associated with traumatic memories, based upon the adaptive information process model of PTSD (Shapiro 2001). EMDR therapy consists of eight phases that includes the individual recalling an image, thought, emotion and a bodily sensation associated with the traumatic event, whilst receiving bilateral stimulation, most commonly in the form of eye movements (Shapiro 2001).

How the intervention might work

Exposure therapy and exposure-based TF-CBT are thought to work by promoting emotional habituation by repeated exposure to the traumatic events or cues associated with the events (Bryant 2003; Ehlers 2005; Marks 1998). Psychoeducation about common reactions to trauma is a key feature of all TF-CBT therapies, which aim to normalise the individual's symptoms and give a rationale for the interventions that follow (Ehlers 2010; NICE 2005). TF-CBT, whilst relying on repeated exposure to the trauma memory and in vivo exposure to situations avoided since the event, also actively incorporates cognitive restructuring to modify the excessively negative appraisals of the trauma or its sequelae, or both (Ehlers 2005; Ehlers 2010). Cognitive therapy for PTSD focuses on identifying and modifying the idiosyncratic meanings of the trauma and problematic appraisal of trauma sequelae (e.g. initial PTSD symptoms, other peoples' responses after the event) and a wide range of behavioural and cognitive maintaining strategies (e.g. rumination, overt and covert safety behaviours that often hamper functioning; Bisson 2013; Ehlers 2005). In some TF-CBT, behavioural experiments are also used to demonstrate the way in which various maintaining processes (such as thought suppression, hypervigilance for danger, avoidance of any cues) operate and support the individual to adopt more adaptive or effective coping mechanisms (Ehlers 2005; Resick 2003). Despite its well-established effectiveness in treating PTSD in the general population, there is no agreed mechanism by which EMDR is thought to operate, hence there is no definitive explanatory model of how it works, although it is suggested that bilateral stimulation aids the processing of traumatic memories (Shapiro 1989).

Why it is important to do this review

People with SMI have been found to be at increased risk of experiencing traumatic events (Bebbington 2004; Fisher 2013; Morrison 2003; Read 2008). These include traumatic events during childhood (such as physical and sexual abuse; Bebbington 2004; Varese 2012), as well as in adulthood (such as being a victim of crime and abusive relationships (Darves-Bornoz 2008; Fisher 2013). Also, there is some evidence to suggest that the illness experience of SMI itself, such as experiences of threatening or persecutory psychotic symptoms (Jackson 2009; Kilcommons 2005), can be traumatic.

Subsequently, it is estimated that around a third of individuals with SMI also suffer from PTSD, across different phases of the illness, from early onset, to acute and remission from positive symptoms (Brunet 2012; Kilcommons 2005; NICE 2014). This rate far exceeds that of the general population. Prolonged and untreated PTSD is associated with exacerbation of both PTSD and psychotic symptoms, associated affective symptoms and a reduction in overall functioning and quality of life in affected individuals (Mueser 2009; Read 2008). However, despite trauma-focused psychological interventions being consistently demonstrated to be effective for the treatment of PTSD (Bisson 2013; Bradley 2005; NICE 2005), empirical studies investigating feasibility, acceptability, and clinical and cost-effectiveness of psychological interventions for PTSD tend to exclude people with psychosis (Mueser 2010; NICE 2014). In routine service settings, provision of psychological interventions (targeting psychotic symptoms specifically or other common co-morbid problems such as PTSD) has also been criticised to be limited for people with psychotic disorders (The Schizophrenia Commission 2012). This may be attributed to clinical and methodological factors, including: 1) diagnostic overshadowing whereby there are overlaps in the symptom presentations of psychosis and PTSD (Calvert 2008; Jones 2014); 2) concerns that this clinical population may find it hard to engage with psychological therapies (Callcott 2004; Gairns 2015); 3) concern that standard treatment/interventions may exacerbate positive symptoms (Gairns 2015); and 4) potential high attrition rates (Callcott 2004; Jackson 2009). Hence, relatively little is known about the utility and effectiveness of such treatments for this co-morbid population. This review aims to address this knowledge gap by investigating the effectiveness of psychological interventions in improving PTSD symptoms and well-being of individuals affected by PTSD and SMI. This information can then be used to inform the development of clinical services for this highly co-morbid group.

OBJECTIVES

To evaluate the effectiveness of psychological interventions for post-traumatic stress disorder (PTSD) symptoms or other symptoms of psychological distress arising from trauma in people with severe mental illness (SMI).

METHODS

Criteria for considering studies for this review

Types of studies

All relevant randomised controlled trials that investigate psychological interventions for the co-morbid post-traumatic stress disorder (PTSD) and severe mental illness (SMI) group. If a trial was described as 'double-blind' and implied randomisation, we planned to include such trials in a sensitivity analysis (see Sensitivity analysis). We excluded quasi-randomised studies, such as those allocating to interventions by alternate days of the week. Where participants were given additional treatments within a psychological intervention for PTSD, we planned to only include the data if the adjunct treatment was evenly distributed between the intervention and control groups, and it was the only psychological intervention (with the primary purpose of treating PTSD or alleviating PTSD symptoms) that was randomised.

Types of participants

Adolescents (aged 11 to 17 years) and adults (aged 18 years and over) with SMI as defined above, and also diagnosed with PTSD, and treated in any (clinical) setting. We also included studies with participants diagnosed with PTSD and co-morbid primary diagnoses other than SMI as defined by this review (e.g. severe depression or bipolar disorder), but only if at least 50% or more of the participants had a psychosis-related disorder; or if data specific to the participants with co-morbid psychosis were reported independently, or obtainable from the study's authors.

Types of interventions

1. Psychological interventions

We included psychological interventions if they were trauma-focused treatments or other psychological treatments that had been used with the explicit intention of treating PTSD, that is, they aimed to reduce PTSD symptoms or other related distress that developed in relation to traumatic events relating to life events, or the experience of SMI. These included the following.

1. Individual trauma-focused cognitive behavioural therapy (TF-CBT): any psychological therapy that predominately used trauma-focused cognitive or behavioural techniques or a combination to address PTSD symptoms or other symptoms of psychological distress arising from trauma (Ehlers 2005). Using the definition adopted by the Cochrane review for psychological therapies for PTSD (Bisson 2013), this category also includes exposure therapy.
2. Group TF-CBT: any approach delivered in a group setting using predominately trauma-focused cognitive, behavioural or cognitive-behavioural techniques.
3. Eye movement desensitisation and reprocessing (EMDR; Shapiro 1989; Shapiro 2001).
4. Any other psychological intervention that did not fit the above categories of modalities, but clearly described its theoretical underpinnings and was intended to target PTSD symptoms and related distress in people with SMI.

2. Control conditions

Comparator interventions included either:

1. usual care/treatment as usual/waiting list: this usually includes care co-ordination or case management and (antipsychotic) medication;
2. any other intervention: any alternative (psychological) intervention other than a specific trauma-focused psychological intervention whose content, mode of delivery and design were clearly defined, e.g. non-trauma-focused CBT, non-directive/supportive counselling (Rogers 1961), stress inoculation training (SIT; Meichenbaum 1988); and less structured approaches such as befriending and psychodynamic therapies.

We conducted separate analyses focusing on each category of active psychological interventions based on a shared modality and format of delivery (i.e. TF-CBT - individual or group based, EMDR, or any other psychological intervention for PTSD), comparing them to all the control conditions pooled together. Whenever there were sufficient data extracted from included studies, we then proceeded to analyse each category of active psychological intervention targeting PTSD comparing each modality and format of active intervention against: 1) active control conditions (i.e. non-PTSD focused intervention/s); 2) usual care/treatment as usual/waiting list; and 3) other modality and format of trauma-focused psychological intervention, for primary outcomes.

Types of outcome measures

We divided all outcomes into short-term (less than six months), medium-term (seven to 12 months) and long-term (over one year) categories.

Primary outcomes

1. PTSD symptom severity - as reported by validated measures

1.1 Average change or endpoint in PTSD symptom severity using a clinician-conducted standardised and validated measure (but not administered by the treating therapist), such as the Clinician Administered PTSD Symptom Scale (CAPS) (Blake 1995).
1.2 Average change or endpoint in self-reported PTSD symptoms using a standardised measure, for example, Impact of Events Scale (IES) by Horowitz 1979), post-traumatic stress diagnostic scale (PDS) by Foa 1995.
1.3 Recovery or remission from PTSD (i.e. no longer meeting diagnostic criteria of PTSD).

2. Quality of life or well-being - as measured by validated self-reported scales

2.1 Clinically important change or endpoint scores in general quality of life or well-being scores, generic or specific to the participants' physical, psychological, social, or cognitive functioning.
2.2 Average change or endpoint scores in general quality of life or well-being scores, generic or specific to the participants' physical, psychological, social, or cognitive functioning.

Secondary outcomes

3. Symptoms of co-morbid psychosis

3.1 Endpoint or average change in severity of overall or general mental state score, as measured by validated scales, such as the Brief Psychiatric Rating Scale (BPRS, Overall 1962) or the Positive and Negative Symptoms Scale (PANSS, Kay 1986).
3.2 Endpoint or average change in severity of positive psychotic symptoms.
3.3 Endpoint or average change in severity of negative psychotic symptoms.
3.4 Recovery or remission from the pre-existing psychotic disorder.

4. Depressive symptoms

4.1 Endpoint or average change in severity of depressive symptoms, as measured by validated scales, for example the Beck Depression Inventory (BDI) (Beck 1996).
4.2 Recovery or remission from depression.

5. Anxiety symptoms

5.1 Endpoint or average change in severity of anxiety symptoms, as reported by validated measures, e.g. the Spielberger State Anxiety Inventory (STAI) (Spielberger 1973) or Beck Anxiety Inventory (BAI) (Beck 1990).
5.2 Recovery or remission from anxiety disorder.

6. Adverse events

6.1 Increased PTSD symptoms or severity.
6.2 Increased severity of overall psychotic symptoms.
6.3 Any other adverse events, e.g. death including suicide and natural causes.

7. Leaving the study early

7.1 Withdrawal from the treatment programme.
7.2 Loss to follow-up.

8. Satisfaction or perceived acceptability of treatment

8.1 Subjective satisfaction with treatment, as measured by validated self-report scales.
8.2 Perceived acceptability of treatment, as measured by validated self-report scales.

9. Health economic outcomes

9.1 Direct costs, e.g. treatment costs, service use.
9.2 Indirect costs.

'Summary of findings' table/s

We used the GRADE approach to interpret findings (Schünemann 2011), and we used the GRADE profiler to import data from RevMan 5.3 to create 'Summary of findings' tables (GRADEPRO; Review Manager). These tables provide outcome-specific information concerning the overall quality of evidence from each included study in the comparison, the magnitude of effect of the interventions examined, and the sum of available data on all outcomes we rated as important to patient-care and decision-making. We aimed to select the following main outcomes for inclusion in the 'Summary of findings' tables:

1. PTSD symptoms
2. Quality of life or well-being
3. Symptoms of co-morbid psychosis
4. Depressive symptoms
5. Anxiety symptoms
6. Adverse events
7. Health economics

Search methods for identification of studies

Electronic searches

1. Cochrane Schizophrenia Group's Trials Register

On January 29, 2015 and March 10, 2016, the information specialist (TSC) searched the Cochrane Schizophrenia Group's Trials Register using the following search strategies:

(*trauma* or *ptsd*):ti,ab,kw of REFERENCE or (*trauma* or *ptsd*):sco of STUDY

The Cochrane Schizophrenia Group's Register of Trials is compiled by systematic searches of major resources (including AMED, BIOSIS, CINAHL, Embase, MEDLINE, PsycINFO, PubMed, and registries of clinical trials) and their monthly updates, handsearches, grey literature, and conference proceedings (see Group Module). There are no language, date, document type, or publication status limitations for inclusion of records into the register.

Searching other resources

1. Reference searching

We inspected the references of all included studies for further relevant studies.

2. Personal contact

We contacted the first and/or corresponding author of each screened study for information regarding unpublished or ongoing trials. We noted the outcome of these contacts in the included or excluded studies tables.

Data collection and analysis

Selection of studies

Review authors DS and MF independently examined citations from the searches and identified relevant abstracts. review authors IN independently re-inspected a random 20% sample to ensure reliability. Where disputes or uncertainty arose, we acquired the full report for more detailed scrutiny. DS and MF obtained and inspected full reports of the abstracts meeting the review criteria independently. Again, IN re-inspected a random 20% of these full reports in order to ensure reliable selection. Where it was not possible to resolve disagreement by discussion, we made contact with the authors of the study for clarification.

Data extraction and management

1. Extraction

Review authors DS and MF extracted data from all included studies. Again, we discussed any disagreement and documented decisions. If necessary, authors of studies were contacted for clarification and for obtaining further unpublished or subgroup data. IN helped clarify issues for any remaining problems and these final decisions were documented. We planned to extract data presented in graphs and figures only, but included these data only if two review authors independently obtained the same result. In the event, we did not need to extract data from graphs and/or figures. We contacted authors through an open-ended request in order to obtain missing information or for clarification whenever necessary. If studies were multi-centre, where possible, we planned to extract data relevant to each component centre independently.

2. Management

2.1 Forms

We extracted data onto simple, standard forms.

2.2 Scale-derived data

We included continuous data from rating scales only if:

1. the psychometric properties of the measuring instrument had been described in a peer-reviewed journal (Marshall 2000); and
2. the measuring instrument had not been written or modified by one of the trialists for that particular trial. Partial use of a validated instrument would be included only if complete subscale results were available for interpretation.

Ideally, the measuring instrument should either be a self-report or a report completed by an independent rater or relative (not the therapist). We realised that this is often not reported clearly; we noted if this was the case or not in the Description of studies section.

2.3 Endpoint versus change data

There are advantages of both endpoint and change data. Change data can remove a component of between-person variability from the analysis, however calculation of change needs two assessments (baseline and endpoint), which can be difficult in unstable and difficult to measure conditions such as schizophrenia. We decided primarily to use endpoint data as much as possible, and only used change data if the former were not available. For continuous outcomes, we calculated the mean difference (MD) and 95% confidence intervals (CI) where all outcomes were measured using the same scale or there was only one trial. We also anticipated that different studies might use different instruments (e.g. different outcome measures or psychological tests) to assess the outcomes. In this case, the scale of measurement would differ from study to study and we decided it would only be meaningful to calculate the standardised mean difference (SMD; i.e. by dividing the MD in each study by that study's standard deviation (SD)). We planned to use a SMD value that was comparable across studies in the analysis (Borenstein 2011), in such circumstances.

2.4 Skewed data

Continuous data on clinical and social outcomes are often not normally distributed. To avoid the pitfall of applying parametric tests to non-parametric data, we applied the following standards to all data before inclusion.

1. SDs and means are reported in the paper or obtainable from the authors.
2. When a scale starts from the finite number zero, we planned to subtract the lowest possible value from the mean, and divide this by the SD. If this value is lower than 1, it strongly suggests a skew and the study would be excluded. If this ratio is higher than one but below two, there is suggestion of skew. We entered the study and tested whether its inclusion or exclusion would change the results substantially; in the event of significant differences in the results, we performed analyses grouping the unskewed and skewed data separately. Finally, if the ratio is larger than 2 the study would have been included, because skew is less likely (Altman 1996; Deeks 2011).
3. If a scale starts from a positive value (such as the Positive and Negative Syndrome Scale (PANSS; Kay 1986), which can have values from 30 to 210), we planned to modify the calculation described above to take the scale starting point into account. In these cases skew is present if 2 SD > (S-S min), where S is the mean score and 'S min' is the minimum score.

Endpoint scores on scales often have a finite start and end point and these rules can be applied. Skewed data pose less of a problem when looking at means if the sample size is large (> 200) (Moore 2010) and we planned to include these data into the syntheses. We planned to present skewed endpoint data from studies of less than 200 participants in 'other tables' within the data analysis section rather than enter such data into statistical analyses together with the unskewed data.

When continuous data are presented on a scale that includes a possibility of negative value (such as change data), it is difficult to tell whether data are skewed or not. We planned to present and enter change data into statistical analyses.

2.5 Common measures

To facilitate comparison between trials, we intended to convert variables that can be reported in different metrics, such as days in hospital (mean days per year, per week or per month) to a common metric (e.g. mean days per month).

2.6 Conversion of continuous data to binary data

Where possible, we intended to convert outcome measures to dichotomous data. This can be done by identifying cut-off points on rating scales and dividing participants accordingly into 'clinically improved' or 'not clinically improved'. In general, we assumed that if there was a 50% reduction in a scale-derived score such as the Brief Psychiatric Rating Scale (BPRS; Overall 1962), or the Positive and Negative Syndrome Scale (PANSS; Kay 1986), this could be considered as a clinically significant response (Leucht 2005a; Leucht 2005b). If data based on these thresholds were not available, we planned to use the primary cut-off presented by the original authors.

2.7 Direction of graphs

Where possible, we entered data in such a way that the area to the left of the line of no effect indicates a favourable outcome for trauma-focused psychological interventions. Where keeping to this made it impossible to avoid outcome titles with clumsy double-negatives (e.g. 'Not un-improved') we reported data where the left of the line indicated an unfavourable outcome. This would have been noted in the relevant graphs.

Assessment of risk of bias in included studies

Review authors DS and MF worked independently to assess risk of bias by using criteria described in the *Cochrane Handbook for Systemic Reviews of Interventions* to assess trial quality (Higgins 2011). This set of criteria is based on evidence of associations between overestimate of effect and high risk of bias of the article, such as sequence generation, allocation concealment, blinding, incomplete outcome data and selective reporting.

If the raters disagreed, the final rating was made by consensus, with the involvement of other members of the review group (TM and IN). Where inadequate details of randomisation and other characteristics of trials were provided, we contacted the authors of the studies to obtain further information. We also planned to report non-concurrence in quality assessment, but if disputes arose regarding the category to which a trial was to be allocated, again, we would have resolved these by discussion.

We noted the level of risk of bias in both the text of the review and in the 'Summary of findings' tables.

Measures of treatment effect

1. Binary data

For binary outcomes we planned to calculate a standard estimation of the risk ratio (RR) and its 95% CI. It has been shown that RR is more intuitive than odds ratios (Boissel 1999), and that odds ratios tend to be interpreted as RR by clinicians (Deeks 2000). The number needed to treat for an additional beneficial outcome (NNTB)/number needed to treat for an additional harmful outcome (NNTH) statistic with its CIs is intuitively attractive to clinicians but is problematic both in its accurate calculation in meta-analyses and interpretation (Hutton 2009). For binary data presented in

the 'Summary of findings' tables, where possible, we planned to calculate illustrative comparative risks.

2. Continuous data

For continuous outcomes, we calculated the mean difference (MD) and its 95% CI where all outcomes were measured using the same scale or where there was only one trial. If different scales had been used, we planned to calculate the standardised mean difference (SMD) and 95% CI. We preferred not to calculate effect size measures (SMD). However, if scales of very considerable similarity had been used, we would have considered that there was a small difference in measurement, and proceeded to calculate effect size and transform the effect back to the units of one or more of the specific instruments.

Unit of analysis issues

1. Cluster trials

Studies increasingly employ 'cluster randomisation' (such as randomisation by clinician or practice) but analysis and pooling of clustered data poses problems. Firstly, authors often fail to account for intra-class correlation in clustered studies, leading to a 'unit of analysis' error whereby P values are spuriously low (Divine 1992), CIs are unduly narrow and statistical significance overestimated. This causes type I errors (Bland 1997; Gulliford 1999).

Where clustering had not been accounted for in primary studies, we planned to present data in a table, with a (*) symbol to indicate the presence of a probable unit of analysis error. In subsequent versions of this review, if we include cluster-randomised trials, we will contact the first or corresponding authors of studies to obtain intra-class correlation coefficients (ICCs) for their clustered data and will adjust for this by using accepted methods (Gulliford 1999). If clustering has been incorporated into the analysis of primary studies, we will present these data as if from a non-cluster randomised study, but adjust for the clustering effect.

We sought statistical advice and have been advised that the binary data as presented in a report should be divided by a 'design effect'. This is calculated using the mean number of participants per cluster (m) and the ICC [Design effect = 1+(m-1)*ICC] (Donner 2002). If the ICC was not reported, we would assume it to be 0.1 (Ukoumunne 1999). If cluster studies have been appropriately analysed taking into account ICCs and relevant data documented in the report, synthesis with other studies will be possible using the generic inverse variance technique.

2. Cross-over trials

A major concern of cross-over trials is the carry-over effect. It occurs if an effect (e.g. pharmacological, physiological or psychological) of the treatment in the first phase is carried over to the second phase. As a consequence, the participants can differ systematically from their initial state on entry to the second phase, despite a wash-out phase. For the same reason cross-over trials are not appropriate if the condition of interest is unstable (Elbourne 2002). As both effects are very likely in severe mental illness, we planned only to use data from the first phase of cross-over studies if included in the review.

3. Studies with multiple treatment groups

We included a study that involved more than two treatment arms: van den Berg 2015 investigated two types of trauma-focused psychological interventions and compared them as a distinctive treatment condition respectively against the waiting-list control condition. We have presented the data of all three treatment arms in comparisons (see Summary of main results). Had the additional treatment arms not been relevant, we would not have used these data.

Dealing with missing data

1. Overall loss of credibility

At some degree of loss of follow-up, the data must lose credibility (Xia 2009). We chose that, for any particular outcome, should more than 50% of the data be unaccounted for, we would not reproduce the data or use them within analyses. If, however, more than 50% of those in one arm of a study were lost, but the total loss across arms was less than 50%, we addressed this within the 'Summary of findings' tables by down-rating quality. This was the case with one included study (Mueser 2008), which had a loss of follow-up rate of 71% (i.e. five out of seven participants allocated to the treatment as usual (TAU) control arm) at six-month follow-up time point, although the overall loss of follow-up combining both active treatment and control arms was 53% (i.e. only three out of 10 participants allocated to the active treatment arm were lost).

2. Binary

In the case where attrition for a binary outcome was between 0% and 50% and where these data were not clearly described, we planned to present data on a 'once-randomised-always-analyse' basis (an intention-to-treat (ITT) analysis). We planned to undertake sensitivity analyses by imputing outcomes for the missing participants with the most optimistic scenario and with the most pessimistic scenario and then compare the results of these two analyses. We also planned to undertake sensitivity analyses to test how prone the primary outcomes were to change when only data from people who completed the study (i.e. available-case analysis) were compared to the ITT analysis using the above assumptions. For the current review, we did not encounter this level of missing binary outcome data and therefore did not undertake the aforementioned sensitivity analyses.

3. Continuous

3.1 Attrition

In the case when attrition for a continuous outcome was between 0 and 50%, and only data from people who completed the study to that point were reported, we planned to reproduce these.

3.2 Standard deviations

If SDs were not reported, as in one included study (van den Berg 2015), we contacted the trial authors who provided us with the raw group means and SDs of all reported outcomes, which we presented and used in the review. If these were not available, where there were missing measures of variance for continuous data, but an exact standard error (SE) and CIs available for group means, and either P value or 't' value available for differences in mean, we could have calculated them according to the rules described in the *Cochrane Handbook for Systemic reviews of Interventions* (Higgins 2011). When only the SE is reported, SDs are calculated by the formula SD = SE * square root (n). Chapters 7.7.3 and 16.1.3 of the *Cochrane Handbook for Systemic reviews of Interventions* present detailed formulae for estimating SDs from P values, t or F values, CIs, ranges or other statistics. If these formulae did not apply, we

would have calculated the SDs according to a validated imputation method that is based on the SDs of the other included studies (Furukawa 2006). Although some of these imputation strategies can introduce error, the alternative would be to exclude a given study's outcome and thus to lose information. We nevertheless also planned to examine the validity of the imputations in a sensitivity analysis excluding imputed values.

3.3 Assumptions about participants who left the trials early or were lost to follow-up

Various methods are available to account for participants who left the trials early or were lost to follow-up. Some trials just present the results of study completers (this was the case with three included studies: Mueser 2008; Mueser 2015; Steel 2010), others use the method of last observation carried forward (LOCF) or more sophisticated approaches, such as multiple imputation or mixed-effects models for repeated measurements (MMRM) (Leon 2006). As all methods of imputation to deal with missing data introduce uncertainty about the reliability of the results (Leucht 2007), we obtained the completers' outcome data from the authors which we presented and used in the review. Moreover, we also addressed this issue in the 'incomplete outcome data' item of the 'Risk of bias' tool.

Assessment of heterogeneity

1. Clinical heterogeneity

We considered all included studies initially, without seeing comparison data, to judge clinical heterogeneity. We simply inspected all studies for clearly outlying people or situations that we had not predicted would arise. If such situations or participant groups arose, these would have been fully discussed by all review authors.

2. Methodological heterogeneity

We considered all included studies initially, without seeing comparison data, to judge methodological heterogeneity. Again, we simply inspected all studies for clearly outlying methods that we had not predicted would arise. When such methodological outliers arose, the review authors discussed these fully.

3. Statistical heterogeneity

3.1 Visual inspection

We inspected graphs visually to investigate the possibility of statistical heterogeneity.

3.2 Employing the I^2 statistic

We investigated heterogeneity between studies by considering the I^2 method alongside the Chi^2 P value. The I^2 provides an estimate of the percentage of inconsistency thought to be due to chance (Higgins 2003). The importance of the observed value of I^2 depends on firstly, magnitude and direction of effects and secondly, the strength of evidence for heterogeneity (e.g. P value from Chi^2 test, or a CI for I^2). We interpreted an I^2 estimate greater than or equal to around 50% accompanied by a statistically significant Chi^2 statistic as evidence of substantial levels of heterogeneity (Section 9.5.2; Deeks 2011). When substantial levels of heterogeneity were found in the primary outcome, we explored reasons for heterogeneity (Subgroup analysis and investigation of heterogeneity).

Assessment of reporting biases

1. Protocol versus full study

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results. These are described in section 10.1 of the *Cochrane Handbook for Systemic reviews of Interventions* (Sterne 2011). We tried to locate protocols of included randomised trials by both searching the databases and by contacting authors of registered trials. Whenever the protocol was available, we compared outcomes in the protocol and in the published report. If the protocol was not available, we compared outcomes listed in the methods section of the trial report with the results reported.

2. Funnel plot

Reporting biases arise when the dissemination of research findings is influenced by the nature and direction of results (Egger 1997). These are again described in Section 10 of the *Cochrane Handbook for Systemic reviews of Interventions* (Sterne 2011). We are aware that funnel plots may be useful in investigating reporting biases but have limited power to detect small-study effects. We therefore did not use funnel plots for outcomes where there were 10 or fewer studies, or where all studies were of similar sizes. In other cases, where funnel plots were possible, we planned to seek statistical advice in their interpretation.

Data synthesis

We understand that there is no closed argument for preference for the use of fixed-effect or random-effects models. The random-effects method incorporates an assumption that the different studies are estimating different, yet related, intervention effects. This often seems to be true to us and the random-effects model takes into account differences between studies, even if there is no statistically significant heterogeneity. There is, however, a disadvantage to the random-effects model. It puts added weight onto small studies which often are the most biased ones. Depending on the direction of effect, these studies can either inflate or deflate the effect size. As there were only few studies (i.e. four studies in total, and a maximum of three included in some analyses), random-effects model analyses may be inadequate to estimate accurately the width of the distribution of intervention effects (Deeks 2011; Kontopantelis 2013). We chose to use the random-effects model for analyses involving more than one study, and check and note if the analysis results were different if using a fixed-effect model. The reader is, however, able to choose to inspect the data using the fixed-effect model.

Subgroup analysis and investigation of heterogeneity

1. Subgroup analyses

1.1 Primary outcomes

We proposed to perform subgroup analyses by age (i.e. adults versus adolescents < 18 years of age) and by types of trauma (i.e. conventional trauma, such as road traffic accidents, physical or sexual assaults versus SMI symptom-related trauma, such as persecutory delusions). We planned to undertake these comparisons only for the primary outcomes to minimise the risk of multiple comparisons.

1.2 Clinical state, stage or problem

We proposed to undertake this review and provide an overview of the effects of psychological interventions for PTSD in people with SMI in general. In addition, however, we planned to report data on subgroups of people with similar clinical presentations and demographics.

2. Investigation of heterogeneity

If inconsistency was high, this would have been reported. Firstly, we planned to investigate whether data had been entered correctly. Secondly, if data were correct, we would proceed to inspect the graph visually and remove outlying studies successively to see if homogeneity was restored. For this review, we decided that, should this occur with data contributing to the summary finding of no more than around 10% of the total weighting, the data would have been presented. If not, data would not be pooled and issues would be discussed. We know of no research that supports this 10% cut-off, but are investigating use of prediction intervals as an alternative to this unsatisfactory state.

When unanticipated clinical or methodological heterogeneity were obvious, we planned to simply state hypotheses regarding these for future reviews or versions of this review. We had not pre-planned any analyses relating to these.

Sensitivity analysis

1. Implication of randomisation

We planned to include trials in a sensitivity analysis if they were described in some way that implied randomisation. For the primary outcomes, we planned to include these studies and, if there was no substantive difference when the implied randomised studies were added to those with better description of randomisation, then all data would have been employed from these studies.

2. Assumptions for lost binary data

If assumptions had to be made regarding people lost to follow-up (see Dealing with missing data), we planned to compare the findings of the primary outcomes when we used our assumptions and when we used only the data from people who completed the study to that point. If there was a substantial difference, we would have reported the results and discuss them, but would have continued to employ our assumption(s).

If assumptions had to be made regarding missing SDs (see Dealing with missing data), we planned to compare the findings of the primary outcomes when we used our assumptions and when we used data only from people who completed the study to that point. We planned to undertake a sensitivity analysis to test how prone results were to change when completer-only data were compared to the imputed data using the above assumptions. If these analyses yielded similar results in terms of the effects of the treatment, we would have presented the results of the available-case analyses. If there was a substantial difference, we would have reported and discussed the difference and presented all results in the 'Summary of findings' tables.

3. Risk of bias

We intended to analyse the effects of excluding trials that were judged to be at high risk of bias across one or more of the domains of randomisation (i.e. implied as randomised with no further details available), allocation concealment, blinding and outcome reporting for the meta-analysis of the primary outcome. If the exclusion of trials at high risk of bias did not substantially alter the direction of effect or the precision of the effect estimates, then we would have included data from these trials in the analysis.

4. Imputed values

If we had included cluster-randomised trials, if necessary, we planned to undertake a sensitivity analysis to assess the effects of including data from trials where we had used imputed values for ICC in calculating the design effect in cluster-randomised trials.

If substantial differences were noted in the direction or precision of effect estimates in any of the sensitivity analyses listed above, we would not have pooled data from the excluded trials with the other trials contributing to the outcome, but would have presented them separately.

5. Fixed-effect and random-effects models

As aforementioned (Data synthesis), we synthesised data using a random-effects model primarily and further compared the results obtained from using both random-effects and fixed-effect models to seek potential bias and heterogeneity (Kontopantelis 2013).

RESULTS

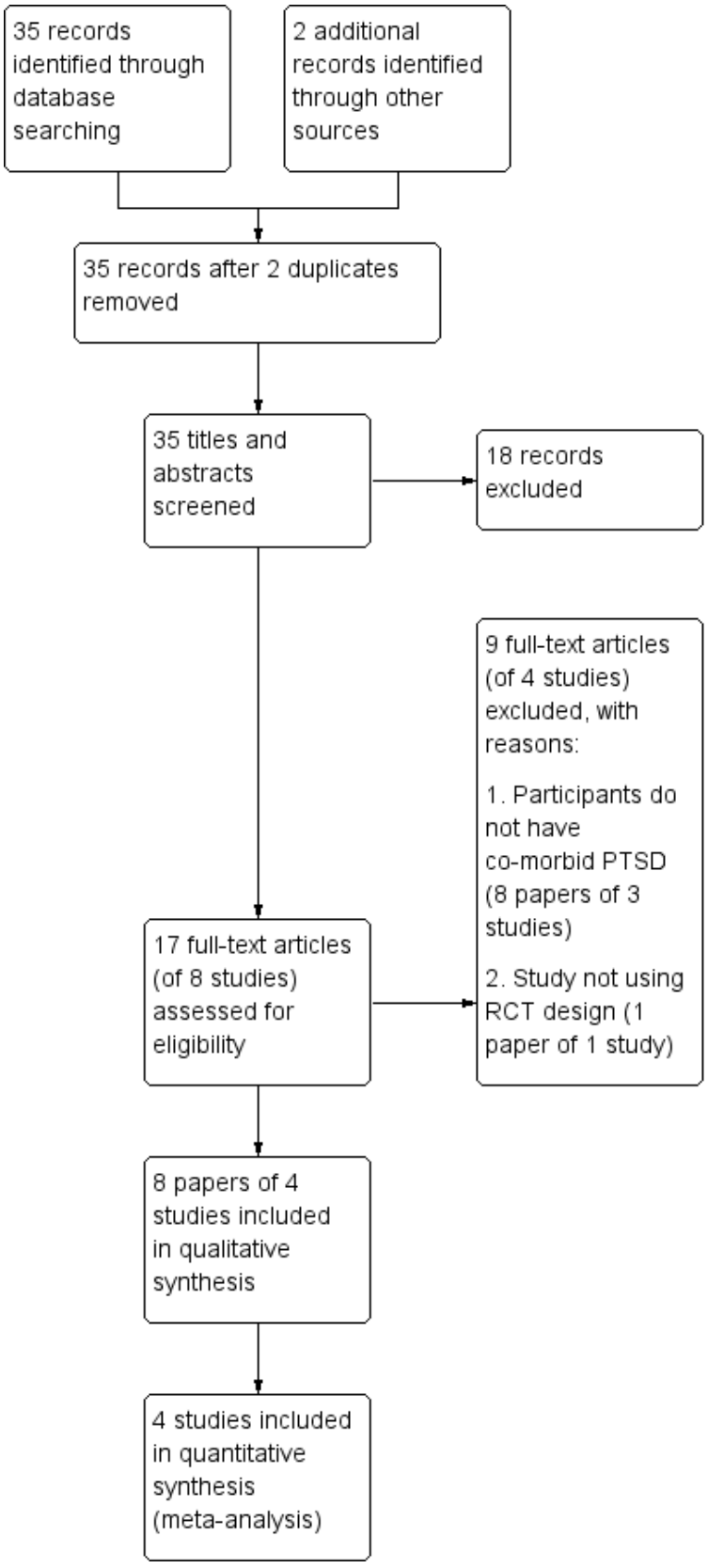
Description of studies

See Characteristics of included studies and Characteristics of excluded studies for detailed description of each screened study.

Results of the search

The search results from the Cochrane Schizophrenia Group Trial Register yielded 35 unique titles and abstracts. After examination, two duplicates were removed and two additional references which belong to two studies were identified by contacting trial authors and updated publication of registered trials (31st March 2015). Seventeen full-text articles or trial registration details of eight studies were assessed for inclusion or exclusion. For trials that included people with severe mental illness (SMI) as participants with others who had a non-SMI diagnosis as defined by this review as their primary diagnosis, we contacted the trial authors by email for specific data in relation to the SMI participants. We also contacted trial authors to inquire if they had unpublished or completed study outcomes relevant for this review, again by email correspondence. Trial authors' responses are summarised in the Characteristics of included studies and Characteristics of excluded studies sections. The results of the search is summarised in Figure 1.

Figure 1. Study flow diagram.



Included studies

With additional subgroup data specific to participants with a psychotic disorder (Mueser 2008; Mueser 2015) and unpublished data obtained from trial authors (Steel 2010), four studies (Mueser 2015; Mueser 2008; Steel 2010; van den Berg 2015) were included that met all the inclusion criteria and provided data specific to individuals with co-morbid psychotic disorder and post-traumatic stress disorder (PTSD) (n = 300). See also Characteristics of included studies for description of the four included studies (including eight papers and/or trial registration detail).

1. Design

All included studies were described as 'randomised'. van den Berg 2015 reported using an independent randomisation bureau to randomise the participants into the three treatment conditions using "stratified randomisation blocks per therapist with equal strata sizes" (van den Berg 2015, p. e3). Altogether, 20 therapists were trained in both active interventions trialled in the study (i.e. Prolonged Exposure (PE) and eye movement desensitisation and reprocessing (EMDR)), they delivered both treatments and it was not possible to blind them to the participant-allocation. Mueser 2008 reported using a computer-based randomisation programme to randomly allocate participants to the two arms in blocks of four within each of the 12 strata (i.e. stratification was devised by four treatment sites and by the three major diagnostic groups, i.e. major mood disorder with or without borderline personality disorder and schizophrenia or schizoaffective disorder). Another study by Mueser (Mueser 2015) also used a computer programme operated by an off-site data manager for randomisation which was stratified by sites (i.e. five) and by primary diagnosis (i.e. three similar to the aforementioned categories used in Mueser 2008). In both USA-based studies, it was not possible to blind the therapists nor the participants to the treatment-allocation (Mueser 2015; Mueser 2008). Steel 2010 did not describe the method used to randomly allocate the participants, however, it was clear that neither the therapist nor the participants were blinded to the treatment allocation.

2. Setting

van den Berg 2015's three-arm randomised controlled trial (RCT) was based in the Netherlands; Mueser 2008's trial was based in the State of New Hampshire, USA, while a more recent trial by Mueser and colleagues (Mueser 2015), was based in the State of New Jersey, USA. Steel 2010's study was based in South East England, UK. Both trials based in the USA (Mueser 2015; Mueser 2008), recruited individuals in community dwellings who had a diagnosis of SMI and a co-morbid PTSD. The UK-based study (Steel 2010), and the Netherlands study (van den Berg 2015), also focused on community-dwelling patients. All patients received the psychological treatment at out-patient clinics.

3. Participants

All participants in Steel 2010 (n = 61) had a diagnosis of schizophrenia or schizoaffective disorder and current symptoms consistent with a diagnosis of PTSD, both with reference to the DSM-IV diagnostic criteria (APA, 2000). van den Berg 2015 recruited 155 adults with a lifetime diagnosis of a psychotic disorder or mood disorder with psychotic features according to the Mini-International Neuropsychiatric Interview-Plus (Sheehan 1997; Sheehan 1998) and a concurrent diagnosis of chronic PTSD meeting all the DSM-IV-tr criteria (APA, 2000). The two USA-based studies recruited individuals meeting the State of New Hampshire (n = 108) (Mueser 2008) or State of New Jersey (n = 201) (Mueser 2015) definition of 'severe mental illness' which included a range of DSM-IV Axis-I disorders (including schizophreniform disorders, schizoaffective disorders, major depression or bipolar disorder) and persistent impairment in the areas of work, school, or ability to care for oneself, and a DSM-IV diagnosis of severe PTSD. Out of the total 108 participants in Mueser 2008, 17 individuals (16%) had co-morbid psychotic disorder and PTSD. And, 67 out of the total 201 participants (33%) in Mueser 2015 met the inclusion criteria of co-morbid SMI and PTSD as defined by this review. All 300 participants across the four studies were adults aged 18 or above, as stipulated in the study eligibility criteria. Apart from Steel 2010 (which was not yet published at the time of writing this review but the lead trialist provided us with some unpublished outcome data), the remaining three studies recruited community-dwelling patients with an average age of early to mid 40s (Mueser 2008; Mueser 2015, van den Berg 2015). There were more female than male patients in both USA studies with female samples ranging from 61% (Mueser 2008) to 71% (Mueser 2015). van den Berg 2015's trial included 71 male patients (46%) and 84 female patients (54%).

4. Nature of trauma and duration of trauma symptoms

Assessment for a current diagnosis of PTSD in all potentially eligible participants across all included studies (Mueser 2015; Mueser 2008; Steel 2010; van den Berg 2015) was conducted by using the Clinician Administered PTSD Scale (CAPS by Blake 1995; Weathers 2001). Mueser 2015 specified that their intervention focused on people with severe PTSD as defined by having a minimum CAPS total score of 65 (Weathers 2001). While van den Berg 2015 specified a diagnosis of chronic PTSD as part of their inclusion criteria for their participants; no minimum duration of PTSD symptoms was stipulated as part of the eligibility criteria, although the baseline data of all participants (n = 155) reported an average duration of PTSD of 21 years (SD = 13.5 years). No details could be found in relation to the nature of traumatic events participants experienced in two studies (Mueser 2015; Steel 2010). Nonetheless, in the remaining studies that reported the nature of the trauma the participants experienced (Mueser 2008; van den Berg 2015), it was reported that most participants experienced multiple childhood traumas, including sexual, emotional and physical abuse. van den Berg 2015 further identified 28 participants (18%) who developed PTSD due to traumatic psychosis experiences.

5. Interventions

5.1 Intervention groups

In order to compare data in a meaningful way, we had made an a priori decision to group different psychological interventions based upon their theoretical basis into four categories when devising our review protocol (see Types of interventions). These four categories of trauma-focused interventions were: individual trauma-focused cognitive behavioural therapy (TF-CBT) including exposure-based therapy; group TF-CBT; EMDR; and any other psychological intervention with an explicit aim to treat PTSD symptoms and related distress.The interventions trialled in the included studies are described below.

5.1.1 Individual trauma-focused cognitive behavioural therapy (TF-CBT)

All four included studies evaluated TF-CBT that was delivered to patients on an individual basis. Mueser 2015 reported devising and trialling a 12- to 16-week CBT programme that was developed based on cognitive models of PTSD (Ehlers 2005; Horowitz 1979): the initial three sessions were dedicated to teaching breathing retraining for anxiety and psychoeducation about PTSD; while the remaining nine to 13 sessions focused on cognitive restructuring. Treatment exposure was a priori defined as completion of at least six sessions. An earlier study by Mueser 2008 also trialled a 12- to 16- session CBT for PTSD programme, with the initial few sessions focusing on psychoeducation and breathing retraining and the remaining sessions split into two parts of cognitive restructuring. Again, participants were required to complete at least six sessions including a minimum of three sessions of cognitive restructuring, to satisfy the definition of treatment exposure. The UK-based study by Steel 2010 adopted the 16-sessions CBT programme developed by Mueser 2008 in which the 12-to 16-session CBT programme was delivered to patients individually over a six-month duration. van den Berg 2015 devised and trialled eight sessions prolonged exposure (PE) therapy run within a 10-week time frame, which was developed based upon a protocol by Foa et al (Foa 2007). Whilst the first of the eight 90-minute PE sessions was used to develop a case conceptualisation between the therapist and the individual patient, the remaining sessions focused on imaginal and in vivo exposure targeting a list of avoided trauma-related stimuli.

5.1.2 Group TF-CBT

No study reported on group-based interventions.

5.1.3 Eye movement desensitisation and reprocessing (EMDR)

An eight weekly 90-minute EMDR therapy delivered to patients individually over a 10-week period was also trialled in van den Berg 2015. The study used the Dutch EMDR therapy protocol (de Jongh 2003), which was translated and adapted from the standard eight-phase protocol by Shapiro (Shapiro 2001). Bilateral eye movements were applied as the dual-attention stimuli when traumatic memories were processed from the second through to the eighth (i.e. last) session, whilst the first session was used to develop a case conceptualisation including identifying a hierarchy of relevant traumatic experiences for the individual patients.

5.1.4 Any other trauma-focused psychological intervention that does not fit the above categories of modality and format

In addition to the TF-CBT programme, Mueser 2015 also trialled a brief PTSD psychoeducation programme, adapted from an earlier therapy the researchers developed to educate persons with SMI about PTSD (Pratt 2005). The brief psychoeducation programme included three sessions, the first of which covered the same breathing retraining and education components as the TF-CBT programme, which was tested in the other arm of the study. The remaining two sessions focused on education on anxiety management and discussion about the causes and nature of PTSD. Treatment exposure was defined a priori as completion of at least two sessions.

5.2 Comparison groups

Comparisons most commonly used were 'Treatment as Usual (TAU)' or 'standard treatment' which usually included out-patient follow-up and case management or care co-ordination, pharmacological treatment and access to a range of supportive psychotherapies excluding any trauma-focused therapies (Mueser 2008; Steel 2010). van den Berg 2015 used a 'wait list' (WL) control group as comparison to the PE and EMDR groups, participants in the WL group received the usual treatment during the 6-month follow-up period and was then offered either PE or EMDR based on their own choice after the follow-up period. Mueser 2015 used the brief PTSD psychoeducation programme (as detailed in Section 5.1.4) as an active comparison against the TF-CBT programme.

6. Outcomes

6.1 Outcome scales

Primary outcomes of the review were PTSD symptom severity and quality of life or well-being of the individuals with co-morbid SMI and PTSD (see Primary outcomes for further details). Secondary outcomes included patients' psychotic symptoms, depressive and anxiety symptoms, adverse events, leaving the study early, satisfaction or perceived acceptability of treatment, and health economic outcomes (see Secondary outcomes). Most of these outcomes were reported by the four included studies, using various scales as described below.

6.1.1 PTSD symptom severity

All four included studies (Mueser 2015; Mueser 2008; Steel 2010; van den Berg 2015) reported clinician-rated PTSD symptom severity and loss of PTSD diagnosis (i.e. remission from PTSD with sub-threshold PTSD symptoms) and/or recovery from PTSD (i.e. asymptomatic of PTSD) as the primary outcome of their study aims. The Clinician Administered PTSD Scale (CAPS by Blake 1995; Weathers 2001) was used as the study's primary outcome measure in all four studies, with Mueser 2015 specifying using the CAPS-schizophrenia version (Gearon 2004). CAPS is a widely used, reliable and valid semi-structured interview for the assessment of PTSD symptoms (Gearon 2004; Weathers 2001). For each PTSD symptom, a frequency and intensity rating is provided, with overall severity scores computed by summing the frequency and intensity scores for all of the PTSD symptoms, i.e. CAPS-total (Blake 1995; Weathers 2001). The higher the CAPs-total scores, the more severe the PTSD symptoms.

In addition, the cut-off of CAPS-total score (i.e. less than 40) (Weathers 2001) was used by three studies (Mueser 2008; Mueser 2015; van den Berg 2015) to determine the number of participants achieving remission from PTSD or sub-threshold PTSD symptom severity (i.e. loss of diagnosis of PTSD) following treatment and at follow-up. Furthermore, van den Berg 2015 used the CAPS-total cut-off of less than 20 (Weathers 2001) as a binary measure to indicate recovery or full remission from PTSD (i.e. asymptomatic or few symptoms of PTSD). Mueser 2015 focused on individuals with SMI and severe PTSD as defined by a minimum CAPS-total score of 65 (Weathers 2001) on entry to the trial, after the intervention and at follow-up time points; this CAPS-total cut-off point of 65 was used again as binary outcome for remission from (or loss of diagnosis of) severe PTSD.

A number of validated outcome measures were used by the included studies to report self-rated PTSD symptoms. These included: the Posttraumatic Cognitions Inventory (PTCI by Foa 1999) - a subjective measure for PTSD patients to report trauma-related cognitions especially negative beliefs about self, others and the world, with higher scores corresponding to greater endorsement of negative beliefs - was used in all studies

(Mueser 2015; Mueser 2008; Steel 2010; van den Berg 2015); the Posttraumatic Stress Symptom Scale Self-Report (PSS-SR by Foa 1993) was also used by van den Berg 2015 to assess patients' self-reported frequency of PTSD symptoms (higher scores indicate poorer symptom severity).

6.1.2 Quality of life or well-being

General quality of life (across different life domains) was assessed and considered as one of the secondary outcomes in two studies (Mueser 2015; Steel 2010) using the Brief Quality of Life Interview (QOLI by Lehman 1995) and the Quality of Life Scale (QoLS by Heinrichs 1984), respectively. Furthermore, overall functioning was evaluated with the Global Assessment of Function scale (GAF by Jones 1995) in both Mueser 2015 and Steel 2010. Mueser 2015 reported further on participants' social functioning using the CAPS-impact on social functioning subscale (Blake 1995). Participants' self-reported mental health and physical functioning were assessed with the Short Form-12 Mental Component and Physical Component respectively (SF12 by Ware 1994) in Mueser 2008.

6.1.3 Symptoms of co-morbid psychosis

Overall and specific psychotic symptoms were assessed as secondary outcomes in three included studies (Mueser 2015; Mueser 2008; Steel 2010). Two studies used the Positive and Negative Syndrome Scale (PANSS by Kay 1986) to assess psychiatric symptoms: Mueser 2015 reported the PANSS total for overall psychotic symptoms severity, the PANSS-positive subscale total for positive symptoms and PANSS-negative subscale total for negative symptoms whilst Steel 2010 reported only the PANSS-positive and -negative subscale totals. The Brief Psychiatric Rating Scale (BPRS by Lukoff 1986) was used by Mueser 2008 to assess overall psychiatric symptoms.

Furthermore, Steel 2010 also assessed specific psychotic symptoms, namely auditory hallucinations and delusions, using the Psychotic Symptom Rating Scale (PSYRATS by Haddock 1999) hallucinations and delusions subscale totals, respectively.

6.1.4 Depressive symptoms

Self-reported depressive symptoms were rated with the Beck Depression Inventory-II (BDI-II by Beck 1990) in three included studies as one of the secondary outcomes (Mueser 2015; Mueser 2008; Steel 2010).

6.1.5 Anxiety symptoms

Three studies (Mueser 2015; Mueser 2008; Steel 2010) reported anxiety symptoms as secondary outcomes and they all used the Beck Anxiety Inventory (BAI by Beck 1996).

6.1.6 Adverse events

van den Berg 2015 reported incidents of severe adverse events, however the nature of the adverse events was not made explicit apart from that they were reported as not related to the interventions trialled. Adverse events, if any, were not reported by the other studies.

6.1.7 Leaving the study early

All included studies reported a priori definition of treatment exposure (i.e. minimal sessions of treatment attended) and reported participants' dropout/attrition rate and loss to follow-up (Mueser 2015; Mueser 2008; Steel 2010; van den Berg 2015).

6.2 Redundant data

6.2.1 Satisfaction or perceived acceptability of treatment

In Steel 2010, participants' perceived acceptability of the TF-CBT was assessed by service user-led interview which implies qualitative data. However, as this study has not published to date, no data are yet available.

6.2.2 Understanding of PTSD

Participants' understanding of PTSD was measured by the PTSD Knowledge Test (Pratt 2005) in both studies led by Mueser (Mueser 2008; Mueser 2015). However, we had not planned to consider PTSD knowledge on its own without subsequent data on any impact of such on PTSD symptoms and/or related distress.

6.3 Missing data

None of the included studies reported health economic outcomes.

7. Follow-up

All studies reported follow-up at post treatment time point while the intervention duration varied across studies, from 10 weeks (van den Berg 2015) to six months (Mueser 2015; Mueser 2008; Steel 2010). Mueser 2015 and van den Berg 2015 collected follow-up outcomes measures up to 12 months post-intervention, although data reporting by van den Berg 2015 was limited to six-month follow-up at the time of data extraction for this review. Mueser 2008 and Steel 2010 followed up their participants for up to six months post-intervention.

Excluded studies

Studies excluded from the review are described in Characteristics of excluded studies section. These included nine full-text papers of four studies, which were examined but excluded at the end of the full-text screening stage, due to the study not using a randomised-controlled design (de Bont 2013), or the study participants not meeting the diagnostic threshold of PTSD (Jackson 2006; ISRCTN43816889; NCT00307216). de Bont 2013 was a feasibility study using a within-group controlled design to test the feasibility and safety of EMDR and prolonged exposure in people with co-morbid psychosis and PTSD. Jackson 2006 investigated the effectiveness of a form of cognitive therapy, which was called the 'recovery intervention', in promoting personal adjustment to psychosis and in reducing depression, trauma and other characteristic negative consequences of psychosis; participants were not assessed for having PTSD or not. ISRCTN43816889 tested the efficacy and safety of EMDR in patients with a psychotic illness but without a co-morbid PTSD. A manual-based individual therapy programme called 'The Gradual Recovery Intervention Programe' (GRIP) investigated by NCT00307216 also focused on individuals recovering from their first episodes of psychosis; no PSTD diagnosis was made.

Please note that Figure 1 - Study flow diagram relates to exclusion of full-text papers.

Studies awaiting assessment

No studies await assessment.

Ongoing Studies

We are not aware of any ongoing studies.

Risk of bias in included studies

Our overall impression of risk of bias in the included studies is represented in Figure 2 and Figure 3, whilst assessment of risk of bias of each included study is reported in Characteristics of included studies. Overall, the methodological quality of all the included studies is good, with clear reporting of the trial design and conduct (except Steel 2010 which was not yet published albeit unpublished outcome data were provided for this review). This suggests that the results can be considered to be at low to medium risk of bias, subject to the available data.

Figure 2. ‚Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

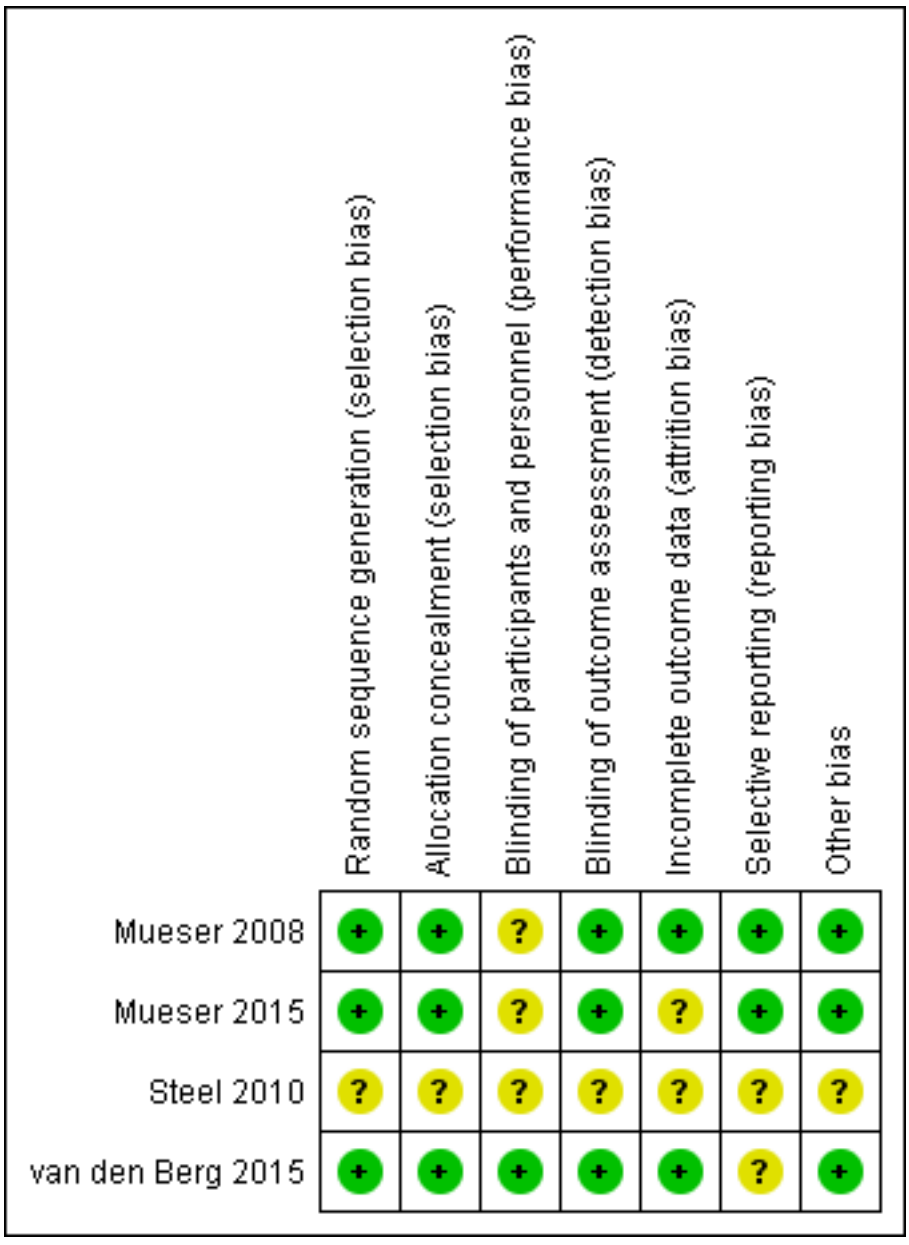
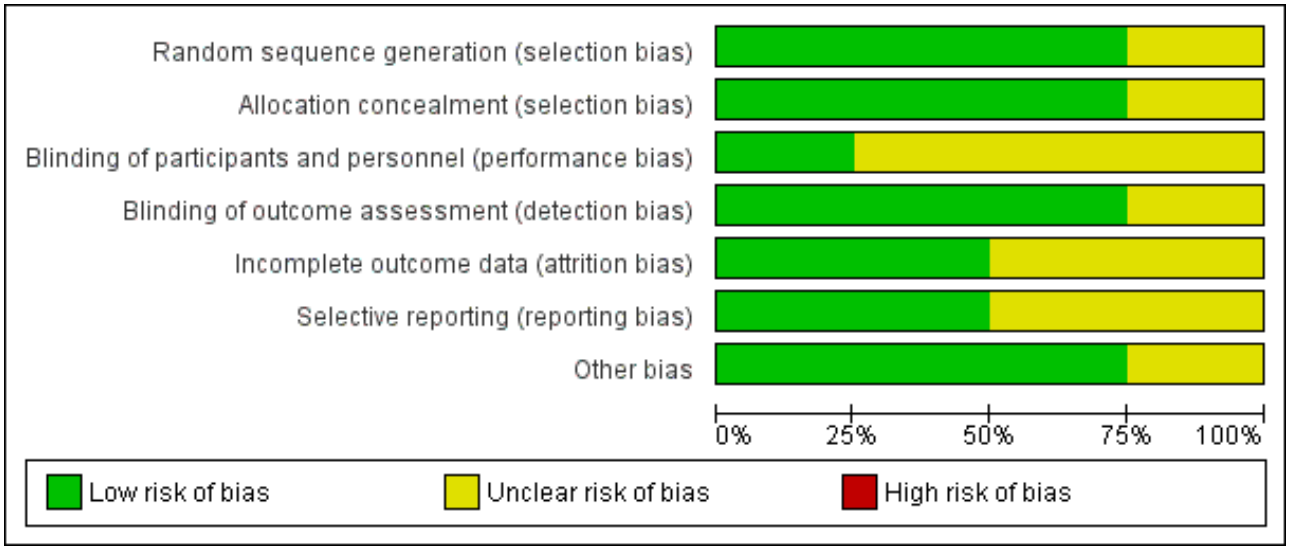


Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

All included studies were randomised controlled trials (RCTs). Apart from Steel 2010, all studies reported the randomisation method used, including the method used to generate the randomisation sequence and strategies to conceal allocation to outcome assessors and participants. It was not possible to obtain further information regarding randomisation methods for Steel 2010 as it was not published at the time of writing this review (i.e. July 2016). Hence, three studies (Mueser 2008; Mueser 2015; van den Berg 2015) were rated as being at low risk of bias and Steel 2010 was rated unclear.

Blinding

Three studies used waiting list or usual care as the comparison (i.e. Mueser 2008; Steel 2010; van den Berg 2015), making it impossible to blind the participants. Due to the design of the trials involving therapists delivering the trauma-focused psychological interventions and/or active control (i.e. brief PTSD-psychoeducation in Mueser 2015), it was not possible to blind the therapists either. Nonetheless, three studies reported clearly their use of blinded assessors for data collection to minimise detection bias (Mueser 2008; Mueser 2015; van den Berg 2015). van den Berg 2015 further described strategies to handle the few unblinding incidents enlisting another independent assessor to re-conduct the assessment, hence this study was rated as at low risk of bias. Both USA studies also reported training and monitoring of blinded assessors, hence we also rated them as at low risk (Mueser 2008; Mueser 2015). Due to inadequate detail, we rated Steel 2010 as at unclear risk.

Incomplete outcome data

All studies reported using intention-to-treat (ITT) method of analysis, except Steel 2010 which is due to limited data available at the time of writing this review. There was also clear reporting of the number of participants completing the treatment exposure (as required as defined a priori) across all studies. However, in two of the studies, these data were difficult to disentangle or were inconsistent. We therefore rated two studies as at low risk of bias (Mueser 2008; van den Berg 2015) and two at unclear risk of bias (Mueser 2015; Steel 2010).

Selective reporting

For all four included studies, we identified either a published trial protocol (i.e. de Bont 2013 for van den Berg 2015) and/or a detailed trial registration (Mueser 2008; Mueser 2015; Steel 2010). Three studies seemed to have reported all outcomes as specified in their study protocol and/or trial registration records (Mueser 2008; Mueser 2015; van den Berg 2015), although van den Berg 2015, which had recently published their six-month follow-up primary outcome results in the previous few months (i.e. e-publication in January 2015), has yet to report its 12-month follow-up results and the secondary to quaternary outcomes in due course. We therefore rated Mueser 2008 and Mueser 2015 as at low risk of bias whilst we rated van den Berg 2015 as at unclear risk of bias at this time. We were provided with unpublished results from Steel 2010, however, since this study was not published at the time of writing this review, we rated it as at unclear risk of bias.

Other potential sources of bias

All included studies provided information on funding sources and any potential conflict of interests. We identified no other potential sources of bias.

Effects of interventions

See: **Summary of findings for the main comparison** Individual TF-CBT compared to waiting list/usual care for PTSD and severe mental illness; **Summary of findings 2** EMDR compared to waiting list/usual care for PTSD and severe mental illness; **Summary of findings 3** Individual TF-CBT compared to EMDR for PTSD and severe mental illness; **Summary of findings 4** Individual TF-CBT compared to Brief PTSD psychoeducation for PTSD and severe mental illness

There are four comparisons, and results of data analyses are summarised below. See also Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3;

Summary of findings 4. Of note, as most of the continuous outcome data were found to be skewed (i.e. un-symmetrically distributed), we conducted analyses grouping unskewed data and skewed data separately (as outlined in Data extraction and management). In the 'Summary of findings' tables, we reported the pre-specified outcomes of interest (Types of outcome measures) whenever data were available, and priority was given to the analyses drawn using unskewed continuous data. In the event of no available analyses using unskewed data, we reported the analyses pooling skewed data and downgraded the quality of evidence.

Comparison 1: Individual trauma-focused cognitive behavioural therapy (TF-CBT) versus waiting list/usual care

Three studies including 178 participants in total contributed to this comparison (Mueser 2008; Steel 2010; van den Berg 2015). See also Summary of findings for the main comparison.

1.1 PTSD symptoms severity: 1a. Clinician-rated PTSD symptom severity - average endpoint CAPS total score (high = poor)

Three studies considered this outcome with a total of 178 individuals.

Short-term unskewed data from one study found no differences in symptom severity between groups (1 RCT, n = 13, mean difference (MD) 13.15, 95% confidence interval (CI) -4.09 to 30.39; *low-quailty evidence*, Analysis 1.1).

1.2 PTSD symptoms severity: 1b. Clinician-rated PTSD symptom severity - average endpoint CAPS total score (high = poor) - skewed data

Short-term skewed data from two studies reported data that showed no significant differences between TF-CBT and waiting-list control groups although there was high heterogeneity (2 RCTs, n = 147, MD -7.44, 95% CI -29.15 to 14.27, I^2 = 87%, Analysis 1.2).

Three studies reported medium-term skewed data. No effect between groups was found (3 RCTs, n = 155, MD -3.92, 95% CI -19.25 to 11.40, Analysis 1.2). There was high heterogeneity (I^2 = 63%),

1.3 PTSD symptoms severity: 2. Self-reported trauma-related cognitions - average endpoint Posttraumatic Cognitions Inventory (PTCI) total score (high = poor)

Three studies reported short-term outcome data, results were equivocal across groups (3 RCTs, n = 136, MD -5.45, 95% CI -33.61 to 22.70; I^2 = 76%) with high heterogeneity detected, however, medium-term data from three studies showed an effect for TF-CBT (3 RCTs, n = 133, MD -15.25, 95% CI -29.48 to -1.02). Analysis 1.3.

1.4 PTSD symptoms severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data

Only one study provided data which were skewed on this outcome. Both short-term (1 RCT, n = 86, MD -9.51, 95% CI -13.84 to -5.18) and medium-term at nine months (1 RCT, n = 85, MD -7.52, 95% CI -12.06 to -2.98) data show an effect for TF-CBT. Analysis 1.4.

1.5 PTSD symptoms severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40

Two studies reported remission from PTSD as measured by below CAPS cut-off score (i.e. <40). Both short-term and medium-term data favoured the TF-CBT group (short term: 2 RCTs, n = 113, risk ratio (RR) 1.99, 95% CI 1.20 to 3.30; medium term: 2 RCTs, n = 109, RR 1.44 95% CI 0.57 to 3.63; Analysis 1.5).

1.6 PTSD symptoms severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20

Only one study provided data on this outcome; recovery was defined as a CAPS total score below 20. The short-term results showed that more participants in the TF-CBT group had achieved full recovery from PTSD when compared with those in the waiting list group and the results were statistically significant (1 RCT, n = 100, RR 4.43, 95% CI 1.37 to 14.37). The medium-term data also favour the TF-CBT group with statistical significant results (1 RCT, n = 100, RR 4.14, 95% CI 1.27 to 13.51; Analysis 1.6).

1.7 Quality of life: 1. General quality of life - average endpoint QLS total score (high = good)

Only one study provided data (unskewed) on this outcome. Both the short-term (1 RCT, n = 38, MD -3.00, 95% CI -8.26 to 2.26) and medium-term results (1 RCT, n =39, MD -0.60, 95% CI -4.47 to 3.27) were equivocal across groups; low-quality evidence, Analysis 1.7.

1.8 Quality of life: 2. Overall functioning - average endpoint GAF total score (high = good)

Again, only one study reported data (unskewed) on this outcome. Neither the short-term (1 RCT, n = 44, MD 0.80, 95% CI -4.61 to 6.21); nor the medium-term (1 RCT, n = 46, MD 2.70, 95% CI -3.32 to 8.72) results showed any significant differences between groups; Analysis 1.8.

1.9 Quality of life: 3. Mental health functioning - average endpoint SF-12 mental component total score (high = good)

Short-term unskewed data from one study (1 RCT, n = 11, MD -9.89, 95% CI -23.35 to 3.57) showed no effect. Medium-term data were also equivocal across the TF-CBT and usual care groups (1 RCT, n = 9, MD 1.96 95% CI -28.15 to 32.07); Analysis 1.9.

1.10 Quality of life: 4. Physical functioning - average endpoint SF-12 physical component total score (high = good)

Again, only one study provided data (unskewed) for this outcome. We found no effect from data across short-term (1 RCT, n = 11, MD 1.32, 95% CI -16.35 to 18.99), and at medium-term follow-up (1 RCT, n = 9, MD -2.52, 95% CI -25.64 to 20.60). Analysis 1.10.

1.11 Symptoms of co-morbid psychosis: 1. Overall mental state - average endpoint BPRS total score (high = poor)

One study reported this outcome using the total BPRS scores; all data were unskewed. Results in the short term (1 RCT, n = 13, MD 1.00, 95% CI -9.96 to 11.96), and medium term (1 RCT, n = 9, MD -6.93 95% CI -34.17 to 20.31, *low-quality evidence)* were equivocal across groups. Analysis 1.11.

1.12 Symptoms of co-morbid psychosis: 2. Positive symptoms - average endpoint PANSS positive subscale total score (high = poor)

Unskewed data showed no significant differences between groups at short term (1 RCT, n = 61, MD -2.00, 95% CI -5.07 to 1.07), and at medium term (1 RCT, n = 61, MD -1.40, 95% CI -4.42 to 1.62). Analysis 1.12.

1.13 Symptoms of co-morbid psychosis: 3. Negative symptoms - average endpoint PANSS negative subscale total score (high = poor)

Again, only one study reported data on this outcome, all data were unskewed. Short-term data across the two groups were equivocal (1 RCT, n = 61, MD -1.40, 95% CI -4.19 to 1.39), as were the medium-term data (1 RCT, n = 61, MD -1.10, 95% CI -3.38 to 1.18). Analysis 1.13.

1.14 Symptoms of co-morbid psychosis: 4. Hallucinations - average endpoint PSYRATS-hallucinations subscale total score (high = poor) - skewed data

Short-term skewed data showed no significant differences between groups (1 RCT, n = 61, MD 2.80, 95% CI -3.88 to 9.48), nor the medium-term skewed data (1 RCT, n = 61, MD -0.30, 95% CI -7.48 to 6.88). Analysis 1.14.

1.15 Symptoms of co-morbid psychosis: 5. Delusions - average endpoint PSYRATS-delusions subscale total score (high = poor) - skewed data

Results between groups across short term (1 RCT, n = 61, MD -0.70, 95% CI -4.73 to 3.33) and medium term (1 RCT, n = 61, MD -2.30, 95% CI -6.22 to 1.62) were equivocal. Of note, all data were skewed. Analysis 1.15.

1.16 Anxiety symptoms - average endpoint BAI total score (high = poor)

One study reported unskewed data for this outcome. Both short-term (1 RCT, n = 13, MD 4.20, 95% CI -7.52 to 15.92) and medium-term (1 RCT, n = 9, MD 12.57, 95% CI -5.54 to 30.68, *very low-quality evidence*) unskewed data showed no significant differences between groups. Analysis 1.16

1.17 Anxiety symptoms - average endpoint BAI total score (high = poor) - skewed data

Another study presented skewed data for this outcome, again no effect between treatments was found at either short term (1 RCT, n = 35, MD 2.00, 95% CI -7.02 to 11.02) or medium term (1 RCT, n = 40, (MD -3.00, 95% CI -12.36 to 6.36). Analysis 1.17.

1.18 Depressive symptoms - average endpoint BDI-II total score (high = poor) - skewed data

Only skewed data from two studies were available for this outcome. No effect was found at short term (2 RCTs, n = 49, MD 1.31, 95% CI -5.81 to 8.44), or medium term (2 RCTs, n = 48, MD 3.26, 95% CI -3.66 to 10.18, *very low-quality evidence*). Analysis 1.18.

1.19 Adverse events - incidents of unspecified severe adverse events

Only one study reported incidents of unspecified severe adverse events, medium-term data were equivocal across TF-CBT and waiting-list control groups (1 RCT, n = 100, RR 0.44, 95% CI 0.09 to 2.31, *low-quality evidence*). These adverse events were specified as not related to the PTSD or psychotic symptoms. See Analysis 1.19.

1.20 Leaving the study early

Three studies with 178 participants in total provided attrition data. No differences in numbers of participants leaving the study early across groups were at short term (3 RCTs, n = 178, RR 0.74, 95% CI 0.38 to 1.44) or medium term (3 RCTs, n = 178, RR 0.80, 95% CI 0.46 to 1.40). Analysis 1.20.

2. Comparison 2: Eye movement desensitisation and reprocessing (EMDR) versus waiting list

Only one study with 102 participants compared EMDR with waiting-list control (van den Berg 2015), meta-analyses on outcomes were therefore not possible using the data. We report the analyses on all available outcome data below. See also Summary of findings 2 for main outcomes of interest.

2.1 PTSD symptoms severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data

All available data were skewed. Both short-term data (1 RCT, n = 83, MD -15.32, 95% CI -25.99 to -4.65) and medium-term data (1 RCT, n = 83, MD -12.31, 95% CI -22.72 to -1.90, *very low-quality evidence*) showed favourable effect for EMDR. Analysis 2.1.

2.2 PTSD symptoms severity: 2. Self-reported trauma-related cognitions - average endpoint PTCI total score (high = poor)

Data reporting this outcome were unskewed. Short-term data favoured EMDR (1 RCT, n = 83, MD -23.27, 95% CI -38.50 to -8.04) and these benefits seemed to be sustained at medium-term follow-up (1 RCT, n = 83, MD -20.66, 95% CI -36.72 to -4.60). Analysis 2.2 .

2.3 PTSD symptoms severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data

The EMDR group fared better in self-reported frequency of PTSD symptoms as measured by PSS-SR, across both short term (1 RCT, n = 83, MD -8.60, 95% CI -13.03 to -4.17) and medium term (1 RCT, n = 83, MD -7.37, 95% CI -12.17 to -2.57), although data reported were skewed. Analysis 2.3.

2.4 PTSD symptoms severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40

A favourable effect for EMDR compared to waiting list was found in both the short-term data (1 RCT, n = 102, RR 2.17, 95% CI 1.30 to 3.61), and the medium-term data (1 RCT, n = 102, RR 1.77, 95% CI 1.10 to 2.85). Analysis 2.4.

2.5 PTSD symptoms severity: 4. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20

There were no significant differences in numbers of participants achieved full recovery from PTSD across EMDR and waiting-list groups, both at short term (1 RCT, n = 102, RR 2.56, 95% CI 0.74 to 8.92) and medium term (1 RCT, n = 102, RR 2.28, 95% CI 0.64 to 8.10). Analysis 2.5.

2.6 Adverse events - incidents of unspecified severe adverse events

No adverse events were recorded at short term. Events were recorded at medium term, with equivocal numbers of adverse events reported across groups in medium term (1 RCT, n = 102, RR 0.21, 95% CI 0.02 to 1.85, *low-quality evidence*). Analysis 2.6.

2.7 Leaving the study early

Short-term data showed no significant differences in number of participants lost to follow-up between groups (1 RCT, n = 102,

RR 1.18, 95% CI 0.52 to 2.68). Equivocal attrition data were also reported at medium term (1 RCT, n = 102, RR 1.46, 95% CI 0.63 to 3.42). Analysis 2.7.

Head to head comparisons of specific category of trauma-focused psychological therapies

We made the following two specific comparisons and reported on primary outcomes only, as pre-specified in our protocol.

Comparison 3: TF-CBT (specifically prolonged exposure) versus EMDR

One study with 108 participants (van den Berg 2015) compared prolonged exposure (PE) therapy which was categorised as a type of TF-CBT (as defined a priori in Types of interventions) with EMDR. We report herewith the analyses on all the available review primary outcomes although meta-analyses were not possible. See also Summary of findings 3.

3.1 PTSD symptoms severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data

No significant differences was found between TF-CBT and EMDR groups based on the short-term data (1 RCT, n = 91, MD -2.94, 95% CI -13.13 to 7.25), as well as the medium-term data (1 RCT, n = 88, MD -1.69, 95% CI -12.61 to 9.23, *very low-quality evidence*). Of note, all available data were skewed. Analysis 3.1.

3.2 PTSD symptoms severity: 2. Self-reported trauma-related cognitions - average endpoint PTCI total score (high = poor)

Results were equivocal between the PE and EMDR groups, both in the short term (1 RCT, n = 91, MD -3.38, 95% CI -21.17 to 14.41) and in the medium term (1 RCT, n = 88, MD 2.05, 95% CI -16.69 to 20.79), based on unskewed data. Analysis 3.2.

3.3 PTSD symptoms severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data

There were no significant differences found between groups, both at short term (1 RCT, n = 91, MD -0.91, 95% CI -5.18 to 3.36) and at medium term (1 RCT, n = 88, MD -0.15, 95% CI -5.49 to 5.19). Of note, data reported were skewed. Analysis 3.3.

3.4 PTSD symptoms severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40

Data showed equivocal results across the PE and EMDR groups, at short term (1 RCT, n = 108, RR 0.94, 95% CI 0.69 to 1.30) and at medium term (1 RCT, n = 108, RR 1.04, 95% CI 0.75 to 1.44). Analysis 3.4.

3.5 PTSD symptoms severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20

Data showed equivocal results across groups, both at short term (1 RCT, n = 108, RR 1.73, 95% CI 0.83 to 3.61) and at medium term (1 RCT, n = 108, RR 1.82, 95% CI 0.83 to 3.97). Analysis 3.5.

Comparison 4: TF-CBT versus brief PTSD psychoeducation

One study compared TF-CBT with brief PTSD psychoeducation (Mueser 2015). We report the analyses on available primary outcomes below although meta-analyses were not possible. See also Summary of findings 4.

4.1 PTSD symptoms severity: 1a. Clinician-rated severity - average endpoint CAPS total score (high = poor)

Short-term unskewed data (1 RCT, n = 54, MD -1.45, 95% CI -14.63 to 11.73) were equivocal across groups as were the medium-term unskewed data (1 RCT, n = 52, MD 0.23, 95% CI -14.66 to 15.12, *low-quality evidence*) Analysis 4.1.

4.2 PTSD symptoms severity: 1b. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data

Long-term skewed data (1 RCT, n = 48, MD -2.13, 95% CI -19.45 to 15.19) also showed no significant differences across groups. Analysis 4.2.

4.3 PTSD symptoms severity: 2. Self-reported trauma-related cognitions - average endpoint PTCI total score (high = poor)

Unskewed data across short term (1 RCT, n = 53, MD 1.64, 95% CI -24.40 to 27.68), medium term (1 RCT, n = 51, MD 7.68, 95% CI -18.64 to 34.00) and long term (1 RCT, n = 49, MD 16.19, 95% CI -10.45 to 42.83) were equivocal across the two treatment groups. Analysis 4.3.

4. 4 PTSD symptoms severity: 3. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40

The data showed no significant differences across groups at short-term (1 RCT, n = 54, RR 1.04, 95% CI 0.47 to 2.30), at medium-term (1 RCT, n = 52, RR 2.00, 95% CI 0.79 to 5.05), and at long-term follow-up (1 RCT, n = 48, RR 1.14, 95% CI 0.49 to 2.65). Analysis 4.4.

4.5 PTSD symptoms severity: 4. Remission from severe PTSD: Loss of severe PTSD diagnosis - CAPS total scores < 65

The results were equivocal across the two treatment groups, at short-term (1 RCT, n = 54, RR 1.21, 95% CI 0.64 to 2.26), at medium-term (1 RCT, n = 52, RR 1.56, 95% CI 0.82 to 2.94), and at long-term follow-up (1 RCT, n = 48, RR 1.30, 95% CI 0.71 to 2.37). Analysis 4.5.

4.6 Quality of life: 1. General quality of life - average endpoint QoLI total score (high = good)

We found no significant differences between the two treatment groups, at short term (1 RCT, n = 54, MD -0.58, 95% CI -1.35 to 0.19), at medium term (1 RCT, n = 52, MD -0.29, 95% CI -1.03 to 0.45), and at long term (1 RCT, n = 49, MD 0.11, 95% CI -0.74 to 0.96, *low-quality evidence*). Analysis 4.6.

4.7 Quality of life: 2. Overall functioning - average endpoint GAF total score (high = good)

No significant differences were found between groups based on short-term data (1 RCT, n = 49, MD -0.86, 95% CI -6.48 to 4.76), medium-term data (1 RCT, n = 50, MD 0.60, 95% CI -4.92 to 6.12); and long-term data (1 RCT, n = 48, MD 1.88, 95% CI -4.93 to 8.69). All data reported were unskewed. See Analysis 4.7.

4.8 Quality of life: 3. Social functioning - average endpoint CAPS social functioning subscale total score (high = poor) - skewed data

We found no significant differences in this outcome across groups (short term: 1 RCT, n = 54, MD -0.29, 95% CI -0.86 to 0.28; medium term: 1 RCT, n = 52, MD -0.61, 95% CI -1.28 to 0.06; long term: 1 RCT, n = 48, MD 0.19, 95% CI -0.46 to 0.84). Data reported were skewed. Analysis 4.8.

Subgroup analyses

No subgroup analyses were conducted on the two pre-specified factors (see Subgroup analysis and investigation of heterogeneity), due to the following reasons.

1. Participants' characteristic, i.e. by age - adults versus adolescents

All included studies recruited adults aged 18 or above. No data were available on adolescents.

2. Clinical characteristics, i.e. by types of trauma

Data on types of trauma experienced by study participants were reported on sample and group levels, but not available on an individual level, to allow for such a subgroup analysis. Furthermore, in all four included studies, it was reported that participants with co-morbid SMI and PTSD commonly experienced multiple traumas, which were often a combination of childhood and adult traumatic events, with the nature of the trauma spanned across conventional events (such as interpersonal violence) and SMI symptom-related experience (e.g. persecutory delusion). These findings raised queries over the feasibility and appropriateness of categorically delineating types of trauma experienced by individuals with such co-morbid conditions and complex presentations. It also raised challenges in our attempt to estimate participants' overall and specific responsiveness to trauma-focused psychological treatment based on types of trauma experienced, even if the individual-level data were available.

Sensitivity analysis

Apart from Comparison 1 (TF-CBT versus usual care/waiting list), which included three studies, the other three comparisons included only one study each which rendered sensitivity analysis impossible.

Overall, all four studies included in the various analyses were of good methodological quality (see Assessment of risk of bias in included studies) and therefore even for Comparison 1, there was no need to undertake a sensitivity analysis based on the following.

1. Implication of randomisation - all included studies were clearly randomised controlled trials.

2. Assumptions for lost binary data - the quantity of included study data lost to follow-up was small (i.e. no studies reported over 50% of missing data).

3. Risk of bias - no included studies were judged to be of high risk of bias.

4. Imputed values - we were provided with the raw data by the trial authors of all four included studies, hence we had not used imputed values for various analyses.

Lastly, regarding meta-analyses using fixed-effect and random-effects models - we had used primarily the random-effects model for analyses when data from more than one study were included; whereas the fixed-effect model was used in analyses when only data from one study were included.

When preparing the 'Summary of findings' tables summarising the pre-specified outcomes together with their respective overall rating of quality of evidence, we prioritised reporting the analyses based on unskewed data (of continuous outcome measures). In the absence of analyses based on unskewed data, we reported analyses based on skewed data with the quality of evidence downgraded.

DISCUSSION

Four randomised controlled trials (RCTs) involving 300 participants were included in this review to investigate the effectiveness of trauma-focused psychological therapies for individuals with both severe mental illness (SMI) and post-traumatic stress disorder (PTSD). We conducted four comparisons to assess the effectiveness of three specific modalities of PTSD psychological interventions, namely: trauma-focused cognitive behavioural therapy (TF-CBT) (including prolonged exposure); eye movement desensitisation and reprocessing (EMDR); and brief PTSD psychoeducation. We have created a "Summary of Findings" table for each of the comparisons (Summary of findings for the main comparison; Summary of findings 2; Summary of findings 3; Summary of findings 4) and the main results are discussed below.

Summary of main results

Trauma-focused cognitive behavioural therapy (TF-CBT)

We included four studies (Mueser 2008; Mueser 2015; Steel 2010; van den Berg 2015) reporting on three specific TF-CBT programmes in this review. The three TF-CBT programmes ranged from a 'prolonged exposure' intervention delivered over eight sessions within a 10-week duration (van den Berg 2015), a 12-to 16-week CBT programme emphasising on cognitive restructuring (Mueser 2015), and a similar 12- to 16-week CBT for PTSD programme with the initial few sessions focusing on psychoeducation and breathing retraining (Mueser 2008 and Steel 2010 whose study adopted the Mueser 2008 CBT treatment manual).

Three studies provided data for comparing individual TF-CBT against non-active control condition, i.e. usual care or waiting-list control (Mueser 2008; Steel 2010; van den Berg 2015). Some continuous outcome data were found to be skewed, and hence meta-analyses grouping unskewed and skewed data separately were conducted on continuous outcome measures whenever both types of data were present. In terms of clinician-rated PTSD symptom severity as measured by Clinician Administered PTSD Symptom Scale (CAPS) total score, only one study including 13 individuals with co-morbid PTSD and SMI (Mueser 2008) reported short-term unskewed data, and these limited results were equivocal across the two groups. Further available data from the other two studies were skewed, but also showed no effect between treatment groups at either short or medium term. Data on self-reported PTSD symptom severity as measured by Post Traumatic Cognitions Inventory (PTCI) total scores were unskewed: short-term outcomes were equivocal across groups although follow-up data at medium term from three studies showed a favourable effect for TF-CBT. Meta-analyses pooling binary data from two included studies (Mueser 2008; van den Berg 2015) that reported the number of participants scoring below 40 on CAPS, provided some preliminary and low-quality evidence (2 RCTs, n = 113) that TF-CBT is more effective than usual care/waiting list in reducing participants' PTSD symptoms to the sub-threshold level leading to remission from PTSD (or loss of PTSD diagnosis) in both short and medium terms. Only one study (van den Berg 2015), reported full recovery from PTSD using a CAPS cut-off score of < 20, and there was some limited and very low-quality evidence favouring TF-CBT in promoting full recovery from PTSD at medium term (1 RCT, n = 100). Only one study

provided data for the remaining primary outcomes focusing on quality of life, and secondary outcomes, hence meta-analysis was not possible. In terms of secondary outcomes, it was not clear from the available data if TF-CBT had any advantages than waiting list or usual care, over a range of general psychiatric symptoms, specific psychotic symptoms, affect or anxiety manifestation. Only one study (van den Berg 2015) reported incidents of unspecified severe adverse events; no significant differences were found between TF-CBT and waiting-list groups. In terms of tolerability of interventions, overall loss to follow-up was equivocal across TF-CBT and usual care/waiting-list groups, as shown by low-quality evidence (3 RCTs, n = 178) throughout the short- to medium-term follow-up.

Only one study compared prolonged exposure therapy against EMDR with 108 individuals with a chronic psychotic disorder and PTSD (van den Berg 2015). Whilst it was not possible to undertake meta-analyses, the study data indicated that outcomes of patients receiving TF-CBT or EMDR did not differ significantly across a range of outcomes focusing on PTSD symptoms.

Another study compared TF-CBT against brief PTSD psychoeducation (Mueser 2015). The results showed no significant differences between the two PTSD psychological therapies in terms of their impacts on patients' PTSD symptoms severity, quality of life and related functioning.

Eye movement desensitisation and reprocessing (EMDR)

We identified one study that compared EMDR against a waiting list as well as against TF-CBT (van den Berg 2015). Meta-analyses were not feasible. Comparing EMDR with waiting list (1 RCT, n = 83), there was some very low-quality evidence indicating that EMDR was much more effective in reducing PTSD symptoms whether they were measured with clinician-rated tools or self-reported cognitions and frequency assessment (of note, continuous outcome data available were skewed). A statistically significant higher number of participants receiving EMDR achieved remission from PTSD (i.e. loss of PTSD diagnosis as defined by a CAPS total score < 40) at short and medium term, respectively, although there was no significant differences in terms of numbers of participants achieving full recovery from PTSD (i.e. CAPS < 20) across EMDR and waiting list. The remaining data indicated equivocal results across EMDR and waiting-list groups in terms of loss to follow-up and unspecified severe adverse events.

The same study also compared EMDR with TF-CBT (van den Berg 2015) and its results suggested both interventions were equivocal in their effectiveness in reducing PTSD symptom severity, as aforementioned. No data were available on other outcomes.

Brief PTSD Psychoeducation

A three-session PTSD psychoeducation programme (Pratt 2005) was identified as an alternative modality of trauma-focused psychological intervention by this review. Only one trial (1 RCT, n = 67) compared TF-CBT head to head with brief PTSD psychoeducation as an active control (Mueser 2015). There was no clear evidence that brief PTSD psychoeducation was either better or worse than TF-CBT across a range of PTSD symptom severity and quality of life outcomes.

Overall completeness and applicability of evidence

Completeness

Our search identified 35 unique titles and abstracts initially. We inspected all of them and contacted a number of authors known to have conducted trials in this field for further unpublished and/or ongoing study data. We also consulted a number of trial authors to establish if their studies targeted people with PTSD or not as sometimes the PTSD diagnostic thresholds used were not clearly described. Many studies implied specially developed psychological therapies focusing on trauma and/or trauma-related experience and sequelae in association with psychotic illness experience and/or other life events (e.g. Jackson 2006; NCT00307216) without establishing if the participants met the diagnostic threshold for PTSD or not. With assistance from the trial authors who provided us with unpublished and/or psychosis data, we were able to include four studies investigating the effects of trauma-focused psychological therapies for people with co-morbid psychosis and PTSD - one newly published online in the beginning of 2015 (van den Berg 2015); one unpublished (Steel 2010); and two studies which originally reported data of participants with psychosis together with others diagnosed with non-psychotic disorder as their primary diagnosis (Mueser 2008; Mueser 2015). Nonetheless, these translate into three studies which were included in the comparison of TF-CBT with usual care/waiting list; and only one study for each of the other comparisons: EMDR with waiting list; TF-CBT with EMDR; and TF-CBT with psychoeducation.

Our pre-specified review primary outcome focusing on PTSD symptoms (severity) was reported by the four included studies using well-established PTSD symptom severity measures, such as CAPS (Blake 1995) and PTCI (Foa 1999). However, we detected skewness in many outcome data reported by continuous measures, which limited the scope of analyses. To avoid the pitfall of applying parametric tests to non-parametric data, we performed analyses grouping the unskewed and skewed data separately and reported these analyses accordingly. We reported the analyses based on unskewed data primarily in the 'Summary of findings' tables, but in the event of no such analyses were available, we reported the analyses drawing on skewed data and downgraded the evidence. When the data were reported as binary outcomes (such as remission or recovery from PTSD as defined by various cut-off of CAPS scores), we reported the risk ratios. The other primary outcome focusing on quality of life/well-being had relatively much less data available; and often limited data from solely one study rendered meta-analysis impossible. This problem also applied to the secondary outcomes including psychotic symptoms and other common concurrent symptoms such as depression and anxiety, whereas continuous outcome data (and often skewed) from one study only were available, limiting the scope and extent of analyses. Unfortunately, there was a distinct lack of data on health economic outcomes.

Lastly, as this review includes a couple of newly emerging trials (Steel 2010; van den Berg 2015), we expect further follow-up data will become available in due course.

Inclusion of trials for this systematic review entailed that study participants reach diagnostic thresholds for both SMI and for PTSD, however it is likely that many of those with SMI have troublesome symptoms relating to trauma without reaching the threshold for a PTSD diagnosis. The automatic exclusion of studies evaluating the

effectiveness of psychological interventions for this population is a limitation of this current review. Another possible limitation is that only trauma-focused therapies were evaluated. It is theoretically possible that other psychological therapies have some efficacy for post-traumatic symptoms even if not specified as such.

Applicability

This review identified four RCTs investigating the effectiveness, acceptability and safety of PTSD psychological treatment, in particular TF-CBT and EMDR, for individuals with co-morbid SMI and PTSD, a population commonly excluded from studies focusing on the general population with PTSD (Bisson 2013; Morrison 2003; NICE 2014). The average profile of the study participants reflects the complexity (such as multiple trauma ranging from childhood to adulthood traumatic experiences) and history of long-standing illness-presentation (such as a life-long diagnosis of psychotic disorder in van den Berg 2015 and severe PTSD in Mueser 2015) of the co-morbid population. All the included studies recruited participants from the community care settings targeting those receiving routine mental health service, with the PTSD psychological therapies delivered in an outpatient clinic setting. These review findings suggest that individual TF-CBT including prolonged exposure and EMDR, can potentially be a feasible and safe evidence-based treatment for the co-morbid group, as for the general population as recommended by several systematic reviews and treatment guidelines (ACPMH 2013; Bisson 2013; NICE 2005; NICE 2013).

There are only data from one study for comparing EMDR with waiting list and the head-to-head comparisons of trauma-focused therapies. This has precluded meta-analyses. While results showed that EMDR was superior than waiting list in reducing PTSD symptom severity, the analyses of the primary outcomes were largely equivocal across TF-CBT versus EMDR, and, TF-CBT versus brief psychoeducation. These analyses with limited data should be interpreted with caution, preliminary evidence of comparative effectiveness of TF-CBT, EMDR and brief psychoeducation is still outstanding.

Meanwhile, we identified further factors which may affect the generalisability of the preliminary findings to routine clinical settings. All included studies reported provision of training and ongoing supervision for therapists who were highly skilled in delivering the treatment manuals with specific considerations to the participants' complex presentations. Examples included an initial phase of breathing retraining and psychoeducation in the studies conducted in the USA and the UK (Mueser 2008; Mueser 2015; Steel 2010), and assessment for treatment adherence to the protocol (Mueser 2015; van den Berg 2015). In addition, all participants who received an intervention also received usual care, which frequently included receipt of multiple services (such as community outreach services, case/care management, psychiatric out-patient follow-up and medication treatment), and so it is not possible to determine from this review the effectiveness of trauma-focused psychological interventions for this co-morbid patient group, in the absence of support from a multi-disciplinary mental health service. All the included studies were conducted in the USA and Europe, therefore the results may have limited generalisability to the countries where the systems for delivering mental health care are substantially different.

Quality of the evidence

Apart from Comparison 1 (comparing TF-CBT with usual care/ waiting list) which included three studies, the other three comparisons included only one study respectively, rendering limited data available and precluding meta-analysis of a number of outcomes. Analyses, with data from a small number of studies and/or participants, should be interpreted with caution, as quite likely, such results are under-powered. Also, it is worth noting that continuous outcome measures were used to report a good proportion of outcomes which may make interpretation of the differences in score points into clinically meaningful or significant changes difficult (e.g. mean difference between groups, or differences of scores across time points versus recovery). Furthermore, much of the continuous data available for the analyses were found to be skewed, with the study sample size relatively small (n < 200) (Moore 2010), further limiting the scope and extent of analyses on outcomes even when data from more than one study were available. We had taken the approach to pooling skewed and unskewed continuous data separately into meta-analyses, reporting the analysis results separately and prioritising those based on unskewed data. However, in doing so to avoid the pitfall in combining parametric and non-parametric data together and applying parametric tests on such data, we might have further diffused the already relatively limited data. Hence, the quality of evidence was often rated as low; and on occasions where only analyses based on skewed data were reported in the 'Summary of findings' tables, we had further downgraded the quality of evidence. In view of these problems with the data available, we suggest further updated reviews may consider prioritising the reporting of binary outcomes, such as remission from PTSD.

Potential biases in the review process

We believe the process of searching for studies was thorough. We followed the review protocol strictly in the process of selecting studies for inclusion, data extraction and analysis. In addition, we also contacted a number of trial authors to seek unpublished and subgroup data specific to patients with co-morbid psychosis and PTSD. We were pleased to have received assistance from many authors who provided further data and clarification on their study design, outcome data and treatment content. Despite the small number of trials included in this review, we were pleased to have been able to include some newly emerging studies. We fully acknowledge the potential conflict of interests which might arise as one of our review authors (JS) was a trial therapist in one of the included trials (Steel 2010); we took steps throughout the review process to remove JS from the screening of search results, data extraction, 'Risk of bias' assessment and data input procedures involving this study.

Agreements and disagreements with other studies or reviews

NICE published a systematic review on the effectiveness of psychological interventions for trauma in people with psychosis, integral to its guideline recommendations on treatment provision for psychosis and schizophrenia (NICE 2014). Only one study was included in the NICE review whose search was undertaken in June 2013: Jackson 2006 devised a specific form of cognitive therapy called "cognitive recovery therapy" and investigated its effectiveness in reducing post-psychotic trauma symptoms, with

the primary outcomes of treatment identified as trauma symptoms, depression, and self-esteem. We had to exclude this study from our review as no PTSD diagnostic threshold was applied to the participants although some might have reached such a threshold if assessed. No other systematic reviews focusing on trauma-focused psychological interventions for the co-morbid population were identified.

Overall, this review identified some limited preliminary, albeit low-quality, evidence that supports the safety and feasibility of TF-CBT for treating PTSD in individuals with psychosis. Existing systematic reviews on psychological therapies for PTSD (e.g. Bisson 2013; Bradley 2005) and current clinical practice guidelines recommend TF-CBT (including exposure therapy) and/or EMDR as an evidence-based treatment for PTSD resulting from single-event trauma in adulthood (ACPMH 2013; NICE 2005; NICE 2013). However, there is insufficient high-quality evidence to determine the effectiveness of TF-CBT for people with co-morbid SMI and PTSD. This review also identified the first study which investigated the effectiveness and safety of EMDR for the co-morbid population (van den Berg 2015). EMDR was found to be more beneficial than usual care/waiting list and equivocal to TF-CBT for individuals with PTSD and psychosis, whilst there were no significant differences reported in adverse events, dropout or loss to follow-up. The findings of this study suggest that EMDR could potentially be applicable and feasible for people with SMI. Finally, this review also compared brief PTSD psychoeducation with TF-CBT using psychosis data from one study (Mueser 2015), although PTSD psychoeducation is not commonly recommended for PTSD in the general population.

AUTHORS' CONCLUSIONS

Implications for practice

For people with co-morbid psychosis and post-traumatic stress disorder (PTSD)

Existing reviews support the effectiveness of trauma-focused cognitive behavioural therapy (TF-CBT) and eye movement desensitisation and reprocessing (EMDR) for PTSD in the general population. TF-CBT and EMDR may be more effective than usual care in promoting recovery from PTSD in the medium term; however the evidence for this is drawn from one or two trials in which all participants also received support from multi-disciplinary mental health services rather than trauma-focused psychological interventions (TFPIs) alone. Due to the limited data available from the few studies carried out to date, the review findings on TF-CBT and EMDR, in terms of their effect on PTSD symptoms, psychotic and other mood and anxiety symptoms remain inconclusive. The evidence-base and availability of TFPIs should be made known to service users who could use this to consider and access treatment.

For clinicians

Clinicians should be alerted to the potentially increased risk of co-morbidity of PTSD and SMI. Increased knowledge in working with the co-morbid illnesses should enhance clinicians' understanding of the often complex presentations of symptoms and needs of service users. This increased awareness may optimise the timely and early assessment of PTSD among people with psychosis. This review has provided some preliminary and limited evidence for the feasibility and safety of TF-CBT and EMDR for individuals with SMI and PTSD, although its effectiveness on improving PTSD, psychotic and other symptoms remain unclear. Clinicians should consider these treatments for mental health service users on an individual basis, as an adjunct to support from a multi-disciplinary mental health service.

For policy makers

Although this review provides some preliminary albeit low-quality evidence on the feasibility and safety of TF-CBT and EMDR, targeting service users with SMI and PTSD, the results of treatment effect on PTSD, psychotic and other symptoms are largely equivocal. Due to a small number of studies of the effects of TFPIs for this co-morbid population, there were limited data, often from only one study, available for the outcomes under investigation for each modality of therapy. Meta-analysis was precluded on many outcomes, and the few analyses undertaken likely lack power. Given that people with SMI require support from multi-disciplinary mental health services, it would be unwise to rely upon evidence from existing reviews of TF-CBT for the general population to guide treatment of people with co-morbid SMI and PTSD. Thus more research is needed of the effectiveness of TFPIs for people with SMI and PTSD to establish the clinical and cost-effectiveness of the intervention with this co-morbid client group.

Implications for research

In general, this review shows that there is a lack of studies exploring PTSD psychological treatment for people with SMI, contrary to their increased vulnerability to developing PTSD and the implications of untreated PTSD in their general prognosis. Despite the small number of trials included in this review, we were pleased to have been able to include three emerging trials (Mueser 2015; Steel 2010; van den Berg 2015), which reflect a significant increase of research and clinical interests in this subject over the recent years. The preliminary findings from the few pioneering trials, need support from further studies including sample sizes powered to detect clinically significant changes in PTSD symptoms and quality of life/well-being in individuals with SMI and PTSD. We expect to see further long-term follow-up data from the included studies alongside other new studies in the coming years which will help expand the evidence base of TFPIs for the co-morbid populations. In addition to extending the follow-up duration to provide data on long-term effects of treatments, future studies should also strive to explore health economic outcomes to inform cost-effectiveness of treatment and policy development.

As most of the included studies focused on people with long-standing psychotic disorders and chronic and/or severe PTSD (e.g. onset of PTSD = 17 years in van den Berg 2015; the average age of participants was mid-40s in Mueser 2008, Mueser 2015, and van den Berg 2015), such patient profiles raise some suggestions for future research. More research efforts focusing on younger people with early-onset psychosis and/or more timely-diagnosed PTSD are needed. It is pertinent to investigate whether the treatment effects identified by this review (when the interventions were applied to a sample with relatively chronic illnesses) will fare equally well for those who have a more recent onset of psychosis and/or PTSD. It is also worthwhile to investigate if the interventions apply effectively in those with SMI and trauma symptoms which may not necessarily meet the diagnostic threshold of PTSD.

While there remains much need for further studies to explore different modalities of PTSD treatment and the optimal adaptation of well-established therapies to suit the complex needs of

individuals with SMI, more comparison studies of one type of psychological therapy against another will also enhance our understanding of comparative effectiveness of different treatments so to promote treatment options and choices for service users and clinicians (NICE 2011; Roth 2005). Future research should also focus on establishing effective training of therapists using various treatment protocols and large-scale implementation of the evidence-based psychological treatment of PTSD for people with SMI, in order to widen provision of treatment.

We suggest an outline design for future trials in Table 1.

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The Cochrane Schizophrenia Group Editorial Base in Nottingham produces and maintains standard text for use in the Methods section of their reviews. We have used this text as the basis of what appears here and adapted it as required.

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CHARACTERISTICS OF STUDIES

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

Mueser 2008

Methods	Allocation: randomised, using a computer-based randomisation programme. Blindness: single-blind (assessor blind). Duration: 4 to 6 months. Setting: community (New Hampshire and Vermont, USA).
Participants	Diagnosis: schizophrenia or schizoaffective disorder (DSM-IV) and co-morbid or current PTSD (assessed with SCID-I for DSM-IV). In addition, PTSD diagnoses and symptom severity based on CAPS (at least CAPS minimum total score of 65) N = 108*. Age: 25 - 57 years (mean ˜ 43.47 years, SD 9.07 years) Sex: 23 M, 85F * Excluded: people with recent psychiatric hospitalisation or suicidal attempt within the past three months; and current DSM-IV diagnosis of substance dependence
Interventions	1. CBT for PTSD programme + TAU: CBT programme: 12 to 16 sessions following a structured format inclusive of handouts, worksheets, and homework assignments. Sessions cover: treatment overview, psychoeducation, breathing retraining and cognitive restructuring as from the sixth sessions. Programme design based on an earlier pilot study focusing on CBT treatment of the co-morbid population (Rosenberg 2004).Treatment exposure was defined a priori as completion of at least six sessions including a minimum of three sessions of cognitive restructuring. N = 54 (n = 10 with PTSD and schizophrenia/schizoaffective disorder)* 2. TAU: usual comprehensive treatment the participants had been receiving for their mental illness, based at local community mental health centre prior to their enrolment in the trial. TAU usually included pharmacological treatment and monitoring, case management, supportive counselling, and access to psychiatric rehabilitation programmes such as vocational rehabilitation. N = 54 (n = 7 with PTSD and schizophrenia /schizoaffective disorder)*

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Xia J, Adams CE, Bhagat N, Bhagat V, Bhoopathi P, El-Sayeh H, et al. Loss to outcomes stakeholder survey: the LOSS study. *Psychiatric Bulletin* 2009;**33**(7):254-7.

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Sin 2015

Sin J, Spain D, Furuta M, Murrells T, Norman I. Psychological interventions for post-traumatic stress disorder (PTSD) in people with severe mental illness. *Cochrane Database of Systematic Reviews* 2015, Issue 1. [DOI: 10.1002/14651858.CD011464]

* Indicates the major publication for the study

Mueser 2008 *(Continued)*

Outcomes	PTSD symptom severity: clinician-rated severity (CAPS), self-reported trauma-related cognition (PTCI), remission from PTSD (CAPS) Quality of life: self-reported mental health functioning (SF-12), self-reported physical functioning (SF-12) Symptoms of co-morbid psychosis: overall mental state (BPRS) Depressive symptoms (BDI-II) Anxiety symptoms (BAI) Leaving the study early Unable to use - Understanding of PTSD: assessed with PKT (outcome not specified in the review protocol) Therapeutic alliance between patient and case manager: rated with client version of WAI (outcome not specified in the review protocol)
Notes	* We only used data from the 17 participants (5M, 12F) with co-morbid PTSD and schizophrenia/schizoaffective disorder. Other participants were diagnosed with concurrent PTSD and a severe mental illness (major depression, bipolar disorder, schizophrenia or schizoaffective disorder) and persistent impairment in the areas of work, school or ability to care for oneself.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation method clearly stated, i.e. computer-based randomisation programme which stratified the randomisation by four recruitment sites and three board diagnostic groups. In addition, to balance the number of participants randomised to the two treatment arms, randomisation was conducted in blocks of four within each of the 12 strata.
Allocation concealment (selection bias)	Low risk	All research staff and therapists providing the CBT programme were unaware of assignments in advance; participants informed of allocation by the project co-ordinator.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Given the study design, both therapists and participants could not be blinded to the treatment allocation.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded assessors, who had no involvement and knowledge of participants' allocation, were used to collect participants' outcomes at all time points. Regardless of their treatment allocation, all participants provided with follow-up appointments according to the CBT treatment schedule.
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete data.
Selective reporting (reporting bias)	Low risk	All outcomes, as stated in the protocol and the papers, were consistently reported.
Other bias	Low risk	None noted. Treatment fidelity of the CBT programme was monitored with 15% of all sessions randomly selected for fidelity monitoring.

Mueser 2015

Methods	Allocation: randomised, using a computer programme Blindness: single-blind, using independent interviewers masked to treatment assignment Duration: 12 to 16 week CBT programme, with + 6 and 12 month-follow-up. Setting: community (in states of New Jersey, USA)
Participants	Diagnosis: schizophrenia or schizoaffective disorder (DSM-IV), and current severe PTSD (CAPS minimum total score of 65) N = 201* Age: mean ˜ 43.7 years, (SD 11 years)* Sex: 63 M 138 F (26 M; 41 F)* Excluded: patients with recent psychiatric hospitalisation or suicidal attempt or substance dependence within the past three months
Interventions	1. CBT for PTSD programme + TAU: 12 to 16 sessions individual CBT programme specially designed and adapted to accommodate the unique challenges of people with SMI, such as psychotic symptoms, cognitive impairment and high levels of stress vulnerability (Mueser 2008; Mueser 2009). The CBT programme included three sessions teaching breathing retraining for anxiety and education about trauma and PTSD, followed by nine to 13 sessions of cognitive restructuring. Treatment exposure was a priori defined as completion of at least six sessions. TAU included usual pharmacological treatment, case management and access to a range of available services within the participants' treatment setting such as individual psychotherapy and vocational rehabilitation excluding intervention specifically targeting PTSD. N = 104 (n = 32 with PTSD and schizophrenia or schizoaffective disorder)* 2. Brief PTSD psychoeducation programme + TAU: A three-session brief treatment programme for PTSD adapted from an earlier PTSD-psychoeducation programme developed by the trial team (Pratt 2005). This brief programme was designed to provide the same breathing retraining and education components as the CBT programme, using the same handouts and worksheets and a video to initiate discussion between the patient and therapist about the causes and nature of PTSD. There was no content on cognitive restructuring in the three-session programme. Treatment exposure was defined a priori as completion of at least two sessions. TAU is same as aforementioned. N = 97 (n = 35 with PTSD and schizophrenia or schizoaffective disorder)*
Outcomes	PTSD symptom severity: clinician-rated severity (CAPS), remission from PTSD (CAPS), self-reported trauma-related cognition (PTCI). Quality of life: overall quality of life (QOLI), overall functioning (GAF), social functioning (CAPS-social functioning). Unable to use - Understanding of PTSD: assessed with average endpoint score of PKT (outcome not specified in the review protocol). Leaving the study early: no data available for the psychosis-specific sample.
Notes	*We could only use data from 67 participants (mean age ˜ 43.4 years, SD 12 years) (26 M, 41 F) with co-morbid PTSD and schizophrenia or schizoaffective disorder out of a total of 201 participants. Other participants were diagnosed with concurrent PTSD and a severe mental illness as defined by the State of New Jersey, USA (i.e. DSM-IV diagnosis of major depression, bipolar disorder, schizophrenia or schizoaffective disorder and significant functional limitations in major life activities within the past three to six months because of the mental disorder and had been receiving supportive services for more than two years).
Risk of bias	

Mueser 2015 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation method was clearly stated, i.e. operated by a computer randomisation programme operated by an off-site data manager which stratified the randomisation by five recruitment sites and three board diagnostic groups.
Allocation concealment (selection bias)	Low risk	All research staff and therapists providing treatments were not involved in the allocation and had no prior knowledge of treatment allocation
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Both therapists and participants could not be blinded to the treatment allocation given the design of the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded interviewers who were masked to treatment allocation were used to collect participants' outcomes at all time points. Regardless of their treatment allocation, all participants were provided with follow-up appointments according to the CBT treatment schedule.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	The study stated using an ITT analysis and a flow chart is provided to outline the sampling frame as well as study participants' progress through the study; however, numbers used at post-treatment analysis seem to be inconsistent with the number of participants having been exposed to the treatment conditions. Also a small number of participants appeared to be un-accounted for (i.e. one in the brief PTSD arm; 3 in CBT arm).
Selective reporting (reporting bias)	Low risk	All outcomes as stated in the protocol and the papers were consistently reported.
Other bias	Low risk	Clinical training and treatment adherence monitoring were reported with 5% to 10% of all sessions were rated for adherence in addition to weekly group supervision for trial therapists

Steel 2010

Methods	Allocation: randomised, undertaken via MHRN database Blindness: single-blind (assessor blind) Duration: 6 months (16 sessions of CBT for PTSD) with a + 6 month-follow-up Setting: community (South East of England)
Participants	Diagnosis: DSM-IV diagnosis of schizophrenia or schizoaffective disorder and current DSM-IV diagnosis of PTSD N = 61 (no baseline demographic data were made available for this review) Excluded: patients with organic disorder, unable to read and write in English, or learning disability
Interventions	1. CBT for PTSD programme + Standard Care: 16 session trauma focused CBT intervention specifically designed and developed for people with psychosis by Mueser 2008 (see above for further details on treatment protocol). N = 30 2. TAU: standard psychiatric care in the UK is based on the care programme approach to case management and typically includes antipsychotic medication, outpatient and community follow-up, and access to community rehabilitative activities such as day centres and drop-ins. N = 31

Steel 2010 *(Continued)*

Outcomes	PTSD symptom severity: clinician-rated severity (CAPS), self-reported trauma-related cognition (PTCI). Quality of life: general quality of life (QLS), overall functioning (GAF) Symptoms of co-morbid psychosis: overall mental state (PANSS-total), positive and negative symptoms (PANSS-positive, PANSS-negative subscales), hallucinations (PSYRATS-hallucination) delusions (PSRATS-delusion) Depressive symptoms: (BDI-II) Anxiety symptoms: (BAI) Leaving the study early Unable to use - Acceptability of the intervention: was assessed through a service-user led interview which appeared to be non-quantitative data. Not made available for this review
Notes	Review author JS was therapist in this trial, therefore, was not involved in the data extraction and assessment of risk of bias of this trial. At the time of writing this review, this trial has not been published, after contacting the lead author of the trial, we used unpublished data provided by the trialists for this review's analyses.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation undertaken via MHRN database, but further detail such as how allocation was generated (e.g. equal sized strata, or permuted block) were not provided.
Allocation concealment (selection bias)	Unclear risk	Insufficient detail provided.
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Due to the design of the study, both the participants and the treatment therapists were unable to be blinded. It was unclear if blinded and independent assessors were used for all data collection.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	A proportion of assessments were undertaken unblinded, but detail of such unblinding incidents (e.g. reasons leading to unblinding, time points at which these occurred, the number of participants affected) and specific measures for managing unblinding, if any were applied, was not reported.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	According to the CONSORT diagram, not all participants allocated to CBT arm received the same number of treatment sessions. Although an ITT analysis was used, the data in Table 1 of their paper are difficult to disentangle.
Selective reporting (reporting bias)	Unclear risk	As yet the data have not been published openly, data reported on this study were provided by the trialists for the current review ahead of publication. Therefore, currently, it is not possible to judge the risk of selective reporting bias.
Other bias	Unclear risk	Although we were provided with unpublished data for the purpose of this review, detail required to estimate the risk of bias, such as with regards to sequence generation, unblinding protocol, and fidelity factors regarding intervention, have not been provided. Therefore the estimation of risk of other bias at this time is difficult to assess.

van den Berg 2015

Methods	Allocation: randomised, stratified randomisation blocks. Blindness: single-blind (assessor blind) Duration: 10 weeks (eight sessions of prolonged exposure (PE) or EMDR therapy) with a + 6 month-follow-up Setting: out-patient services in the Netherlands
Participants	Diagnosis: a lifetime diagnosis of a psychotic disorder or mood disorder with psychotic features according to the Mini-International Neuropsychiatric Interview-Plus (Sheehan 1997; Sheehan 1998), and DSM-IV-tr diagnosis (APA, 2000) of chronic PTSD as assessed with CAPS (Blake 1995) N = 155 Age: mean ˜ 41.2 years, SD 10.5 years Sex: 71 M, 84 F History: duration of psychosis: mean ˜ 17.7 years (SD 11.8 years), duration of PTSD: mean ˜ 21.0 years (SD 13.5 years) Excluded: patients with an extremely high acute suicide risk, or who had changes in antipsychotic or antidepressant medication regimen within two months before the assessments, or with insufficient competence in the Dutch language; or with intellectual impairment (as defined as an estimated IQ of 70 or less; or not being able to travel to the outpatient service (including current involuntary hospitalisation)
Interventions	1. Prolonged exposure (PE) + TAU*: eight weekly 90-minute sessions offered within a 10-week period. The PE intervention comprised development of a case formulation including a hierarchy of former experiences, and then use of imaginal exposure, audio recordings of sessions were made and listened to for homework, in vivo exposure was also included. N = 53 2. EMDR + TAU*: eight weekly 90-minute sessions (offered within a 10-week period); the standard eight phase protocol was used after being translated into Dutch (de Jongh 2003). N = 55 3. Waiting-list control + TAU*: in addition to usual care, participants were seen at the outset following randomisation and then approximately six months later at which time they could choose their treatment of choice. N = 47
Outcomes	PTSD symptom severity: clinician-rated severity (CAPS), remission and recovery from PTSD (CAPS), self-reported frequency PTSD symptoms (PSS-SR), self-reported trauma-related cognition (PTCI) Adverse events: number of severe adverse events Leaving the study early
Notes	*Treatment as usual comprised typically care provided by multidisciplinary assertive outreach teams, usually consisting of antipsychotic medication and treatment and/or non-trauma focused supportive counselling

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Sequence generation was undertaken by an independent randomisation bureau, using stratified randomisation blocks with equal strata sizes.

van den Berg 2015 *(Continued)*

Allocation concealment (selection bias)	Low risk	Treatment allocation was conducted by the independent bureau.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Single-blind given the study design that both participants and therapists were not able to be blinded to treatment they received or delivered.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessments were undertaken by independent assessors who were blind to treatment allocation; trial authors reported a small proportion of assessments were unblinded (27 occasions), however, measures by means of implementing a further independent assessor were implemented that minimised detection bias.
Incomplete outcome data (attrition bias) All outcomes	Low risk	The study used an ITT analysis and a flow chart is provided to outline the sampling frame as well as the reasons for excluding participants and a clear description of participants' journey through the study.
Selective reporting (reporting bias)	Unclear risk	Only some selected outcome data focusing on PTSD diagnosis, PTSD symptom severity and self-report of PTSD symptoms and trauma-related cognition were reported in the main paper (albeit they are the study primary outcomes); many other outcomes as stated in the protocol (such as paranoid thinking, verbal hallucinations, delusions, depression, social functioning, and cost-effectiveness data) which are reported as secondary, tertiary and quaternary objectives of the trial, were not reported. We understand other publications reporting on these other outcomes and further follow-up data, are planned. Nonetheless, we have to rate the reporting bias, as best, unclear.
Other bias	Low risk	None noted; treatment therapist training and fidelity monitoring are reported with 10% of all treatment sessions which were videotaped, randomly selected and rated by trained and blinded raters. Treatment adherence to protocols of both PE and EMDR is reported as good and excellent respectively.

BAI: Beck Anxiety Inventory (Beck 1990)
BDI-II: Beck Depression Inventory-II (Beck 1996)
BPRS: Brief Psychiatric Rating Scale (Lukoff 1986)
CAPS: Clinician Administered PTSD Scale (Blake 1995)
CBT Cognitive Behavioural Therapy
DSM-IV: Diagnostic and Statistical Manual of Mental Disorders(4th edition)
EMDR: eye movement desensitisation and reprocessing
F: Female
GAF: Global Assessment of Functioning Scale (Jones 1995)
ITT: intention-to-treat
M: Male
N: total number
N: number
QOLI: Brief Quality of Life interview (Lehman 1995)
QOLS: Quality of Life Scale(Heinrichs 1984)
PANSS: Positive and Negative Syndrome Scale (Kay 1986)
PKT – PTSD: knowledge Test (Pratt 2005)
PSYRATS: Psychotic Symptom Rating Scale (Haddock 1999)
PSS-SR: Posttraumatic Stress Symptom Scale Selt Report (Foa 1993)
PTCI: Posttraumatic Cognitions Inventory (Foa 1999)
PTSD: post-traumatic stress disorder
SCID: Structured Clinical Interview (First 1996)
SD: Standard deviation
SF-12: Short Form-12 (Ware 1994)
SMI: severe mental illness
TAU: treatment as usual

WAI: Working Alliance Inventory (Horvath 1989)

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

Study	Reason for exclusion
de Bont 2013	Allocation: not randomised but used a within-group controlled design
ISRCTN43816889	Allocation: randomised Participants: individuals with a psychotic illness without co-morbid PTSD
Jackson 2006	Allocation: randomised Participants: Individuals with first episode psychosis without co-morbid PTSD
NCT00307216	Allocation: randomised Participants: individuals recovering from their first episodes of psychosis but with no PTSD

PTSD - post-traumatic stress disorder

DATA AND ANALYSES

Comparison 1. TF-CBT versus WAITING LIST/TAU

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor)	1	13	Mean Difference (IV, Fixed, 95% CI)	13.15 [-4.09, 30.39]
1.1 short term	1	13	Mean Difference (IV, Fixed, 95% CI)	13.15 [-4.09, 30.39]
2 PTSD symptom severity: 1a. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1 short term - skewed data	2	147	Mean Difference (IV, Random, 95% CI)	-7.44 [-29.15, 14.27]
2.2 medium term - skewed data	3	155	Mean Difference (IV, Random, 95% CI)	-3.92 [-19.25, 11.40]
3 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor)	3		Mean Difference (IV, Random, 95% CI)	Subtotals only
3.1 short term	3	136	Mean Difference (IV, Random, 95% CI)	-5.45 [-33.61, 22.70]

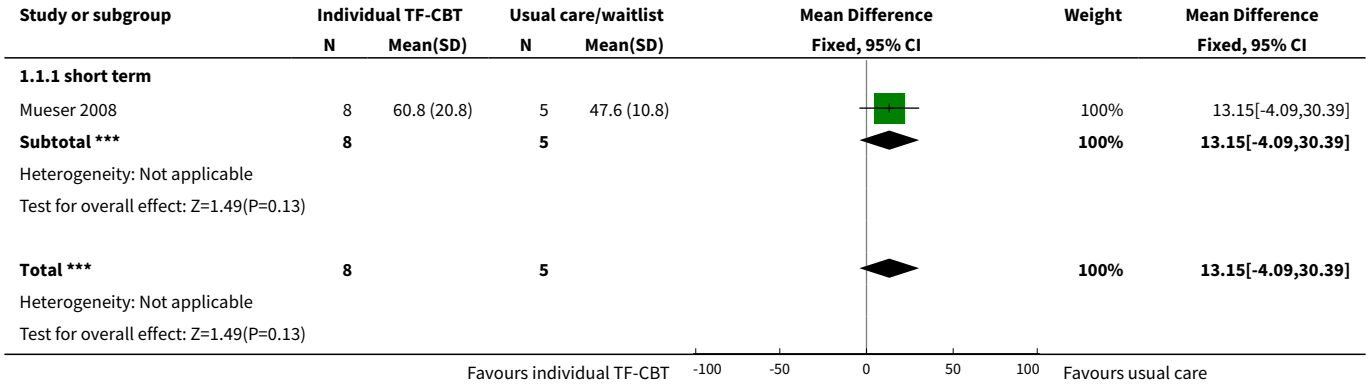
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.2 medium term	3	133	Mean Difference (IV, Random, 95% CI)	-15.25 [-29.48, -1.02]
4 PTSD symptom severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1 short term - skewed data	1	86	Mean Difference (IV, Fixed, 95% CI)	-9.51 [-13.84, -5.18]
4.2 medium term - skewed data	1	85	Mean Difference (IV, Fixed, 95% CI)	-7.52 [-12.06, -2.98]
5 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40	2		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
5.1 short term	2	113	Risk Ratio (M-H, Random, 95% CI)	1.99 [1.20, 3.30]
5.2 medium term	2	109	Risk Ratio (M-H, Random, 95% CI)	1.44 [0.57, 3.63]
6 PTSD symptom severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 short term	1	100	Risk Ratio (M-H, Fixed, 95% CI)	4.43 [1.37, 14.37]
6.2 medium term	1	100	Risk Ratio (M-H, Fixed, 95% CI)	4.14 [1.27, 13.51]
7 Quality of life: 1. General quality of life - average endpoint QLS total score (high = good)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 short term	1	38	Mean Difference (IV, Fixed, 95% CI)	-3.0 [-8.26, 2.26]
7.2 medium term	1	39	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-4.47, 3.27]
8 Quality of life: 2. Overall functioning - average endpoint GAF total score (high = good)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 short term	1	44	Mean Difference (IV, Fixed, 95% CI)	0.80 [-4.61, 6.21]
8.2 medium term	1	46	Mean Difference (IV, Fixed, 95% CI)	2.70 [-3.32, 8.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9 Quality of life: 3. Mental health functioning - average endpoint SF-12 mental component total score (high = good)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
9.1 short term	1	11	Mean Difference (IV, Fixed, 95% CI)	-9.89 [-23.35, 3.57]
9.2 medium term	1	9	Mean Difference (IV, Fixed, 95% CI)	1.96 [-28.15, 32.07]
10 Quality of life: 4. Physical functioning - average endpoint SF-12 physical component total score (high = good)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
10.1 short term	1	11	Mean Difference (IV, Fixed, 95% CI)	1.32 [-16.35, 18.99]
10.2 medium term	1	9	Mean Difference (IV, Fixed, 95% CI)	-2.52 [-25.64, 20.60]
11 Symptoms of co-morbid psychosis: 1. Overall mental state - average endpoint BPRS total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
11.1 short term	1	13	Mean Difference (IV, Fixed, 95% CI)	1.0 [-9.96, 11.96]
11.2 medium term	1	9	Mean Difference (IV, Fixed, 95% CI)	-6.93 [-34.17, 20.31]
12 Symptoms of co-morbid psychosis: 2. Positive symptoms - average endpoint PANSS positive subscale total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
12.1 short term	1	61	Mean Difference (IV, Fixed, 95% CI)	-2.0 [-5.07, 1.07]
12.2 medium term	1	61	Mean Difference (IV, Fixed, 95% CI)	-1.40 [-4.42, 1.62]
13 Symptoms of co-morbid psychosis: 4. Negative symptoms - average endpoint PANSS negative subscale total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
13.1 short term	1	61	Mean Difference (IV, Fixed, 95% CI)	-1.40 [-4.19, 1.39]
13.2 medium term	1	61	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-3.38, 1.18]
14 Symptoms of co-morbid psychosis: 3. Hallucinations - average endpoint	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

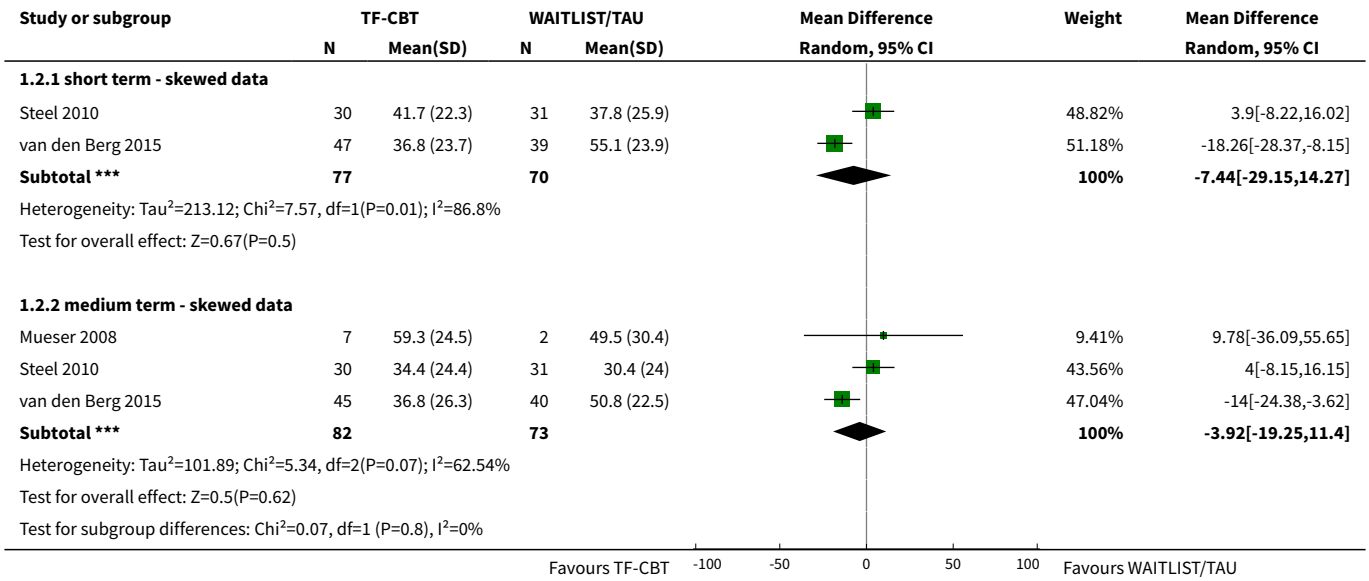
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
PSYRATS-hallucinations subscale total score (high = poor) - skewed data				
14.1 short term - skewed data	1	61	Mean Difference (IV, Fixed, 95% CI)	2.80 [-3.88, 9.48]
14.2 medium term - skewed data	1	61	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-7.48, 6.88]
15 Symptoms of co-morbid psychosis: 5. Delusions - average endpoint PSYRATS-delusions subscale total score (high = poor) - skewed data	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
15.1 short term - skewed data	1	61	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-4.73, 3.33]
15.2 medium term - skewed data	1	61	Mean Difference (IV, Fixed, 95% CI)	-2.30 [-6.22, 1.62]
16 Anxiety symptoms: 1a. average endpoint BAI total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
16.1 Short term	1	13	Mean Difference (IV, Fixed, 95% CI)	4.20 [-7.52, 15.92]
16.2 Medium term	1	9	Mean Difference (IV, Fixed, 95% CI)	12.57 [-5.54, 30.68]
17 Anxiety symptoms: 1b. average endpoint BAI total score (high = poor) - skewed data	1	75	Mean Difference (IV, Fixed, 95% CI)	-0.41 [-6.90, 6.09]
17.1 Short term - skewed data	1	35	Mean Difference (IV, Fixed, 95% CI)	2.0 [-7.02, 11.02]
17.2 medium term - skewed data	1	40	Mean Difference (IV, Fixed, 95% CI)	-1.00 [-12.36, 6.36]
18 Depressive symptoms: 1. average endpoint BDI-II total (high = poor) - skewed data	2		Mean Difference (IV, Random, 95% CI)	Subtotals only
18.1 short term - skewed data	2	49	Mean Difference (IV, Random, 95% CI)	1.31 [-5.81, 8.44]
18.2 medium term - skewed data	2	48	Mean Difference (IV, Random, 95% CI)	3.26 [-3.66, 10.18]
19 Adverse events - incidents of unspecified severe adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
19.1 Medium term	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.44 [0.09, 2.31]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
20 Leaving the study early	3		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
20.1 short term	3	178	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.38, 1.44]
20.2 medium term	3	178	Risk Ratio (M-H, Random, 95% CI)	0.80 [0.46, 1.40]

Analysis 1.1. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 1 PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor).



Analysis 1.2. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 2 PTSD symptom severity: 1a. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data.



Analysis 1.3. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 3 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor).

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.3.1 short term							
Mueser 2008	8	102.9 (23.3)	6	85.5 (26.4)		31.87%	17.38[-9.17,43.93]
Steel 2010	18	140.1 (42.9)	18	142.3 (49.8)		29.31%	-2.2[-32.57,28.17]
van den Berg 2015	47	115.9 (45.9)	39	142.6 (29.8)		38.82%	-26.65[-42.76,-10.54]
Subtotal ***	**73**		**63**			**100%**	**-5.45[-33.61,22.7]**
Heterogeneity: Tau^2=463.9; Chi^2=8.27, df=2(P=0.02); I^2=75.82%							
Test for overall effect: Z=0.38(P=0.7)							
1.3.2 medium term							
Mueser 2008	7	100 (18.8)	2	104.5 (65.8)		2.38%	-4.5[-96.7,87.7]
Steel 2010	20	127.7 (49.7)	19	132.5 (47.2)		21.9%	-4.8[-35.21,25.61]
van den Berg 2015	45	120.3 (46)	40	138.9 (30.1)		75.72%	-18.61[-34.96,-2.26]
Subtotal ***	**72**		**61**			**100%**	**-15.25[-29.48,-1.02]**
Heterogeneity: Tau^2=0; Chi^2=0.67, df=2(P=0.72); I^2=0%							
Test for overall effect: Z=2.1(P=0.04)							
Test for subgroup differences: Chi^2=0.37, df=1 (P=0.54), I^2=0%							

Favours individual TF-CBT — Favours usual care

Analysis 1.4. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 4 PTSD symptom severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data.

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.4.1 short term - skewed data							
van den Berg 2015	47	15.2 (10.3)	39	24.7 (10.1)		100%	-9.51[-13.84,-5.18]
Subtotal ***	**47**		**39**			**100%**	**-9.51[-13.84,-5.18]**
Heterogeneity: Not applicable							
Test for overall effect: Z=4.3(P<0.0001)							
1.4.2 medium term - skewed data							
van den Berg 2015	45	16.2 (12.4)	40	23.7 (8.9)		100%	-7.52[-12.06,-2.98]
Subtotal ***	**45**		**40**			**100%**	**-7.52[-12.06,-2.98]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=3.25(P=0)							
Test for subgroup differences: Chi^2=0.39, df=1 (P=0.53), I^2=0%							

Favours individual TF-CBT — Favours waitlist

Analysis 1.5. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 5 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40.

Study or subgroup	Individual TF-CBT n/N	Usual care/ waitlist n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
1.5.1 short term					
Mueser 2008	2/8	1/5		5.63%	1.25[0.15,10.46]
van den Berg 2015	30/53	13/47		94.37%	2.05[1.22,3.44]
Subtotal (95% CI)	**61**	**52**		**100%**	**1.99[1.2,3.3]**
Total events: 32 (Individual TF-CBT), 14 (Usual care/waitlist)					
Heterogeneity: Tau^2=0; Chi^2=0.2, df=1(P=0.66); I^2=0%					
Test for overall effect: Z=2.68(P=0.01)					
1.5.2 medium term					
Mueser 2008	2/7	1/2		20.66%	0.57[0.09,3.51]
van den Berg 2015	31/53	15/47		79.34%	1.83[1.14,2.95]
Subtotal (95% CI)	**60**	**49**		**100%**	**1.44[0.57,3.63]**
Total events: 33 (Individual TF-CBT), 16 (Usual care/waitlist)					
Heterogeneity: Tau^2=0.22; Chi^2=1.49, df=1(P=0.22); I^2=32.67%					
Test for overall effect: Z=0.77(P=0.44)					
Test for subgroup differences: Chi^2=0.36, df=1 (P=0.55), I^2=0%					

Analysis 1.6. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 6 PTSD symptom severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20.

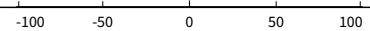
Study or subgroup	Individual TF-CBT n/N	Usual care/ waitlist n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
1.6.1 short term					
van den Berg 2015	15/53	3/47		100%	4.43[1.37,14.37]
Subtotal (95% CI)	**53**	**47**		**100%**	**4.43[1.37,14.37]**
Total events: 15 (Individual TF-CBT), 3 (Usual care/waitlist)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.48(P=0.01)					
1.6.2 medium term					
van den Berg 2015	14/53	3/47		100%	4.14[1.27,13.51]
Subtotal (95% CI)	**53**	**47**		**100%**	**4.14[1.27,13.51]**
Total events: 14 (Individual TF-CBT), 3 (Usual care/waitlist)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.35(P=0.02)					
Test for subgroup differences: Chi^2=0.01, df=1 (P=0.94), I^2=0%					

Analysis 1.7. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 7 Quality of life: 1. General quality of life - average endpoint QLS total score (high = good).

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.7.1 short term							
Steel 2010	19	23 (9.8)	19	26 (6.4)		100%	-3[-8.26,2.26]
Subtotal ***	**19**		**19**			**100%**	**-3[-8.26,2.26]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.12(P=0.26)							
1.7.2 medium term							
Steel 2010	20	25.4 (7.2)	19	26 (5)		100%	-0.6[-4.47,3.27]
Subtotal ***	**20**		**19**			**100%**	**-0.6[-4.47,3.27]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.3(P=0.76)							
Test for subgroup differences: Chi^2=0.52, df=1 (P=0.47), I^2=0%							

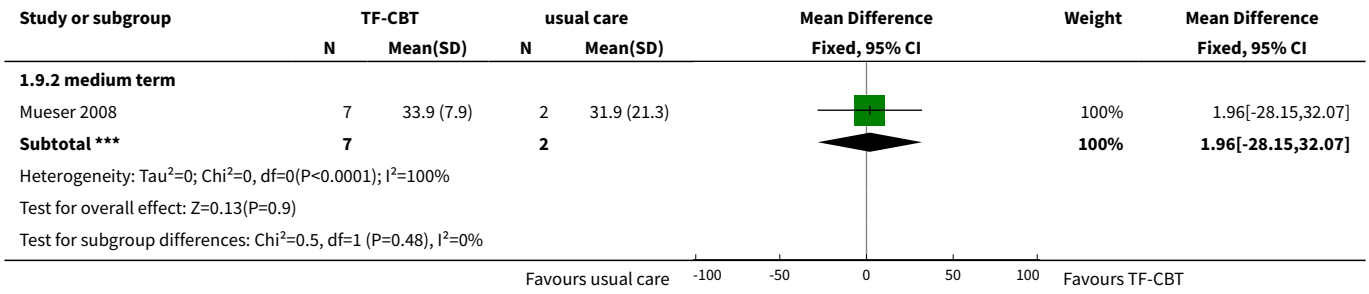
Analysis 1.8. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 8 Quality of life: 2. Overall functioning - average endpoint GAF total score (high = good).

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.8.1 short term							
Steel 2010	23	61.6 (10)	21	60.8 (8.3)		100%	0.8[-4.61,6.21]
Subtotal ***	**23**		**21**			**100%**	**0.8[-4.61,6.21]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.29(P=0.77)							
1.8.2 medium term							
Steel 2010	23	61.3 (9.8)	23	58.6 (11)		100%	2.7[-3.32,8.72]
Subtotal ***	**23**		**23**			**100%**	**2.7[-3.32,8.72]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.88(P=0.38)							
Test for subgroup differences: Chi^2=0.21, df=1 (P=0.65), I^2=0%							

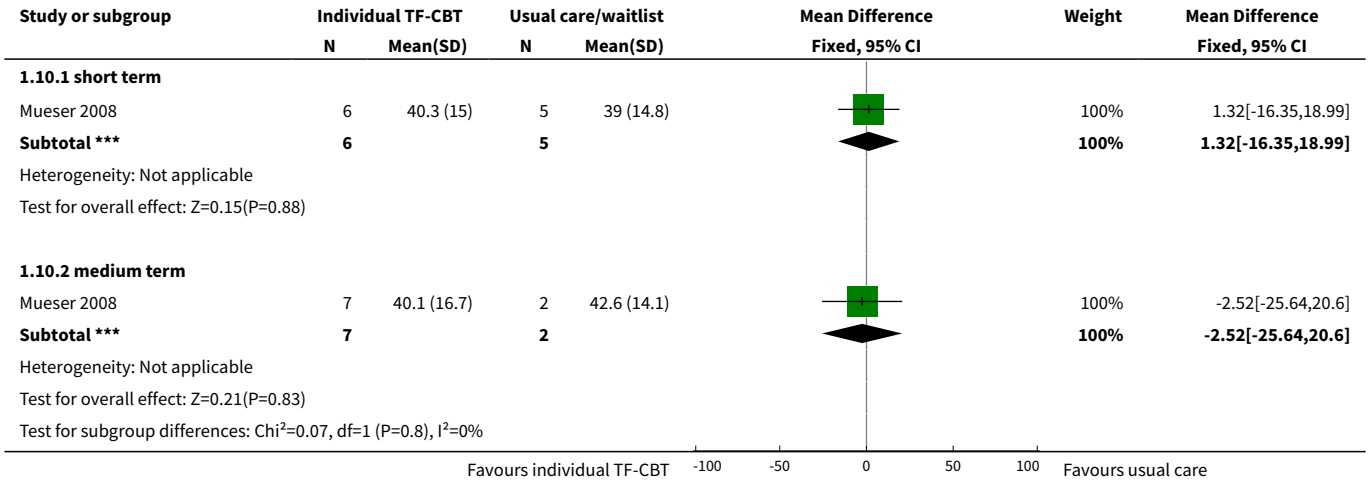


Analysis 1.9. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 9 Quality of life: 3. Mental health functioning - average endpoint SF-12 mental component total score (high = good).

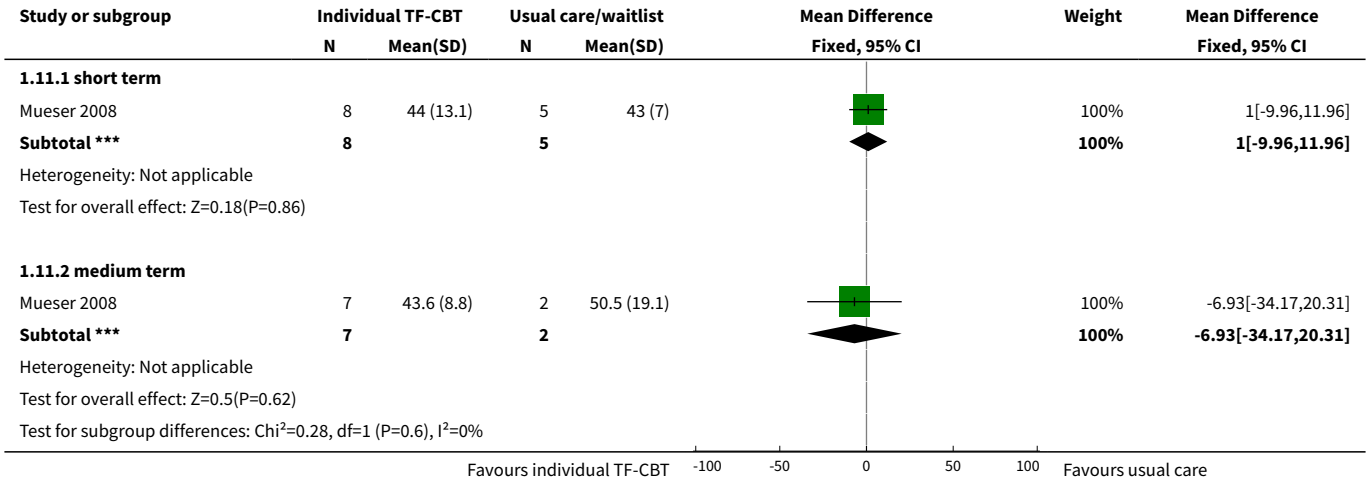
Study or subgroup	TF-CBT N	TF-CBT Mean(SD)	usual care N	usual care Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.9.1 short term							
Mueser 2008	6	31 (7.6)	5	40.9 (13.7)		100%	-9.89[-23.35,3.57]
Subtotal ***	**6**		**5**			**100%**	**-9.89[-23.35,3.57]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.44(P=0.15)							



Analysis 1.10. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 10 Quality of life: 4. Physical functioning - average endpoint SF-12 physical component total score (high = good).



Analysis 1.11. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 11 Symptoms of co-morbid psychosis: 1. Overall mental state - average endpoint BPRS total score (high = poor).



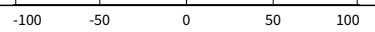
Analysis 1.12. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 12 Symptoms of co-morbid psychosis: 2. Positive symptoms - average endpoint PANSS positive subscale total score (high = poor).

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.12.1 short term							
Steel 2010	30	17.8 (5.6)	31	19.8 (6.6)		100%	-2[-5.07,1.07]
Subtotal ***	**30**		**31**			**100%**	**-2[-5.07,1.07]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.28(P=0.2)							
1.12.2 medium term							
Steel 2010	30	17 (5.6)	31	18.4 (6.4)		100%	-1.4[-4.42,1.62]
Subtotal ***	**30**		**31**			**100%**	**-1.4[-4.42,1.62]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.91(P=0.36)							
Test for subgroup differences: Chi^2=0.07, df=1 (P=0.78), I^2=0%							

Favours individual TF-CBT — Favours usual care

Analysis 1.13. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 13 Symptoms of co-morbid psychosis: 4. Negative symptoms - average endpoint PANSS negative subscale total score (high = poor).

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.13.1 short term							
Steel 2010	30	15 (5.7)	31	16.4 (5.4)		100%	-1.4[-4.19,1.39]
Subtotal ***	**30**		**31**			**100%**	**-1.4[-4.19,1.39]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.98(P=0.33)							
1.13.2 medium term							
Steel 2010	30	15 (4.6)	31	16.1 (4.5)		100%	-1.1[-3.38,1.18]
Subtotal ***	**30**		**31**			**100%**	**-1.1[-3.38,1.18]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.94(P=0.35)							
Test for subgroup differences: Chi^2=0.03, df=1 (P=0.87), I^2=0%							

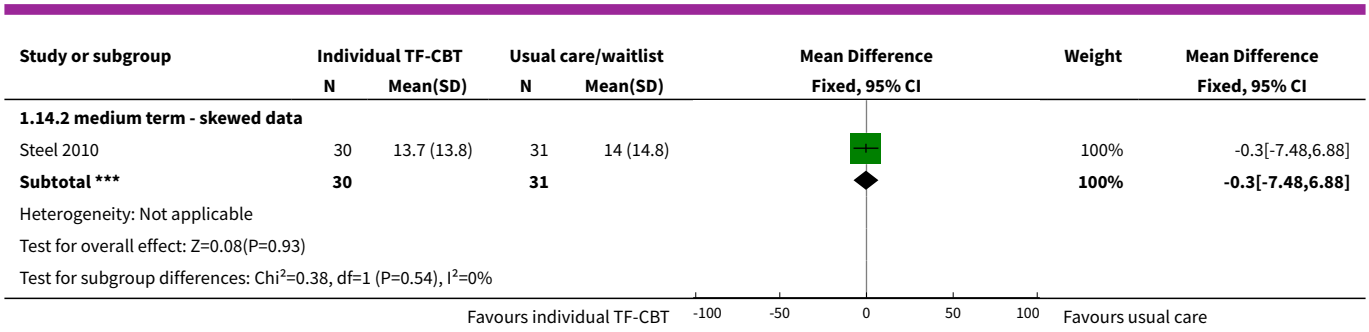


Favours individual TF-CBT — Favours usual care

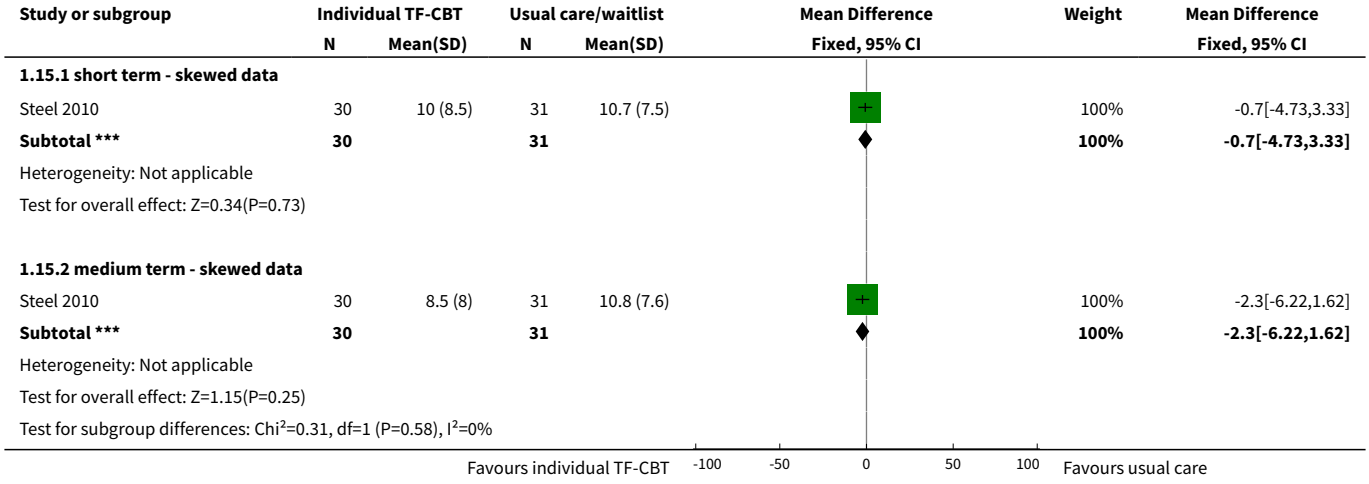
Analysis 1.14. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 14 Symptoms of co-morbid psychosis: 3. Hallucinations - average endpoint PSYRATS-hallucinations subscale total score (high = poor) - skewed data.

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.14.1 short term - skewed data							
Steel 2010	30	16.8 (13.4)	31	14 (13.2)		100%	2.8[-3.88,9.48]
Subtotal ***	**30**		**31**			**100%**	**2.8[-3.88,9.48]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.82(P=0.41)							

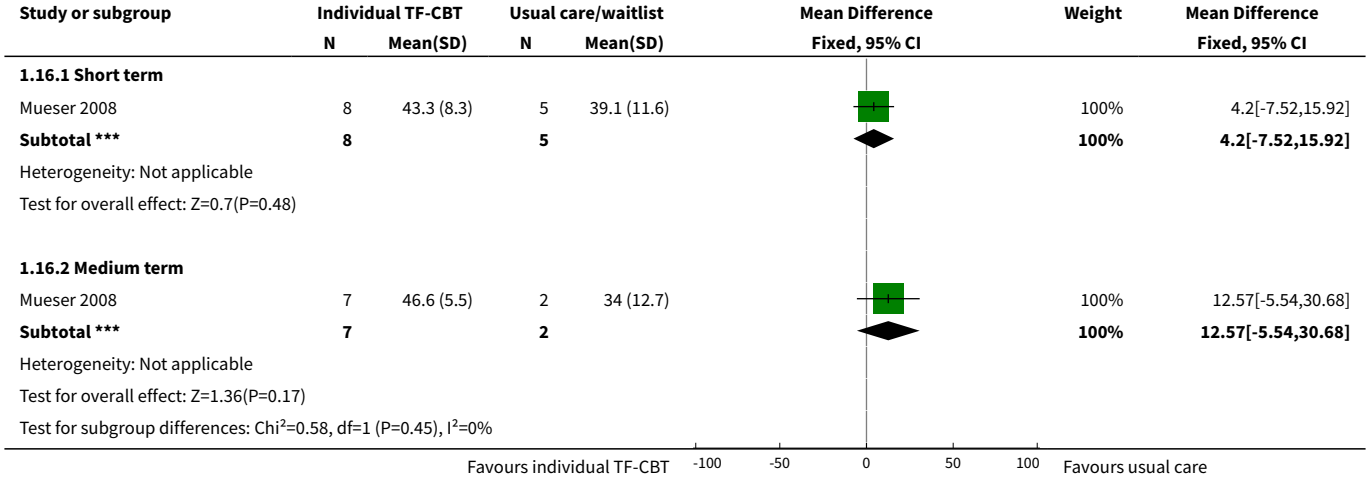
Favours individual TF-CBT — Favours usual care



Analysis 1.15. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 15 Symptoms of co-morbid psychosis: 5. Delusions - average endpoint PSYRATS-delusions subscale total score (high = poor) - skewed data.

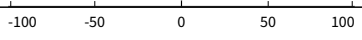


Analysis 1.16. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 16 Anxiety symptoms: 1a. average endpoint BAI total score (high = poor).



Analysis 1.17. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 17 Anxiety symptoms: 1b. average endpoint BAI total score (high = poor) - skewed data.

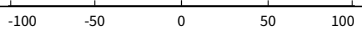
Study or subgroup	TF-CBT N	TF-CBT Mean(SD)	WAITLIST/TAU N	WAITLIST/TAU Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1.17.1 Short term - skewed data							
Steel 2010	18	21.8 (15.2)	17	19.8 (11.9)		51.89%	2[-7.02,11.02]
Subtotal ***	**18**		**17**			**51.89%**	**2[-7.02,11.02]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.43(P=0.66)							
1.17.2 medium term - skewed data							
Steel 2010	20	19.4 (14.6)	20	22.4 (15.6)		48.11%	-3[-12.36,6.36]
Subtotal ***	**20**		**20**			**48.11%**	**-3[-12.36,6.36]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=0.63(P=0.53)							
Total ***	**38**		**37**			**100%**	**-0.41[-6.9,6.09]**
Heterogeneity: Tau^2=0; Chi^2=0.57, df=1(P=0.45); I^2=0%							
Test for overall effect: Z=0.12(P=0.9)							
Test for subgroup differences: Chi^2=0.57, df=1 (P=0.45), I^2=0%							



Favours TF-CBT — Favours WAITLIST/TAU

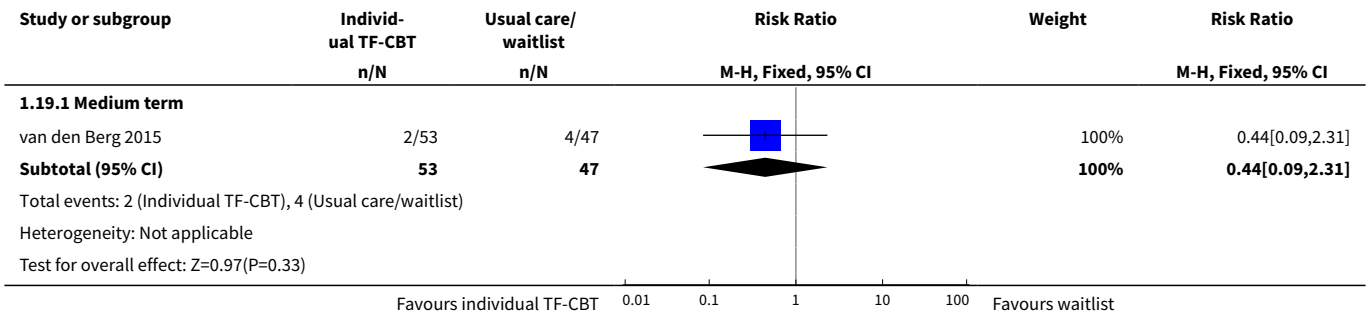
Analysis 1.18. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 18 Depressive symptoms: 1. average endpoint BDI-II total (high = poor) - skewed data.

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	Usual care/waitlist N	Usual care/waitlist Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1.18.1 short term - skewed data							
Mueser 2008	8	21 (9.3)	5	24.2 (14.2)		25.98%	-3.2[-17.18,10.78]
Steel 2010	19	24.3 (14.2)	17	21.4 (11.1)		74.02%	2.9[-5.38,11.18]
Subtotal ***	**27**		**22**			**100%**	**1.31[-5.81,8.44]**
Heterogeneity: Tau^2=0; Chi^2=0.54, df=1(P=0.46); I^2=0%							
Test for overall effect: Z=0.36(P=0.72)							
1.18.2 medium term - skewed data							
Mueser 2008	7	25 (11.2)	2	22.5 (21.9)		4.83%	2.5[-28.98,33.98]
Steel 2010	20	21.9 (11.3)	19	18.6 (11.3)		95.17%	3.3[-3.8,10.4]
Subtotal ***	**27**		**21**			**100%**	**3.26[-3.66,10.18]**
Heterogeneity: Tau^2=0; Chi^2=0, df=1(P=0.96); I^2=0%							
Test for overall effect: Z=0.92(P=0.36)							
Test for subgroup differences: Chi^2=0.15, df=1 (P=0.7), I^2=0%							

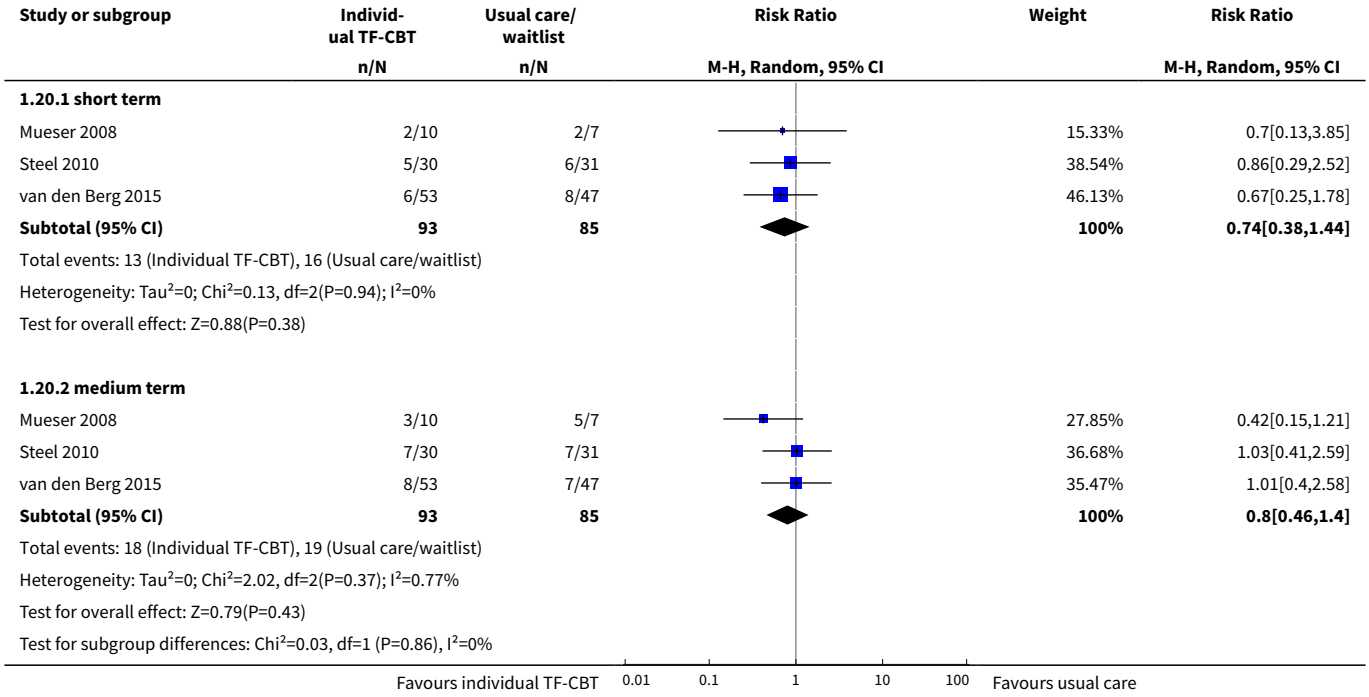


Favours individual TF-CBT — Favours usual care

Analysis 1.19. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 19 Adverse events - incidents of unspecified severe adverse events.



Analysis 1.20. Comparison 1 TF-CBT versus WAITING LIST/TAU, Outcome 20 Leaving the study early.



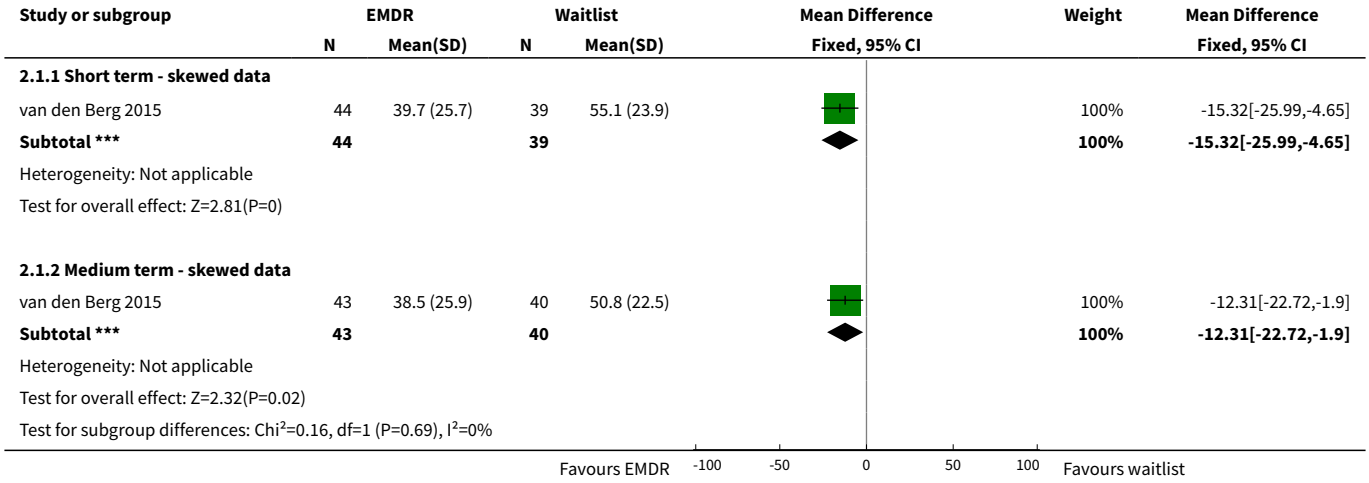
Comparison 2. EMDR versus WAITING LIST

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Short term - skewed data	1	83	Mean Difference (IV, Fixed, 95% CI)	-15.32 [-25.99, -4.65]

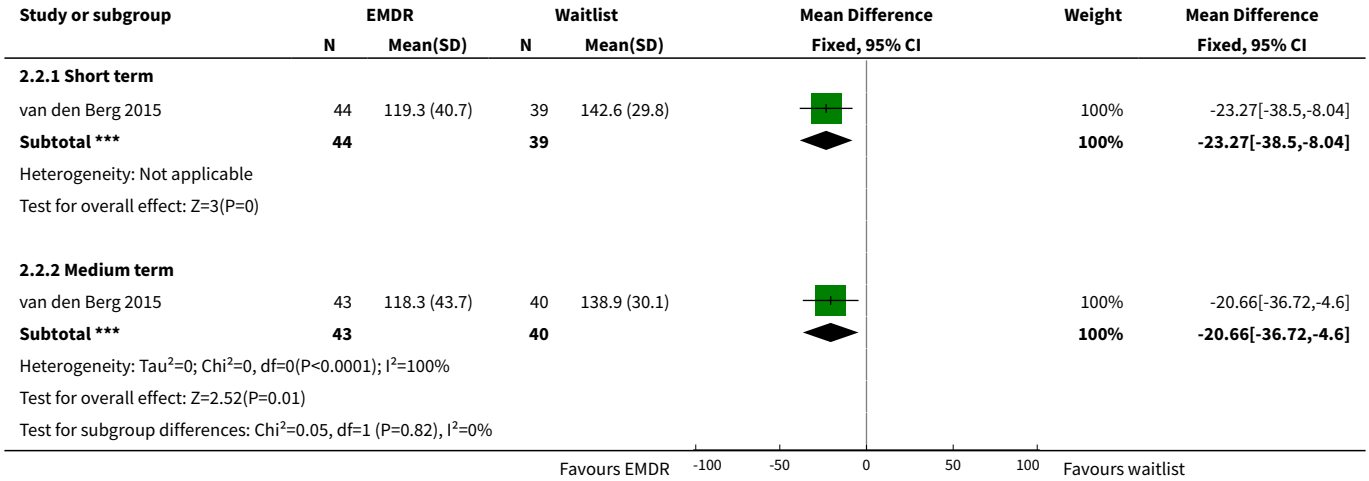
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 Medium term - skewed data	1	83	Mean Difference (IV, Fixed, 95% CI)	-12.31 [-22.72, -1.90]
2 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Short term	1	83	Mean Difference (IV, Fixed, 95% CI)	-23.27 [-38.50, -8.04]
2.2 Medium term	1	83	Mean Difference (IV, Fixed, 95% CI)	-20.66 [-36.72, -4.60]
3 PTSD symptom severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Short term - skewed data	1	83	Mean Difference (IV, Fixed, 95% CI)	-8.60 [-13.03, -4.17]
3.2 Medium term - skewed data	1	83	Mean Difference (IV, Fixed, 95% CI)	-7.37 [-12.17, -2.57]
4 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Short term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	2.17 [1.30, 3.61]
4.2 Medium term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	1.77 [1.10, 2.85]
5 PTSD symptom severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Short term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	2.56 [0.74, 8.92]
5.2 Medium term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	2.28 [0.64, 8.10]
6 Adverse events - incidents of unspecified severe adverse events	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
6.1 Short term	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
6.2 Medium term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	0.21 [0.02, 1.85]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7 Leaving the study early	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
7.1 Short term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.52, 2.68]
7.2 Medium term	1	102	Risk Ratio (M-H, Fixed, 95% CI)	1.46 [0.63, 3.42]

Analysis 2.1. Comparison 2 EMDR versus WAITING LIST, Outcome 1 PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data.

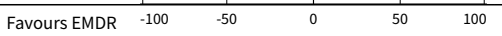


Analysis 2.2. Comparison 2 EMDR versus WAITING LIST, Outcome 2 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor).



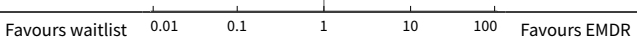
Analysis 2.3. Comparison 2 EMDR versus WAITING LIST, Outcome 3 PTSD symptom severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data.

Study or subgroup	EMDR N	EMDR Mean(SD)	Waitlist N	Waitlist Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
2.3.1 Short term - skewed data							
van den Berg 2015	44	16.1 (10.5)	39	24.7 (10.1)		100%	-8.6[-13.03,-4.17]
Subtotal ***	**44**		**39**			**100%**	**-8.6[-13.03,-4.17]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.81(P=0)							
2.3.2 Medium term - skewed data							
van den Berg 2015	43	16.3 (13.1)	40	23.7 (8.9)		100%	-7.37[-12.17,-2.57]
Subtotal ***	**43**		**40**			**100%**	**-7.37[-12.17,-2.57]**
Heterogeneity: Not applicable							
Test for overall effect: Z=3.01(P=0)							
Test for subgroup differences: Chi²=0.14, df=1 (P=0.71), I²=0%							



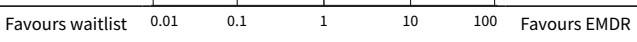
Analysis 2.4. Comparison 2 EMDR versus WAITING LIST, Outcome 4 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40.

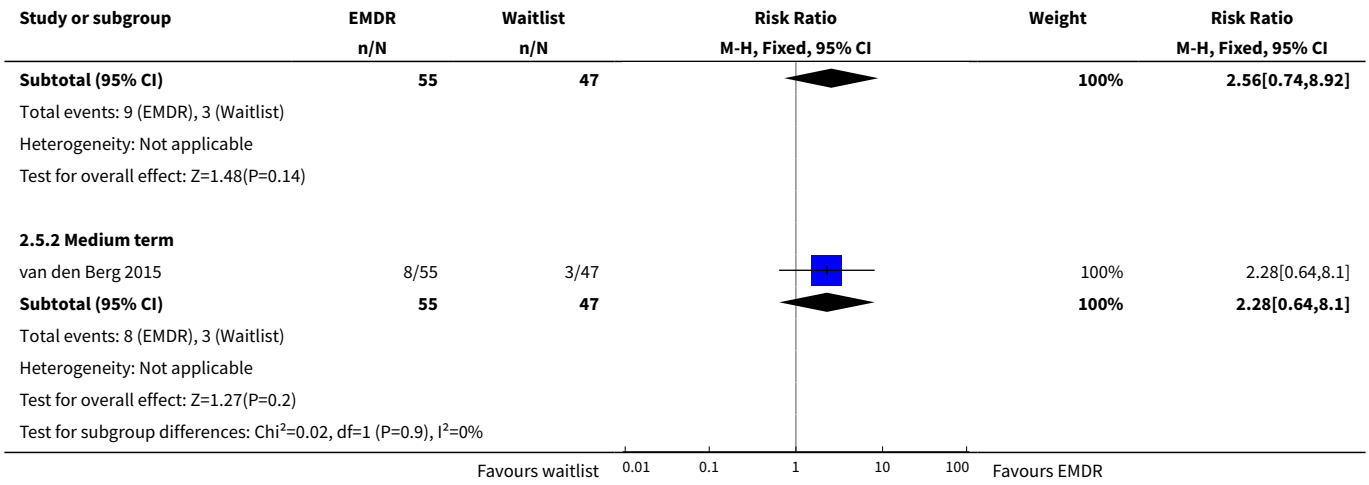
Study or subgroup	EMDR n/N	Waitlist n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.4.1 Short term					
van den Berg 2015	33/55	13/47		100%	2.17[1.3,3.61]
Subtotal (95% CI)	**55**	**47**		**100%**	**2.17[1.3,3.61]**
Total events: 33 (EMDR), 13 (Waitlist)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.97(P=0)					
2.4.2 Medium term					
van den Berg 2015	31/55	15/47		100%	1.77[1.1,2.85]
Subtotal (95% CI)	**55**	**47**		**100%**	**1.77[1.1,2.85]**
Total events: 31 (EMDR), 15 (Waitlist)					
Heterogeneity: Not applicable					
Test for overall effect: Z=2.33(P=0.02)					
Test for subgroup differences: Chi²=0.33, df=1 (P=0.56), I²=0%					



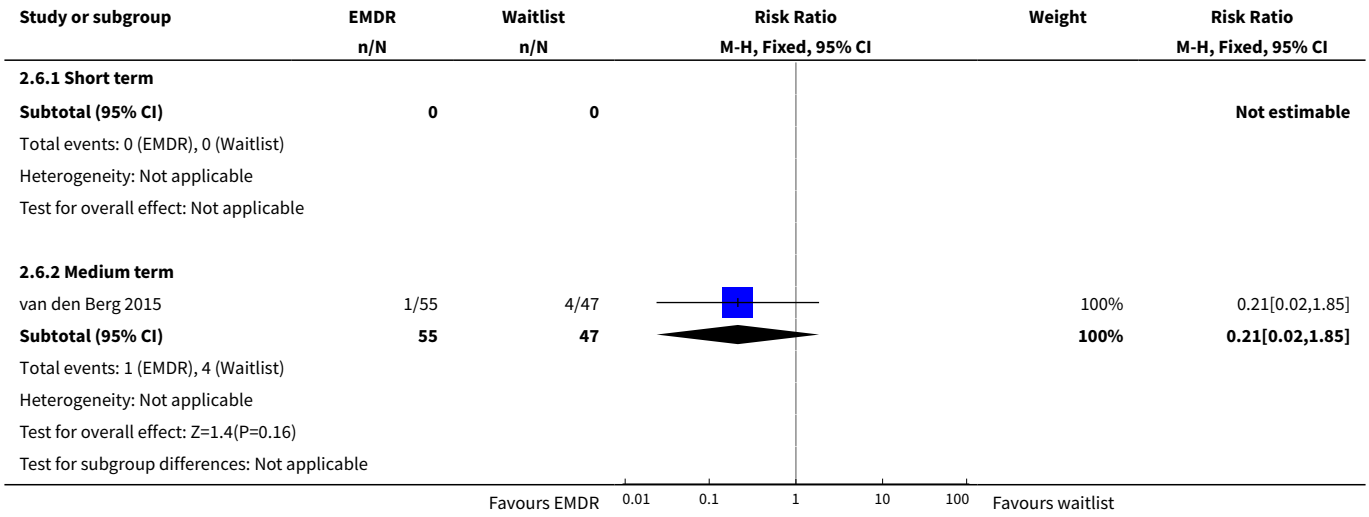
Analysis 2.5. Comparison 2 EMDR versus WAITING LIST, Outcome 5 PTSD symptom severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20.

Study or subgroup	EMDR n/N	Waitlist n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
2.5.1 Short term					
van den Berg 2015	9/55	3/47		100%	2.56[0.74,8.92]

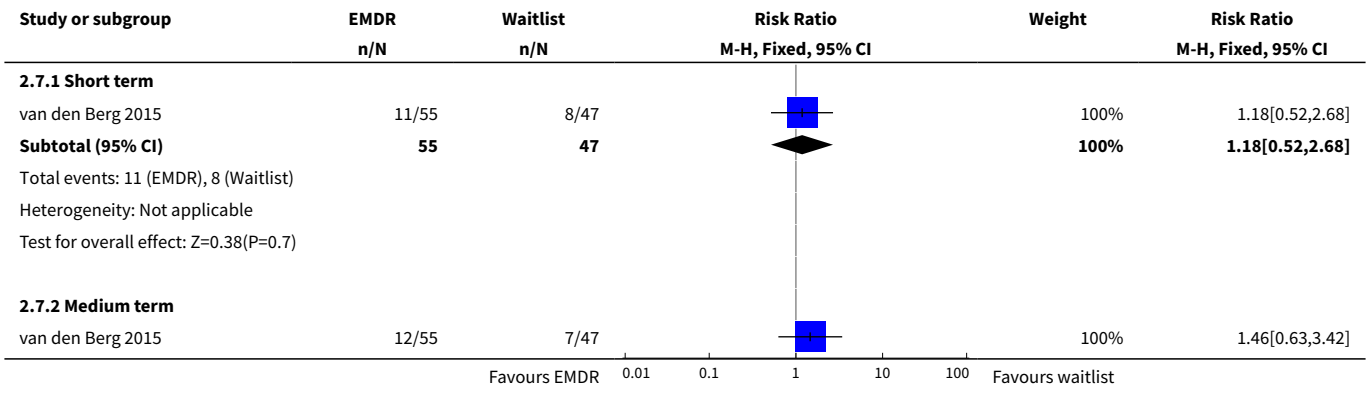


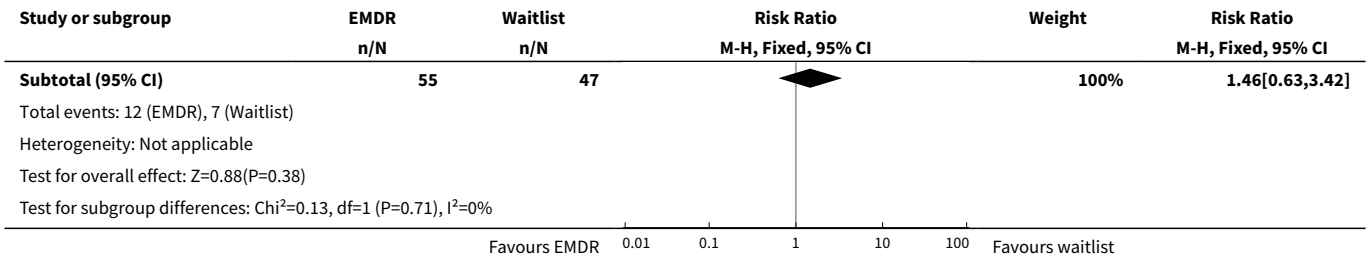


Analysis 2.6. Comparison 2 EMDR versus WAITING LIST, Outcome 6 Adverse events - incidents of unspecified severe adverse events.



Analysis 2.7. Comparison 2 EMDR versus WAITING LIST, Outcome 7 Leaving the study early.





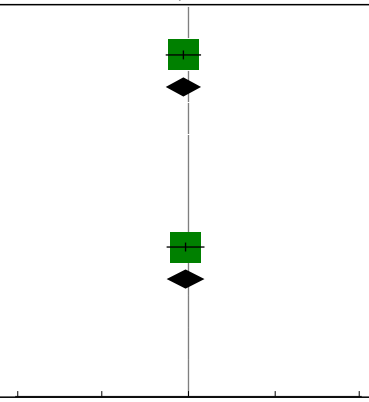
Comparison 3. TF-CBT versus EMDR

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Short term - skewed data	1	91	Mean Difference (IV, Fixed, 95% CI)	-2.94 [-13.13, 7.25]
1.2 Medium term - skewed data	1	88	Mean Difference (IV, Fixed, 95% CI)	-1.69 [-12.61, 9.23]
2 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Short term	1	91	Mean Difference (IV, Fixed, 95% CI)	-3.38 [-21.17, 14.41]
2.2 Medium term (7-9 months)	1	88	Mean Difference (IV, Fixed, 95% CI)	2.05 [-16.69, 20.79]
3 PTSD symptom severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Short term - skewed data	1	91	Mean Difference (IV, Fixed, 95% CI)	-0.91 [-5.18, 3.36]
3.2 Medium term - skewed data	1	88	Mean Difference (IV, Fixed, 95% CI)	-0.15 [-5.49, 5.19]
4 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Short term	1	108	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.69, 1.30]
4.2 Medium term	1	108	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.75, 1.44]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5 PTSD symptom severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Short term	1	108	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [0.83, 3.61]
5.2 Medium term	1	108	Risk Ratio (M-H, Fixed, 95% CI)	1.82 [0.83, 3.97]

Analysis 3.1. Comparison 3 TF-CBT versus EMDR, Outcome 1 PTSD symptom severity: 1. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data.

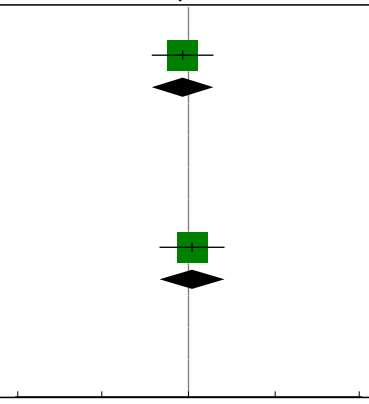
Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	EMDR N	EMDR Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
3.1.1 Short term - skewed data							
van den Berg 2015	47	36.8 (23.7)	44	39.7 (25.7)		100%	-2.94[-13.13,7.25]
Subtotal ***	**47**		**44**			**100%**	**-2.94[-13.13,7.25]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.57(P=0.57)							
3.1.2 Medium term - skewed data							
van den Berg 2015	45	36.8 (26.3)	43	38.5 (25.9)		100%	-1.69[-12.61,9.23]
Subtotal ***	**45**		**43**			**100%**	**-1.69[-12.61,9.23]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.3(P=0.76)							
Test for subgroup differences: Chi^2=0.03, df=1 (P=0.87), I^2=0%							



Favours individual TF-CBT — Favours EMDR

Analysis 3.2. Comparison 3 TF-CBT versus EMDR, Outcome 2 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor).

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	EMDR N	EMDR Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
3.2.1 Short term							
van den Berg 2015	47	115.9 (45.9)	44	119.3 (40.7)		100%	-3.38[-21.17,14.41]
Subtotal ***	**47**		**44**			**100%**	**-3.38[-21.17,14.41]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.37(P=0.71)							
3.2.2 Medium term (7-9 months)							
van den Berg 2015	45	120.3 (46)	43	118.3 (43.7)		100%	2.05[-16.69,20.79]
Subtotal ***	**45**		**43**			**100%**	**2.05[-16.69,20.79]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.21(P=0.83)							
Test for subgroup differences: Chi^2=0.17, df=1 (P=0.68), I^2=0%							



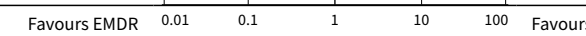
Favours individual TF-CBT — Favours EMDR

Analysis 3.3. Comparison 3 TF-CBT versus EMDR, Outcome 3 PTSD symptom severity: 3. Self-reported frequency of PTSD symptoms - average endpoint PSS-SR total score (high = poor) - skewed data.

Study or subgroup	Individual TF-CBT N	Individual TF-CBT Mean(SD)	EMDR N	EMDR Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
3.3.1 Short term - skewed data							
van den Berg 2015	47	15.2 (10.3)	44	16.1 (10.5)		100%	-0.91[-5.18,3.36]
Subtotal ***	**47**		**44**			**100%**	**-0.91[-5.18,3.36]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=0.42(P=0.68)							
3.3.2 Medium term - skewed data							
van den Berg 2015	45	16.2 (12.4)	43	16.3 (13.1)		100%	-0.15[-5.49,5.19]
Subtotal ***	**45**		**43**			**100%**	**-0.15[-5.49,5.19]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.06(P=0.96)							
Test for subgroup differences: Chi^2=0.05, df=1 (P=0.83), I^2=0%							

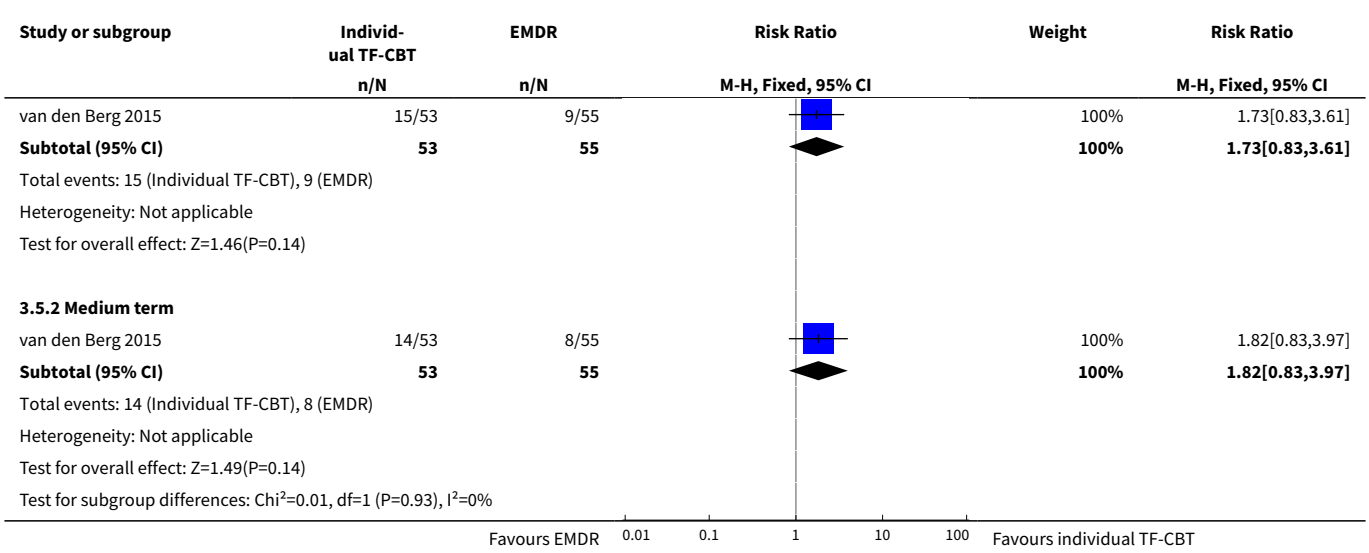
Analysis 3.4. Comparison 3 TF-CBT versus EMDR, Outcome 4 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40.

Study or subgroup	Individual TF-CBT n/N	EMDR n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.4.1 Short term					
van den Berg 2015	30/53	33/55		100%	0.94[0.69,1.3]
Subtotal (95% CI)	**53**	**55**		**100%**	**0.94[0.69,1.3]**
Total events: 30 (Individual TF-CBT), 33 (EMDR)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.36(P=0.72)					
3.4.2 Medium term					
van den Berg 2015	31/53	31/55		100%	1.04[0.75,1.44]
Subtotal (95% CI)	**53**	**55**		**100%**	**1.04[0.75,1.44]**
Total events: 31 (Individual TF-CBT), 31 (EMDR)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.22(P=0.82)					
Test for subgroup differences: Chi^2=0.17, df=1 (P=0.68), I^2=0%					



Analysis 3.5. Comparison 3 TF-CBT versus EMDR, Outcome 5 PTSD symptom severity: 5. Recovery from PTSD: Asymptomatic or few symptoms - CAPS total score < 20.

Study or subgroup	Individual TF-CBT n/N	EMDR n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
3.5.1 Short term					



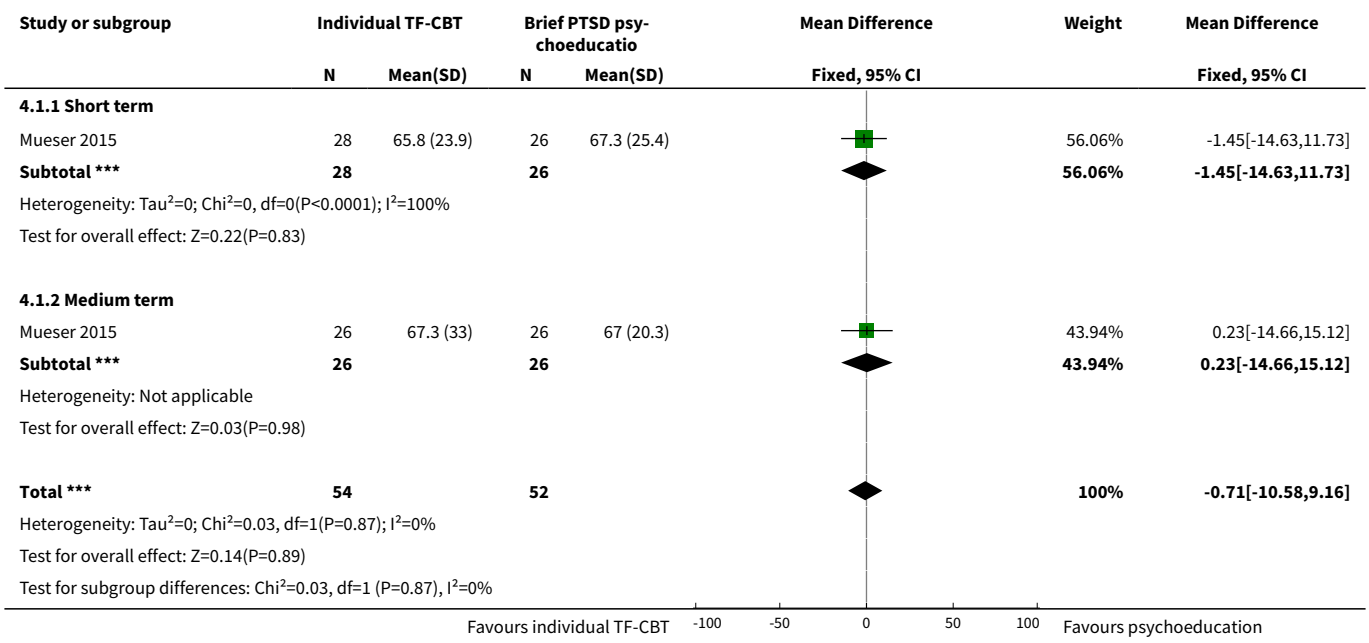
Comparison 4. Individual TF-CBT versus brief PTSD psychoeducation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 PTSD symptom severity: 1a. Clinician-rated severity - average endpoint CAPS total score (high = poor)	1	106	Mean Difference (IV, Fixed, 95% CI)	-0.71 [-10.58, 9.16]
1.1 Short term	1	54	Mean Difference (IV, Fixed, 95% CI)	-1.45 [-14.63, 11.73]
1.2 Medium term	1	52	Mean Difference (IV, Fixed, 95% CI)	0.23 [-14.66, 15.12]
2 PTSD symptom severity: 1b. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data	1	48	Mean Difference (IV, Fixed, 95% CI)	-2.13 [-19.45, 15.19]
2.1 Long term - skewed data	1	48	Mean Difference (IV, Fixed, 95% CI)	-2.13 [-19.45, 15.19]
3 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Short term	1	53	Mean Difference (IV, Fixed, 95% CI)	1.64 [-24.40, 27.68]
3.2 Medium term	1	51	Mean Difference (IV, Fixed, 95% CI)	7.68 [-18.64, 34.00]
3.3 Long term	1	49	Mean Difference (IV, Fixed, 95% CI)	16.19 [-10.45, 42.83]

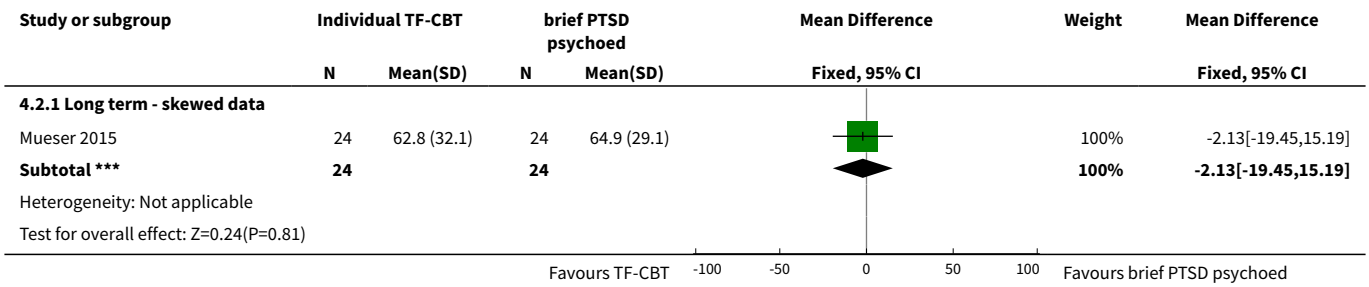
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
4.1 Short term	1	54	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.47, 2.30]
4.2 Medium term	1	52	Risk Ratio (M-H, Fixed, 95% CI)	2.0 [0.79, 5.05]
4.3 Long term	1	48	Risk Ratio (M-H, Fixed, 95% CI)	1.14 [0.49, 2.65]
5 PTSD symptom severity: 5. Remission from severe PTSD: Loss of severe PTSD diagnosis - CAPS total score < 65	1		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Short term	1	54	Risk Ratio (M-H, Fixed, 95% CI)	1.21 [0.64, 2.26]
5.2 Medium term	1	52	Risk Ratio (M-H, Fixed, 95% CI)	1.56 [0.82, 2.94]
5.3 Long term	1	48	Risk Ratio (M-H, Fixed, 95% CI)	1.3 [0.71, 2.37]
6 Quality of life: 1. General quality of life - average endpoint QoLI total score (high = good)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 Short term	1	54	Mean Difference (IV, Fixed, 95% CI)	-0.58 [-1.35, 0.19]
6.2 Medium term	1	52	Mean Difference (IV, Fixed, 95% CI)	-0.29 [-1.03, 0.45]
6.3 Long term	1	49	Mean Difference (IV, Fixed, 95% CI)	0.11 [-0.74, 0.96]
7 Quality of life: 2. Overall functioning - average endpoint GAF total score (high = good)	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 Short term	1	49	Mean Difference (IV, Fixed, 95% CI)	-0.86 [-6.48, 4.76]
7.2 Medium term	1	50	Mean Difference (IV, Fixed, 95% CI)	0.60 [-4.92, 6.12]
7.3 Long term	1	48	Mean Difference (IV, Fixed, 95% CI)	1.88 [-4.93, 8.69]
8 Quality of life: 3. Social functioning - average endpoint CAPS social func-	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only

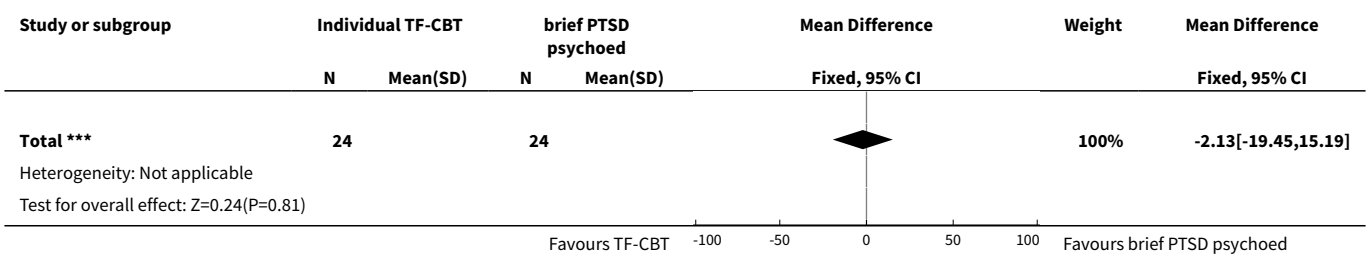
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
tioning subscale total score (high = poor) - skewed data				
8.1 Short term - skewed data	1	54	Mean Difference (IV, Fixed, 95% CI)	-0.29 [-0.86, 0.28]
8.2 Medium term - skewed data	1	52	Mean Difference (IV, Fixed, 95% CI)	-0.61 [-1.28, 0.06]
8.3 Long term - skewed data	1	48	Mean Difference (IV, Fixed, 95% CI)	0.19 [-0.46, 0.84]

Analysis 4.1. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 1 PTSD symptom severity: 1a. Clinician-rated severity - average endpoint CAPS total score (high = poor).

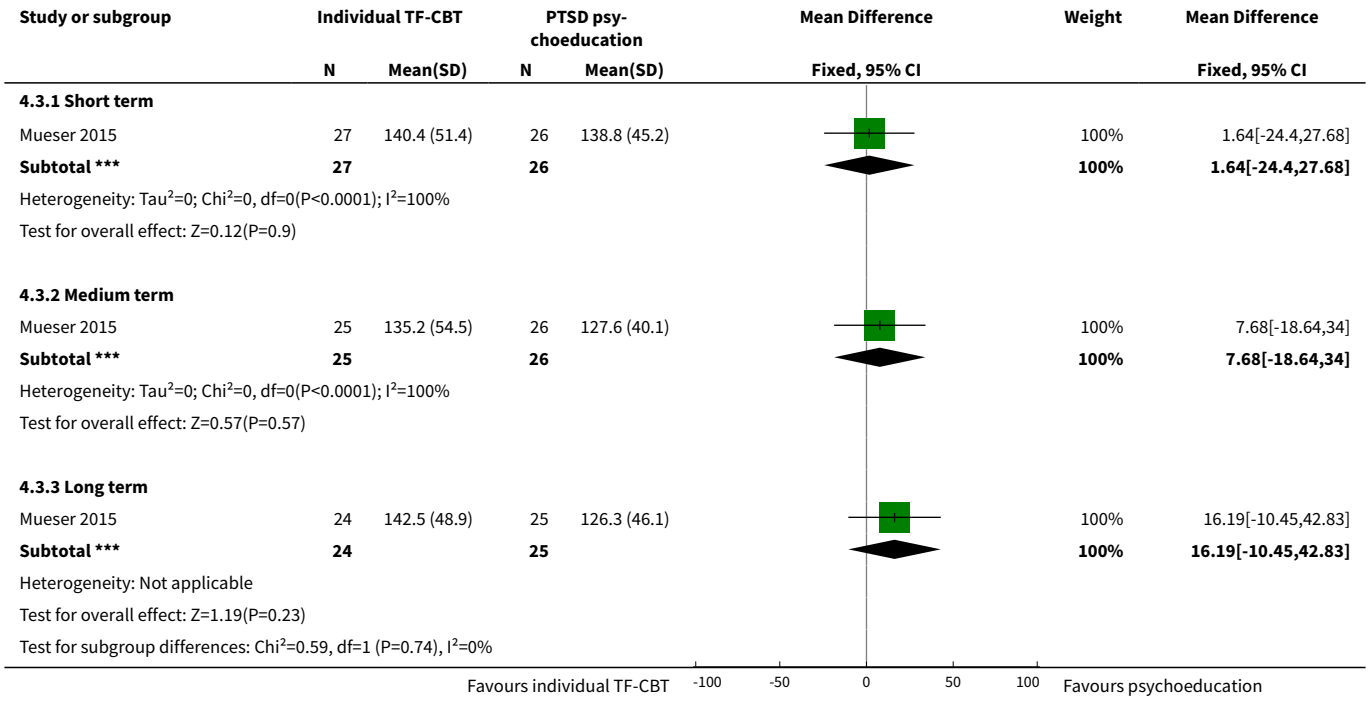


Analysis 4.2. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 2 PTSD symptom severity: 1b. Clinician-rated severity - average endpoint CAPS total score (high = poor) - skewed data.

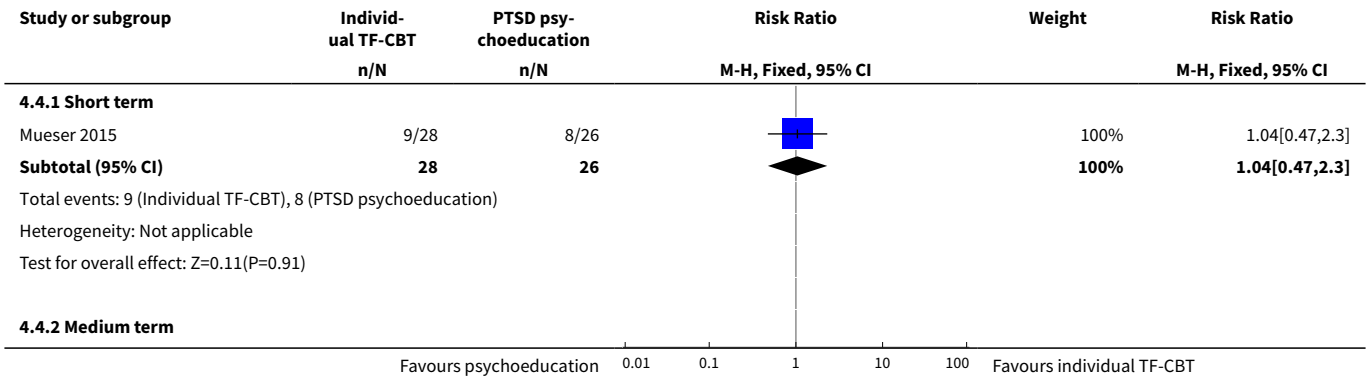


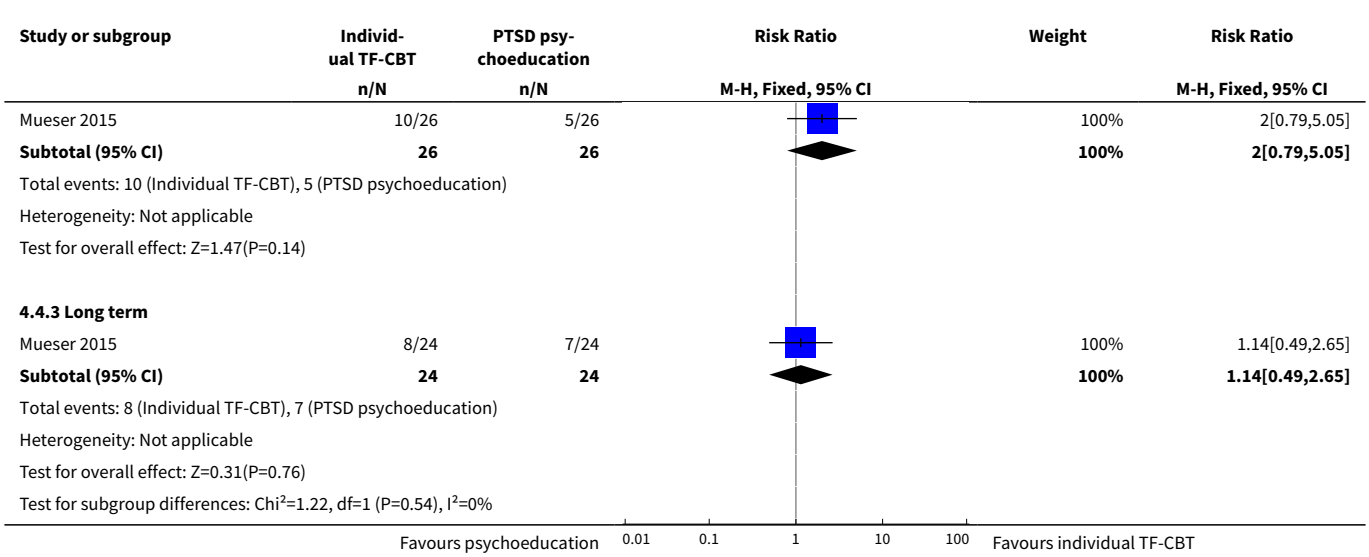


Analysis 4.3. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 3 PTSD symptom severity: 2. Self-reported trauma-related cognition - average endpoint PTCI total score (high = poor).

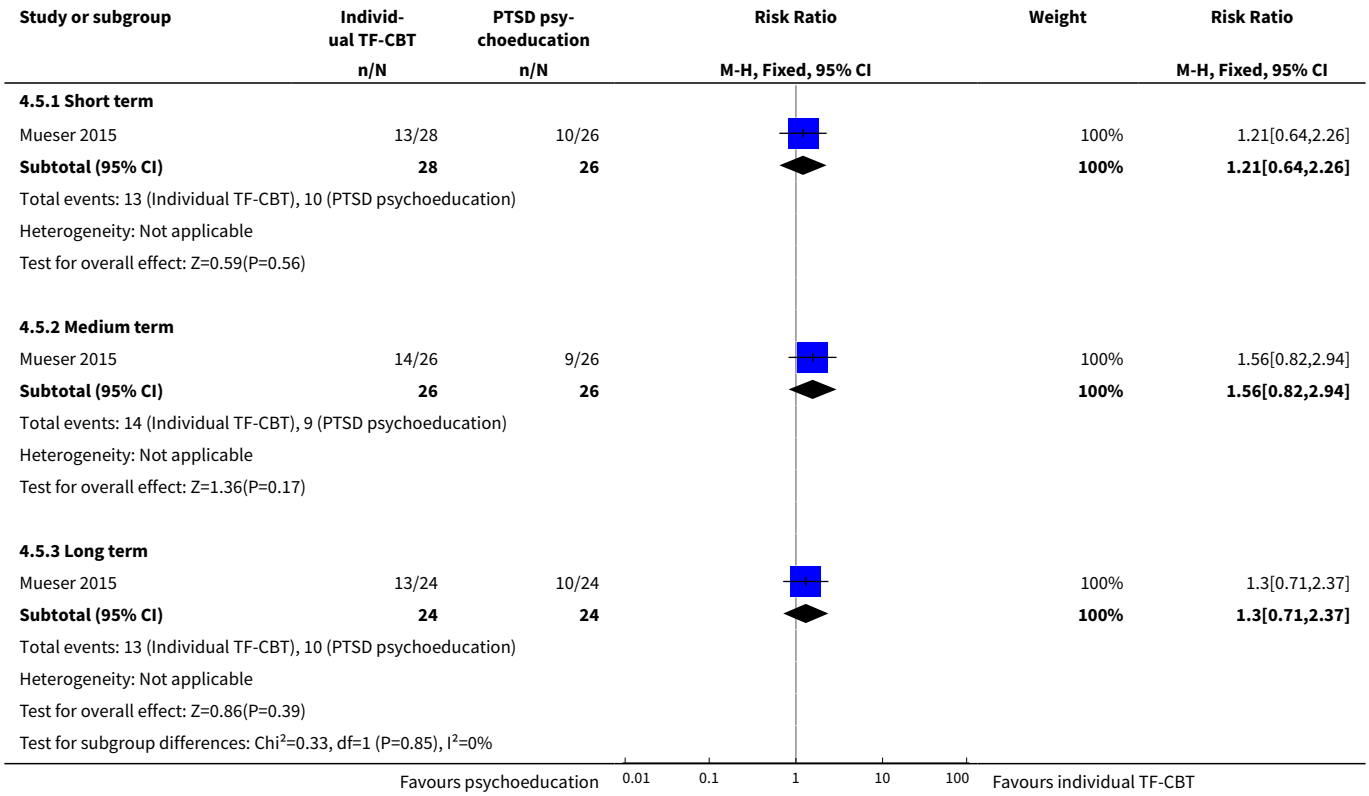


Analysis 4.4. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 4 PTSD symptom severity: 4. Remission from PTSD: Symptoms below diagnostic threshold - CAPS total score < 40.





Analysis 4.5. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 5 PTSD symptom severity: 5. Remission from severe PTSD: Loss of severe PTSD diagnosis - CAPS total score < 65.



Analysis 4.6. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 6 Quality of life: 1. General quality of life - average endpoint QoLI total score (high = good).

Study or subgroup	Individual TF-CBT		PTSD psy-choeducation		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
4.6.1 Short term							
Mueser 2015	28	4 (1.3)	26	4.6 (1.5)		100%	-0.58[-1.35,0.19]
Subtotal ***	**28**		**26**			**100%**	**-0.58[-1.35,0.19]**
Heterogeneity: Not applicable							
Test for overall effect: Z=1.47(P=0.14)							
4.6.2 Medium term							
Mueser 2015	26	4.1 (1.4)	26	4.4 (1.3)		100%	-0.29[-1.03,0.45]
Subtotal ***	**26**		**26**			**100%**	**-0.29[-1.03,0.45]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.77(P=0.44)							
4.6.3 Long term							
Mueser 2015	24	4.4 (1.2)	25	4.2 (1.8)		100%	0.11[-0.74,0.96]
Subtotal ***	**24**		**25**			**100%**	**0.11[-0.74,0.96]**
Heterogeneity: Tau^2=0; Chi^2=0, df=0(P<0.0001); I^2=100%							
Test for overall effect: Z=0.25(P=0.8)							
Test for subgroup differences: Chi^2=1.39, df=1 (P=0.5), I^2=0%							

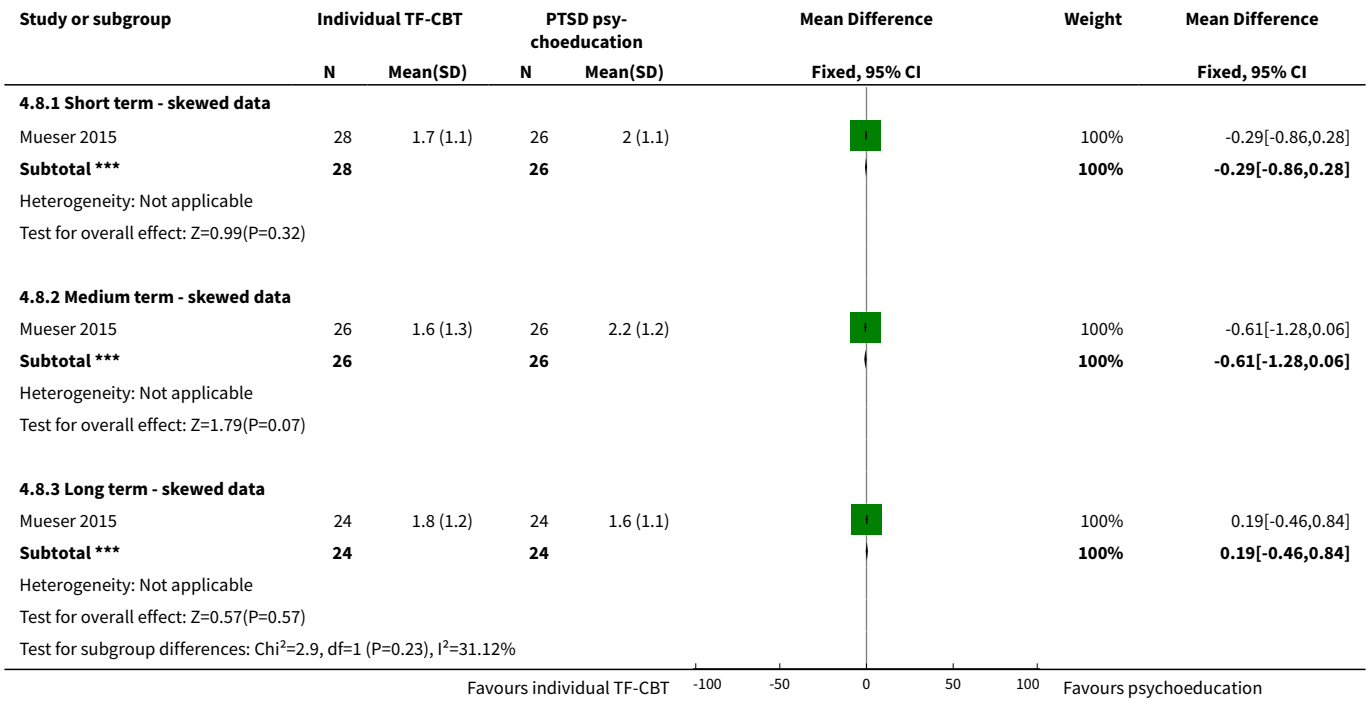
Favours psychoeducation — Favours individual TF-CBT

Analysis 4.7. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 7 Quality of life: 2. Overall functioning - average endpoint GAF total score (high = good).

Study or subgroup	Individual TF-CBT		PTSD psy-choeducation		Mean Difference	Weight	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI		Fixed, 95% CI
4.7.1 Short term							
Mueser 2015	24	54.5 (10.5)	25	55.4 (9.6)		100%	-0.86[-6.48,4.76]
Subtotal ***	**24**		**25**			**100%**	**-0.86[-6.48,4.76]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.3(P=0.76)							
4.7.2 Medium term							
Mueser 2015	24	53.8 (10.1)	26	53.2 (9.8)		100%	0.6[-4.92,6.12]
Subtotal ***	**24**		**26**			**100%**	**0.6[-4.92,6.12]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.21(P=0.83)							
4.7.3 Long term							
Mueser 2015	24	56 (9.8)	24	54.1 (13.9)		100%	1.88[-4.93,8.69]
Subtotal ***	**24**		**24**			**100%**	**1.88[-4.93,8.69]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.54(P=0.59)							
Test for subgroup differences: Chi^2=0.38, df=1 (P=0.83), I^2=0%							

Favours psycheoducation — Favours individual TF-CBT

Analysis 4.8. Comparison 4 Individual TF-CBT versus brief PTSD psychoeducation, Outcome 8 Quality of life: 3. Social functioning - average endpoint CAPS social functioning subscale total score (high = poor) - skewed data.



ADDITIONAL TABLES

Table 1. Suggested design for future studies

Methods	Allocation: randomised, full explicit description of methods of randomisation and allocation concealment
Participants	Diagnosis: Individuals with schizophrenia or psychosis (ICD or DSM) and co-morbid PTSD (DSM) N = 450* Age: adolescents and adults Sex: both
Inteventions	1. Trauma-focused cognitive behavioural therapy (modality and format to be specified), n = 150 2. Eye movement desensitisation and reprocessing (or another well-defined trauma-focused therapy as a comparative treatment), n = 150 3. Standard care/waiting list, n = 150
Outcomes	1. PTSD symptoms 2. Quality of life or well-being 3. Psychotic symptoms 4. Depressive symptoms 5. Anxiety symptoms 6. Adverse events 7. Health economic outcomes

Table 1. Suggested design for future studies *(Continued)*

Notes	*Powered to be able to identify a difference of 20% between groups for primary outcome with adequate degree of certainty

ICD: International Classification of Diseases
DSM: Diagnostic and Statistical Manual of Mental Disorders
PTSD: post-traumatic stress disorder

Table 2. Differences between protocol and review

Protocol stated comparisons as:	The current review states comparisons as:
We will conduct separate analyses focusing on each category of active psychological interventions based on a shared modality and format of delivery (i.e. TF-CBT - individual or group based, EMDR, or any psychological intervention for PTSD), comparing them to all the control conditions pooled together. If there are sufficient data extracted from included studies, we will then proceed to analyse each category of active psychological intervention targeting PTSD comparing each modality and format of active intervention against: 1) active control conditions (i.e. non-PTSD focused intervention/s); and 2) usual care/treatment as usual/waiting list, for primary outcomes.	We conducted separate analyses focusing on each category of active psychological interventions based on a shared modality and format of delivery (i.e. TF-CBT - individual or group based, EMDR, or any psychological intervention for PTSD), comparing them to all the control conditions pooled together. Whenever there were sufficient data extracted from included studies, we then proceeded to analyse each category of active psychological intervention targeting PTSD comparing each modality and format of active intervention against: 1) active control conditions (i.e. non-PTSD focused intervention/s); 2) usual care/treatment as usual/waiting list; and 3) other modality and format of active intervention, for primary outcomes.

EMDR: eye movement desensitisation and reprocessing
PTSD: post-traumatic stress disorder
TF-CBT: trauma-focused cognitive behavioural therapy

CONTRIBUTIONS OF AUTHORS

JS: proposing and designing the review, protocol development, initiating contacts with trial authors for data and information, analysis and interpretation of data, and writing and reviewing the final report.

DS: design of the review and protocol development, abstract and paper screening, data extraction, and reviewing the final report.

MF: design of the review and protocol development, data extraction, analysis of data, and reviewing the final report.

TM: design of the review and protocol development, checking data analysis and interpretation of data, and reviewing the final report.

IN: design of the review, protocol development, abstract and paper screening, checking data extraction and analysis, and reviewing the final report.

DECLARATIONS OF INTEREST

JS was involved in the Cognitive Behaviour Therapy for Post-traumatic stress disorder and Schizophrenia (C-PAS) study (ISRCTN67096137) in the capacity of a trial therapist from 2009 to 2012. JS is also based, in part, at the Berkshire Traumatic Stress Service (2004 onwards). JS is now supported by the National Institute for Health Research (NIHR) Post Doctoral Research Fellowship (Reference: PDF-2015-08-035, 2016 - 2020) and also in part by the NIHR Biomedical Research Centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London (2015 - 2017). DS is funded by a NIHR Clinical Doctoral Research Fellowship (Reference: CDRF-03-059, 2013 - 2016). The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

DS: no known conflict of interest.

MF: no known conflict of interest.

TM: no known conflict of interest.

IN: no known conflict of interest.

SOURCES OF SUPPORT

Internal sources

- Berkshire Healthcare NHS Foundation Trust, UK.

  JS is based, in part, in the Berkshire Traumatic Stress Service (BTSS), Berkshire Healthcare NHS Foundation Trust, as Consultant Nurse Therapist (from 2004 to the current time, except the period from 2012 to 2014 when her position with BTSS was of a honorary nature during her NIHR doctoral research fellowship).
- King's College London, UK.
- Kyoto University, Japan.
- South London & Maudsley NHS Foundation Trust, UK.

  Review authors DS and IN hold honorary clinical posts at South London & Maudsley NHS Foundation Trust: DS - Honorary Consultant Nurse & Cognitive Behaviour Therapist (2014 onwards); and IN - Honorary Cognitive Behavioural Psychotherapist (2009 onwards).
- St George's, University of London, UK.

  JS is based, in part, in Population Health Research Institute, St George's, University of London, from 2016 onward.

External sources

- National Institute for Health Research (NIHR), UK.

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- National Institute for Health Research (NIHR) Biomedical Research Centre based at Guy's & St Thomas' NHS Foundation Trust and King's College London, UK.

  JS is, in part, supported by a King's College London Prize Fellowship - NIHR BRC Clinical Lecturer position (August 2015 - March 2017), with BRC funded research sessions.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Minor changes

Differences made on the presentation of comparisons between interventions whilst both the types of psychological interventions and control conditions remained the same across the protocol and the review is summarised in Table 2.

The review authors acknowledged the changes made to the comparisons which allowed for comparisons of active trauma-focused interventions differing in modality and format. The rationale for doing so, was to ascertain comparative effectiveness of interventions, hence informing treatment options and choices for clinicians and patients (NICE 2011; Roth 2005).

Outcomes of interest for the 'Summary of findings' tables: We renamed a prespecified outcome 'psychotic symptoms' to 'symptoms of co-morbid psychosis' for consistency between 'Outcomes of interest' and 'Types of outcome measures' sections of the review.

INDEX TERMS

Medical Subject Headings (MeSH)

Cognitive Behavioral Therapy [*methods]; Eye Movement Desensitization Reprocessing [*methods]; Mental Disorders [*psychology]; Psychotherapy, Brief [*methods]; Quality of Life; Randomized Controlled Trials as Topic; Stress Disorders, Post-Traumatic [etiology] [*therapy]; Waiting Lists

MeSH check words

Adult; Humans