EUROPEAN JOURNAL OF PSYCHOTRAUMATOLOGY
2020, VOL. 11, 1729633
https://doi.org/10.1080/20008198.2020.1729633

EUROPEAN JOURNAL OF PSYCHO-TRAUMATOLOGY
THE OFFICIAL JOURNAL OF THE EUROPEAN SOCIETY FOR TRAUMATIC STRESS STUDIES

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REVIEW ARTICLE

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Psychological therapies for post-traumatic stress disorder in adults: systematic review and meta-analysis

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ABSTRACT

Background: Psychological therapies are the recommended first-line treatment for post-traumatic stress disorder (PTSD). Previous systematic reviews have grouped theoretically similar interventions to determine differences between broadly distinct approaches. Consequently, we know little regarding the relative efficacy of the specific manualized therapies commonly applied to the treatment of PTSD.
Objective: To determine the effect sizes of manualized therapies for PTSD.
Methods: We undertook a systematic review following Cochrane Collaboration guidelines. A pre-determined definition of clinical importance was applied to the results and the quality of evidence was appraised using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.
Results: 114 randomized-controlled trials (RCTs) of 8171 participants were included. There was robust evidence that the therapies broadly defined as CBT with a trauma focus (CBT-T), as well as Eye Movement Desensitization and Reprocessing (EMDR), had a clinically important effect. The manualized CBT-Ts with the strongest evidence of effect were Cognitive Processing Therapy (CPT); Cognitive Therapy (CT); and Prolonged Exposure (PE). There was also some evidence supporting CBT without a trauma focus; group CBT with a trauma focus; guided internet-based CBT; and Present Centred Therapy (PCT). There was emerging evidence for a number of other therapies.
Conclusions: A recent increase in RCTs of psychological therapies for PTSD, results in a more confident recommendation of CBT-T and EMDR as the first-line treatments. Among the CBT-Ts considered by the review CPT, CT and PE should be the treatments of choice. The findings should guide evidence informed shared decision-making between patient and clinician.

ARTICLE HISTORY
Received 26 October 2019
Revised 23 December 2019
Accepted 24 January 2020

KEYWORDS
PTSD; systematic review; psychological therapy

PALABRAS CLAVES
TEPT; revisión sistemática; terapia psicológica

关键字
PTSD; 系统评价; 心理治疗

HIGHLIGHTS

- This review informed the latest ISTSS treatment guidelines. It summarises the current evidence-base in relation to the effect of specific therapies for PTSD.

Terapias psicológicas para el trastorno de estrés postraumático en adultos: revisión sistemática y metaanálisis

Objetivo: determinar los tamaños del efecto de las terapias manualizadas para el TEPT.
Métodos: Realizamos una revisión sistemática siguiendo las guías de la Colaboración Cochrane. Se aplicó una definición predeterminada de importancia clínica a los resultados y se evaluó la calidad de la evidencia utilizando el enfoque de calificación de recomendaciones, evaluación, desarrollo y evaluaciones (GRADE).
Resultados: se incluyeron 114 ensayos controlados aleatorizados (ECA) de 8.171 participantes. Hubo evidencia robusta de que las terapias ampliamente definidas como TCC con un enfoque de trauma (TCC-T), así como la desensibilización y reprocesamiento POR movimientos oculares (EMDR), tuvieron un efecto clínicamente importante. Las CBT-Ts manualizados con la mayor evidencia de efecto fueron la terapia de procesamiento cognitivo (CPT); Terapia cognitiva (CT); y exposición prolongada (PE). También hubo alguna evidencia que apoya la TCC sin un enfoque traumático; TCC grupal con enfoque en trauma; TCC basada en Internet guiada; y terapia centrada en el presente (PCT). Hubo evidencia emergente para una serie de otras terapias.
Conclusiones: Un aumento reciente en ECA de terapias psicológicas para el TEPT, da como resultado una recomendación más confiable de CBT-T y EMDR como los tratamientos de primera línea. Entre los CBT-Ts considerados por la revisión CPT, CT y PE deberían ser los tratamientos de elección. Los hallazgos deben guiar la toma de decisiones compartida informada por la evidencia entre el paciente y el médico.

成人创伤后应激障碍的心理治疗：系统综述和元分析

目的: 确定创伤后应激障碍的规范疗法的效应量大小。
方法: 我们按照Cochrane协作指南进行了系统综述。临床重要性的预定义用于结果中, 并使用'建议, 评估, 发展和评估等级' (GRADE) 方法评估证据的质量。

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结果: 纳入了8171名参与者的114项随机对照试验 (RCT) 。有力的证据表明, 广泛定义为创伤中心CBT (CBT-T) 以及眼动脱敏再加工 (EMDR) 疗法具有重要的临床效果。效果最强的CBT-T是认知加工疗法 (CPT), 认知疗法 (CT), 和延长暴露 (PE) 。也有一些证据支持非创伤中心的CBT, 以创伤中心的团体CBT, 有指导的基于互联网的CBT, 现实中心疗法 (PCT) 。越来越多的证据表明存在其他许多疗法。
结论: 创伤后应激障碍心理治疗的RCT最近增加, 结果更加支持CBT-T和EMDR作为一线治疗方法。在本综述考虑的CBT-T中, CPT, CT和PE应该是首选的治疗方法。研究结果应指导患者和临床医生之间循证知情的共同决策。

1. Introduction

Post-traumatic stress disorder (PTSD) is a common mental disorder that can develop as a consequence of exposure to a serious traumatic event (American Psychiatric Association, 2013; World Health Organisation, 2018). Diagnostic criteria for PTSD specify the presence of symptoms including re-experiencing the traumatic event; avoiding reminders of the trauma; alterations in arousal and reactivity; and changes in cognition and mood (American Psychiatric Association, 2013). PTSD is a debilitating disorder, which is commonly comorbid with other conditions such as depression, substance use and anxiety disorders (Kessler, 2000; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995).

Previous systematic reviews have converged on the general finding that psychological therapies are effective for the treatment of PTSD (Bisson, Roberts, Andrew, Cooper, & Lewis, 2013; Bradley, Greene, Russ, Dutra, & Westen, 2005, Cusack, Grubaugh, Knapp, & Frueh, 2006; Jonas et al., 2013, Watts et al., 2013). Reviews to date have grouped psychological therapies together based on similar theoretical underpinnings and overlapping techniques. A broad distinction has been made between therapies that focus on the traumatic event and those that aim to reduce traumatic stress symptoms without directly targeting the trauma memory or related thoughts, with the strongest evidence for the effect of those with a trauma-focus (Bisson et al., 2013; Bradley et al., 2005; Cusack et al., 2006; Jonas et al., 2013). A further distinction has been made based on the theoretical model from which a therapy stems, for example, grouping those based on cognitive behavioural principles. Despite the benefits to the methodology in terms of detecting differences between broadly different therapeutic approaches, categorizing interventions for meta-analysis has hindered the reporting of effect sizes for specific manualized therapies.

A recent proliferation of randomized-controlled trials (RCTs) has resulted in adequate data to move beyond grouping therapies for meta-analysis, allowing the estimation of effect sizes for specific manualized therapies. In addition to the benefits of being able to inform more detailed and precise treatment recommendations, this approach may indicate the procedures shared by the most effective interventions to inform an understanding of the crucial components when developing and modifying therapies. An in-depth understanding is also required to aid patients and clinicians in the co-production of treatment plans. These should take patient characteristics and preferences into account, alongside the evidence-base for the many psychological therapies currently available for the treatment of PTSD in adults.

We conducted a comprehensive systematic review and meta-analyses of RCTs of all psychological therapies for PTSD. The aim was to determine effect sizes for specific manualized therapies for PTSD and to apply a pre-determined definition of clinically important effect in order to inform a detailed understanding of the relative efficacy of the specific psychological therapies commonly applied to the treatment of PTSD. The review informed the 2018 update of the International Society for Traumatic Stress Studies (ISTSS) treatment guidelines (ISTSS, 2018).

2. Method

2.1. Selection criteria

The review included RCTs of any defined psychological therapy aimed at the reduction of PTSD-symptoms in comparison with a control group (e.g., usual care/waiting list); other psychological therapy; or psychosocial intervention (e.g., psychoeducation/relaxation training). At least 70% of study participants were required to be diagnosed with PTSD with a duration of 3 months or more, according to DSM or ICD criteria determined by clinician diagnosis or an established diagnostic interview. This review considered studies of adults aged 18 or over, only. There were no restrictions based on symptom-severity or trauma-type. The diagnosis of PTSD was required to be primary, but there were no other exclusions based on co-morbidity. Studies that conducted secondary analyses of data already included in the meta-analyses were excluded. Studies were also excluded if a continuous measure of PTSD severity post-treatment was not available.

2.2. Search strategy

This systematic review was undertaken alongside a number of reviews for an update of the ISTSS Treatment Guidelines (ISTSS, 2018). A search was

conducted by the Cochrane Collaboration, which updated a previously published Cochrane review with the same inclusion criteria, which was published in 2013 (Bisson et al., 2013). The updated search aimed to identify all RCTs related to the prevention and treatment of PTSD, published from January 2008 to the 31 May 2018, using the search terms PTSD or posttrauma* or post-trauma* or 'post trauma*' or 'combat disorder*' or 'stress disorder*'. The searches included results from PubMed, PsycINFO, Embase and the Cochrane database of randomized trials. This produced a group of papers related to the psychological treatment of PTSD in adults. We checked reference lists of the included studies. We searched the World Health Organization's, and the U.S. National Institutes of Health's trials portals to identify additional unpublished or ongoing studies. We contacted experts in the field with the aim of identifying unpublished studies and studies that were in submission. A complementary search of the Published International Literature on Traumatic Stress (PILOTS) was also conducted.

2.3. Data extraction

Study characteristics and outcome data were extracted by two reviewers using a form that had been piloted on five of the included studies. In order to categorize therapies, information on the protocol used was sought from the methods sections of the included studies and authors were contacted if there was uncertainty regarding the type of therapy delivered. The outcome measure for the review was reduction in the severity of PTSD symptoms post-treatment using a standardized measure. When available, clinician-rated measures were included in meta-analyses (e.g., the Clinician-Administered PTSD Scale (CAPS); Blake et al., 1995). If no clinician-rated measure was used or reported, self-report measures were included (e.g., the PTSD Checklist for DSM-5 (PCL-5); Weathers et al., 2013). Study authors were contacted to obtain missing data. Therapy classifications were agreed with the ISTSS treatment guidelines committee.

2.4. Risk of bias assessment

All included studies were assessed for risk of bias using Cochrane criteria (Higgins et al., 2011). This included: (1) sequence allocation for randomization (the methods used for randomly assigning participants to the treatment arms and the extent to which this was truly random); (2) allocation concealment (whether or not participants or personnel were able to foresee allocation to a specific group); (3) assessor blinding (whether the assessor was aware of group allocation); (4) incomplete outcome data (whether missing outcome data was handled appropriately); (5) selective outcome reporting (whether reported outcomes matched with those that were pre-specified); and (6) any other notable threats to validity (for example, baseline imbalances between groups, small sample size, or premature termination of the study). Two researchers independently assessed each study and any conflicts were discussed with a third researcher with the aim of reaching a unanimous decision.

2.5. Quality of evidence assessment

The quality of evidence for each comparison was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system (GRADE, 2018). Evidence was categorized as high quality (indicating that further research is very unlikely to change confidence in the estimate of effect); moderate quality (indicating that further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate); low quality (indicating that 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) or very low quality (indicating that we are very uncertain about the estimate).

2.6. Data synthesis

Meta-analyses were conducted using the Cochrane's Review Manager 5 (RevMan) software (RevMan, 2014). Continuous measures of post-treatment PTSD severity were analysed as standardized mean differences (SMDs). All outcomes were presented using 95% confidence intervals. Clinical heterogeneity was assessed in terms of variability in the experimental and control interventions; participants; settings; and outcomes. Heterogeneity was assessed further using both the I^2 statistic and the chi-squared test of heterogeneity, as well as visual inspection of the forest plots. Data were pooled using fixed-effect meta-analyses, except where heterogeneity was present, when random-effect models were used. Since combining waitlist and usual care in a single comparison was a potential limitation of the review, sensitivity analyses looked at the influence of removing studies that adopted a usual care control group from meta-analyses making this comparison. To determine the impact of risk of bias within the included studies on outcome, sensitivity analyses were conducted by removing studies with high risk of bias in three or more domains. Sensitivity analyses were only conducted for meta-analyses including 10 or more studies, since it was unlikely that meaningful differences would be determined among a smaller number of studies. A funnel plot was constructed for the meta-analysis containing the largest number of studies and

visually inspected, with signs of asymmetry taken to indicate publication bias.

2.7. Clinical importance

A definition of clinical importance, which was developed by the ISTSS treatment guidelines committee, after consultation with the ISTSS membership, and approved by the ISTSS Board, was applied to the meta-analytic results (ISTSS, 2018). To be rated as clinically important, an intervention had to demonstrate an effect size of >0.80 for wait list control comparisons; >0.5 for attention control comparisons; >0.4 for placebo control comparisons; and >0.2 for active treatment control comparisons. If there was only one RCT, an intervention was not rated as clinically important unless it included over 300 participants. Non-inferiority RCT evidence alone was not enough to rate an intervention as clinically important.

3. Results

The original Cochrane review included 70 RCTs. The update search identified 5500 potentially eligible studies published since 2008. Abstracts were reviewed and full-text copies obtained for 203 potentially relevant studies. Forty-four new RCTs met inclusion criteria for the review. This resulted in a total of 114 RCTs of 8171 participants. Figure 1 presents a flow diagram for study selection.

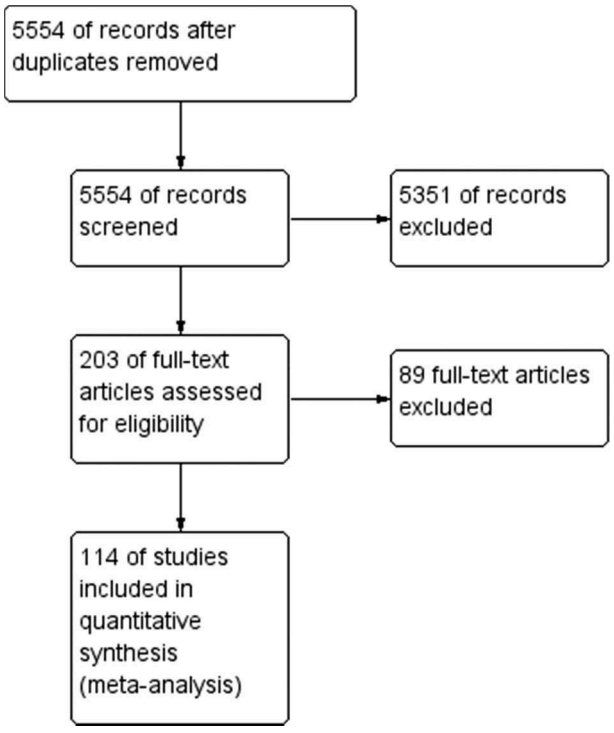

Figure 1. Study flow diagram.

3.1. Study characteristics

Study characteristics are summarized in Table 1. Twenty-nine defined psychological therapies were evaluated. Eight of these were broadly categorized as CBT-T delivered on an individual basis: Brief Eclectic Psychotherapy (BEP); Cognitive Processing Therapy (CPT); Cognitive Therapy (CT); Narrative Exposure Therapy (NET): Prolonged Exposure (PE); Single Session CBT; Reconsolidation of Traumatic Memories (RTM); Virtual Reality Exposure Therapy (VRE). Twelve other therapies delivered to individuals were evaluated: EMDR; CBT without a Trauma Focus; Present Centred Therapy (PCT); Supportive Counselling; Written Exposure Therapy; Observed and Experiential Integration (OEI); Interpersonal Psychotherapy; Psychodynamic Psychotherapy; Relaxation Training; REM Desensitization; Emotional Freedom Technique (EFT); Dialogical Exposure Therapy (DET); Relaxation Training; Psychoeducation; Guided Internet-based CBT with a Trauma Focus. There were five different types of group therapy: Group CBT-T; Group and Individual CBT-T; Group Interpersonal Therapy; Group Stabilizing Treatment; Group Supportive Counselling. Couples CBT with a Trauma Focus was also evaluated. It was decided a priori that therapies delivered in a group format would be grouped, due to the small number of studies.

The number of randomized participants ranged from 10 to 366. Studies were conducted in Australia (9), Canada (2), China (2), Denmark (1), Germany (5), Iran (2), Israel (1), Italy (2), Japan (1), the Netherlands (4), Norway (1), Portugal (1), Romania (1), Rwanda (1), Spain (1), Sweden (3), Switzerland (1), Syria (1), Thailand (1), Turkey (3), Uganda (2), UK (11), USA (61). Participants were traumatized by military combat (27 studies), sexual assault or rape (11 studies), war/persecution (8 studies), road traffic accidents (6 studies), earthquakes (4 studies), childhood sexual abuse (7 studies), political detainment (1 study), terrorism (2 studies), physical assault (2 studies), domestic violence (4 studies), trauma from a medical diagnosis/emergency (4 studies) and crime/organized violence (4 studies). The remainder (41 studies) included individuals traumatized by a variety of different traumatic events. There were 27 studies of females only and 9 of only males; the percentage of females in the remaining studies ranged from 1.75% to 96%. The percentage with a University education ranged from 4% to 90%. Exclusion criteria varied across studies, with the most common being: current or lifetime psychosis (69 studies); bipolar disorder (18 studies) or severe depression (12 studies); substance use (63 studies); suicidal ideation (55 studies). Participants were recruited from health or social care settings (71 studies); from the general public

Table 1. Study characteristics.

Study	*N*	Country	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	Trauma type	% Female	% Unemployed	% University educated
Acarturk et al. (2016)	98	Turkey/Syria	EMDR	WL			Refugees	War/Persecution	74	Unknown	4
Adenauer et al. (2011)	34	Germany	NET (CBT-T)	WL			Refugees	War/Persecution	44	Unknown	Unknown
Ahmadi, Hazrati, Ahmadizadeh, and Noohi (2015)	48	Iran	EMDR	REM desensitization	WL		Military Personnel/Veterans	Military Trauma	0	Unknown	33.3
Akbarian et al. (2015)	40	Iran	Group CBT-T	MC/RA			General Population	Various	79	Unknown	Unknown
Asukai, Saito, Tsuruta, Kishimoto, and Nishikawa (2010)	24	Japan	PE (CBT-T)	TAU			General Population	Various	88	Unknown	Unknown
Basoglu, Şalcıoğlu, Livanou, Kalender, and Acar (2005)	59	Turkey	Single-session CBT-T	WL			General Population	Earthquake	85	Unknown	5.1
Basoglu, Salcioglu, and Livanou (2007)	31	Turkey	Single-session CBT-T	MC/RA			General Population	Earthquake	93	Unknown	10
Beck, Coffey, Foy, Keane, and Blanchard (2009)	44	USA	Group CBT-T	MC/RA			General Population	Road Traffic Accident	82	54	Unknown
Bichescu, Neuner, Schauer, and Elbert (2007)	18	Romania	NET (CBT-T)	Psychoeducation			General Population	Political detainment	94	0%	72
Blanchard et al. (2003)	98	USA	CBT-T	SC	WL		General Population	Road Traffic Accident	73	Unknown	Unknown
Bradshaw, McDonald, Grace, Detwiler, and Austin (2014)	10	Canada	OEI	WL			General Population	Various	70	0	Unknown
Brom, Kleber, and Defares (1989)	83	Netherlands	CBT-T	Psychodynamic therapy	WL		General Population	Various	79	49	Unknown
Bryant, Moulds, Guthrie, Dang, and Nixon (2003)	58	Australia	CBT-T	SC			General Population	Various	52	Unknown	Unknown
Bryant et al. (2011)	28	Thailand	CBT-T	SC			General Population	Terrorist Attack	96	84%	Unknown
Buhmann, Nordentoft, Ekstroem, Carlsson, and Mortensen (2016)	138	Denmark	CBT-T	WL			Refugees	Organized Violence	41	Unknown	Unknown
Butollo, Karl, König, and Rosner (2016)	148	Germany	CPT (CBT-T)	DET			General Population	Various	66	Unknown	Unknown
Capezzani et al. (2013)	21	Italy	EMDR	CBT-T			General Population	Cancer	90	Unknown	Unknown
Carletto et al. (2016)	50	Italy	EMDR	Relaxation training			General Population	Multiple Sclerosis	81	Unknown	Unknown
Carlson, Chemtob, Rusnak, Hedlund, and Muraoka (1998)	35	USA	EMDR	Relaxation training	TAU		Military Personnel/Veterans	Military Trauma	0	62	Unknown
Castillo et al. (2016)	86	USA	Group CBT-T	WL			Military Personnel/Veterans	Military Trauma	100	44%	Unknown
Chard (2005)	71	USA	CPT (CBT-T)	WL			General Population	Child Sexual Abuse	100	Unknown	Unknown
Cloitre, Koenen, Cohen, and Han (2002)	58	USA	CBT-T	WL			General Population	Child Abuse	100	24%	52
Cloitre et al. (2010)	71	USA	CBT-T	CBT without a trauma focus			General Population	Child Abuse	100	31%	Unknown
Devilly, Spence, and Rapee (1998)	35	Australia	EMDR	TAU			Military Personnel/Veterans	Military Trauma	0	Unknown	Unknown

(*Continued*)

Table 1. (Continued).

Study	*N*	Country	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	Trauma type	% Female	% Unemployed	% University educated
Devilly and Spence (1999)	32	Australia	EMDR	CBT-T			General Population	Various	100	Unknown	Unknown
Dorrepaal et al. (2012)	71	Netherlands	Group Stabilizing Treatment	TAU			General Population	Child Abuse	Unknown	83%	Unknown
Duffy, Gillespie, and Clark (2007)	58	UK	CT (CBT-T)	WL			General Population	Various	40	Unknown	Unknown
Dunne, Kenardy, and Sterling (2012)	26	Australia	CBT-T	WL			General Population	Road Traffic Accident	50	31%	73
Echeburua, De Corral, Zubizarreta, and Sarasua (1997)	20	Spain	CBT-T	Relaxation training			General Population	Child Abuse or Adult RaPE (CBT-T)	100	Unknown	20
Ehlers, Clark, Hackmann, McManus, and Fennell (2005)	28	UK	CT (CBT-T)	WL			General Population	Various	50	25%	35
Ehlers et al. (2003)	57	UK	CT (CBT-T)	MC/RA			General Population	Road Traffic Accident	Unknown	Unknown	Unknown
Ehlers et al. (2014)	91	UK	CT (CBT-T)	SC	WL		General Population	Various	58.7	23	26
Falsetti, Resnick, and Davis (2008)	60	USA	Group CBT-T	WL			General Population	Various	100	Unknown	Unknown
Fecteau and Nicki (1999)	20	Canada	CBT-T	WL			General Population	Road Traffic Accident	70	Unknown	Unknown
Feske (2008)	21	USA	PE (CBT-T)	TAU			General Population	Various	100	29%	90%
Foa, Rothbaum, Riggs, and Murdock (1991)	45	USA	PE (CBT-T)	CBT without a trauma focus	Supportive counselling	WL	General Population	Sexual Assault	100	Unknown	Unknown
Foa et al. (1999)	66	USA	PE (CBT-T)	CBT without a trauma focus	WL		General Population	Assault/Sexual assault	100	38%	41%
Foa et al. (2005)	179	USA	PE (CBT-T)	WL			General Population	Assault	100	17%	34%
Foa et al. (2018)	256	USA	Spaced PE (CBT-T)	PCT	MC/RA		Military Personnel/Veterans	Military Trauma	12	100%	66%
Fonzo et al. (2017)	66	USA	PE (CBT-T)	WL			General Population	Various	65	Unknown	Unknown
Forbes et al. (2012)	59	Australia	CPT (CBT-T)	TAU			Military Personnel/Veterans	Military Trauma	4	36%	Unknown
Ford, Steinberg, and Zhang (2011)	146	USA	CBT without a trauma focus	PCT	WL		General Population	Various	100	Unknown	22%
Ford, Chang, Levine, and Zhang (2013)	80	USA	Group CBT-T	Group supportive counselling			Incarcerated Women	Various	100	Unknown	Unknown
Galovski, Blain, Mott, Elwood, and Houle (2012)	100	USA	CPT (CBT-T)	MC/RA			General Population	Various	69	Unknown	Unknown
Gamito et al. (2010)	10	Portugal	VRE (CBT-T)	Control exposure	WL		Military Personnel/Veterans	Military Trauma	0	Unknown	Unknown
Gersons, Carlier, Lamberts, and Van der Kolk (2000)	42	Netherlands	BEP (CBT-T)	WL			General Population	Various	Unknown	Unknown	Unknown
Gray, Budden-Potts, and Bourke (2017)	74	USA	RTM (CBT-T)	WL			Military Personnel/Veterans	Military Trauma	0	Unknown	Unknown
Hensel-Dittmann et al. (2011)	28	Germany	NET (CBT-T)	CBT without a trauma focus			Asylum Seekers	Organized Violence	Unknown	Unknown	Unknown
Hinton et al. (2005)	40	USA	CBT-T	WL			Refugees	Genocide	60	Unknown	Unknown
Hinton, Hofmann, Rivera, Otto, and Pollack (2011)	24	USA	Group CBT-T	WL			General Population	Various	100	Unknown	Unknown

(*Continued*)

Table 1. (Continued).

Study	*N*	Country	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	Trauma type	% Female	% Unemployed	% University educated
Hogberg et al. (2007)	24	Sweden	EMDR	WL			General Population	Various	38	Unknown	Unknown
Hollifield, Sinclair-Lian, Warner, and Hammerschlag (2007)	55	USA	Group trauma-focused CBT	WL			General Population	Various	68	Unknown	40%
Ironson, Freund, Strauss, and Williams (2002)	22	USA	EMDR	PE (CBT-T)			General Population	Various	77	Unknown	Unknown
Ivarsson et al. (2014)	62	Sweden	I-CBT	WL			General Population	Various	82	8%	65%
Jacob, Neuner, Maedl, Schaal, and Elbert (2014)	76	Rwanda	NET (CBT-T)	WL			Genocide Survivors	Genocide	92	Unknown	Unknown
Jensen (1994)	25	USA	EMDR	WL			Military Personnel/Veterans	Military Trauma	0	68	Unknown
Johnson, Zlotnick, and Perez (2011)	70	USA	CBT without a trauma focus	TAU			General Population	Intimate Partner Violence	100	73	7%
Johnson, Johnson, Perez, Palmieri, and Zlotnick (2016)	60	USA	CBT without a trauma focus	TAU			General Population	Intimate Partner Violence	100	77	5%
Karatzias et al. (2011)	46	UK	EMDR	EFT			General Population	Various	57	37	47%
Keane, Fairbank, Caddell, and Zimering (1989)	24	USA	CBT-T	WL			Military Personnel/Veterans	Military Trauma	0	Unknown	Unknown
Krupnick et al. (2008)	48	USA	Group IPT	WL			General Population	Interpersonal Trauma	100	80	13%
Kubany, Hill, and Owens (2003)	37	USA	CBT-T	WL			General Population	Domestic Abuse	100	Unknown	Unknown
Kubany et al. (2004)	107	USA	CBT-T	WL			General Population	Domestic Abuse	100	Unknown	Unknown
Laugharne et al. (2016)	20	Australia	EMDR	PE (CBT-T)			General Population	Various	70	Unknown	Unknown
Lee, Gavriel, Drummond, Richards, and Greenwald (2002)	24	Australia	CBT-T	EMDR			General Population	Various	46	Unknown	Unknown
Lewis et al. (2017)	42	UK	I-CBT	WL			General Population	Various	57	19	62%
Littleton, Grills, Kline, Schoemann, & Dodd (2016)	87	USA	I-CBT	I-Psychoeducation			General Population	Rape	100	Unknown	Unknown
Litz, Engel, Bryant, and Papa (2007)	45	USA	I-CBT	I-SC			Military Personnel/Veterans	Terrorism/Military Trauma	Unknown	Unknown	Unknown
Marcus, Marquis, and Sakai (1997)	67	USA	EMDR	TAU			General Population	Various	79	Unknown	Unknown
Markowitz et al. (2015)	110	USA	IPT	PE (CBT-T)	Relaxation Therapy		General Population	Various	70	21	Unknown
Marks, Lovell, Noshirvani, Livanou, and Thrasher (1998)	87	UK	PE (CBT-T)	Cognitive restructuring	PE (CBT-T) (CBT-T) (CBT-T)and Cognitive Restructuring	Relaxation without PE (CBT-T) (CBT-T)(CBT-T)or CR	General Population	Various	36	54	Unknown
McDonagh et al. (2005)	74	USA	PE (CBT-T)	PCT	WL		General Population	Child Sexual Abuse	100	17	Unknown
McLay et al. (2011)	20	USA	VRE (CBT-T)	TAU			Military Personnel/Veterans	Military Trauma	5	Unknown	Unknown
McLay et al. (2017)	81	USA	VRE (CBT-T)	Control exposure therapy			Military Personnel/Veterans	Military Trauma	4	Unclear	Unclear
Monson et al. (2012)	20	USA	Couples CBT-T	WL			General Population	Various	25	40	Unknown
Monson et al. (2006)	60	USA	CPT (CBT-T)	WL			Military Personnel/Veterans	Military Trauma	10	Unknown	Unknown

(*Continued*)

Table 1. (Continued).

Study	*N*	Country	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	Trauma type	% Female	% Unemployed	% University educated
Morath et al. (2014)	38	Germany	NET (CBT-T)	WL			Refugees	Organized Violoence	32	Unknown	Unknown
Mueser et al. (2008)	108	USA	CBT-T	TAU			General Population	Various	79	Unknown	Unknown
Nacasch et al. (2011)	30	Israel	PE (CBT-T)	TAU			Military Personnel/Veterans	Military Trauma	Unknown	63	Unknown
Neuner et al. (2010)	32	Germany	NET (CBT-T)	TAU			Refugees	Torture	31	Unknown	Unknown
Neuner et al. (2008)	277	Uganda	NET (CBT-T)	SC	Monitoring		Refugees	War	51	49	Unknown
Neuner, Schauer, Klaschik, Karunakara, and Elbert (2004)	43	Uganda	NET (CBT-T)	SC	Psychoeducation		Refugees	War	60	28	Unknown
Nijdam, Gersons, Reitsma, de Jongh, and Olff (2012)	140	Netherlands	BEP (CBT-T)	EMDR			General Population	Vaious	56	Unknown	30
Pacella et al. (2012)	66	USA	PE (CBT-T) (CBT-T)	MC/RA			General Population	HIV Diagnosis	37	Unknown	Unknown
Paunovic (2011)	29	Sweden	CBT-T	WL			General Population	Crime	63	74	11
Peniston and Kulkosky (1991)	29	USA	CBT-T	TAU			Military Personnel/Veterans	Military Trauma	Unknown	Unknown	Unknown
Power et al. (2002)	105	UK	EMDR	CBT-T	WL		General Population	Various	42	Unknown	Unknown
Rauch et al. (2015)	36	USA	PE (CBT-T) (CBT-T)	PCT			Military Personnel/Veterans	Military Trauma	9	Unknown	Unknown
Ready, Gerardi, Backscheider, Mascaro, and Rothbaum (2010)	11	USA	VRE (CBT-T)	PCT			Military Personnel/Veterans	Military Trauma	Unknown	Unknown	Unknown
Reger et al. (2016)	162	USA	VRE (CBT-T)	PE (CBT-T)	WL		Military Personnel/Veterans	Military Trauma	4	Active duty	7
Resick et al. (2015)	108	USA	Group CBT-T	Group PCT			Military Personnel/Veterans	Military Trauma	8	0	8
Resick, Nishith, Weaver, Astin, and Feuer (2002)	171	USA	CPT (CBT-T) (CBT-T)	PE (CBT-T)	Minimal Attention		General Population	Rape	100	Unknown	Unknown
Resick et al. (2017)	268	USA	CPT (CBT-T) (CBT-T)	Group CBT-T			Military Personnel/Veterans	Military Trauma	9	100	19
Rothbaum (1997)	18	USA	EMDR	WL			General Population	Sexual Assault	100	19	43
Rothbaum, Astin, and Marsteller (2005)	60	USA	PE (CBT-T)	EMDR	WL		General Population	Rape	100	Unknown	Unknown
Sautter, Glynn, Cretu, Senturk, and Vaught (2015)	57	USA	Couples CBT without a trauma focus	Couples psychoeducation			Military Personnel/Veterans	Military Trauma	1.75	12	75
Scheck, Schaeffer, and Gillette (1998)	60	USA	EMDR	SC			General Population	Various	100	Unknown	Unknown
Schnurr et al. (2003)	360	USA	Group CBT-T	Group PCT			Military Personnel/Veterans	Military Trauma	0	51	Unknown
Schnurr et al. (2007)	284	USA	PE (CBT-T) (CBT-T)	Group PCT			Military Personnel/Veterans	Military Trauma	100	38	Unknown
Schnyder, Müller, Maercker, and Wittmann (2011)	30	Switzerland	BEP (CBT-T)	MC/RA			General Population	Various	46.7	Unknown	Unknown
Sloan, Marx, Bovin, Feinstein, and Gallagher (2012)	46	USA	WET	WL			General Population	Road Traffic Accident	Unclear	78	41
Sloan, Marx, Lee, and Resick (2018)	126	USA	WET	CPT (CBT-T)			General Population	Various	49	Unknown	13
Spence et al. (2011)	42	Australia	I-CBT	WL			General Population	Various	81	41	Not Clear

(*Continued*)

Table 1. (Continued).

Study	*N*	Country	Intervention 1	Intervention 2	Intervention 3	Intervention 4	Population	Trauma type	% Female	% Unemployed	% University educated
Stenmark, Catani, Neuner, Elbert, and Holen (2013)	81	Norway	NET (CBT-T)	TAU			Refugees	Various	31	Unknown	25
Suris, Link-Malcolm, Chard, Ahn, and North (2013)	86	USA	CPT (CBT-T)	PCT			Military Personnel/Veterans	Military Sexual Trauma	85	43	16
Taylor et al. (2003)	60	USA	PE (CBT-T)	Relaxation therapy	EMDR		General Population	Various	75	13	Unknown
Tylee, Gray, Glatt, and Bourke (2017)	30	USA	RTM (CBT-T)	WL			General Population	Military Trauma	0	Unknown	Unknown
Vaughan et al. (1994)	36	Australia	CBT-T	Relaxation training	EMDR		General Population	Various	64	Unknown	Unknown
Wells, Walton, Lovell, and Proctor (2015)	32	UK	PE (CBT-T)	CBT without a trauma focus	WL		General Population	Various	38	6	Unknown
Wells and Sembi (2004)	20	UK	CBT without a trauma focus	WL			General Population	Various	55	Unknown	Unknown
Yehuda et al. (2014)	52	USA	PE (CBT-T)	MC/RA			Military Personnel/Veterans	Military Trauma	Unclear	Unknown	Unknown
Zang, Hunt, and Cox (2014)	20	China	NET (CBT-T)	WL			General Population	Earthquake	90	Unknown	Unknown
Zang, Hunt, and Cox (2013)	22	China	NET (CBT-T)	WL			General Population	Earthquake	77	Unknown	Unknown
Zlotnick et al. (1997)	48	USA	Group CBT-T	WL			General Population	Child Sexual Abuse	100	Unknown	33

BEP, brief eclectic psychotherapy; NET, narrative exposure therapy; CBT, cognitive behavioural therapy; OEI, observed and experimental integration; CBT-T, cognitive behavioural therapy with a trauma focus; PCT, present centred therapy; CPT, cognitive processing therapy; PE, prolonged exposure; CR, cognitive restructuring; REM Desensitization, rapid eye movement desensitization; CT, cognitive therapy; RTM, reconsolidation of traumatic memories; DET, dialogical exposure therapy; SC, supportive counselling; EFT, emotional freedom technique; TAU, treatment as usual; EMDR, eye movement desensitization and reprocessing; VRE, virtual reality exposure; I-CBT, Internet-based cognitive behavioural therapy; WET, written emotion therapy; I-Psychoeducation, Internet-based psychoeducation; WL, waiting list; IPT, interpersonal psychotherapy; I-SC, Internet-based supportive counselling; MC/RA, medical checks/repeated assessments.

via advertisements (21); or through a combination of the two approaches (7 studies).

3.2. Risk of bias

Risk of bias assessments for the included studies is summarized in Table 2. Fifty-three studies reported a method of sequence allocation judged to pose a 'low' risk of bias; four reported a method with a 'high' risk of bias; the remainder reported insufficient details and were, therefore, rated as 'unclear'. Forty-one studies reported methods of allocation concealment representing a 'low' risk of bias; one a method with a 'high' risk of bias; with the remainder rated as 'unclear'. The outcome assessor was aware of the participant's allocation in 12 of the included studies; it was unclear whether the outcome assessor was aware of group allocation in 18 studies; with the remainder using blind-raters or self-report questionnaires delivered in a way that could not be influenced by members of the research team. Twenty-three studies were judged as posing a 'high' risk of bias in terms of incomplete outcome data; 80 studies were felt to have dealt with dropouts appropriately ('low' risk of bias); it was unclear in the remaining studies. The majority of studies failed to reference a published protocol, resulting in an 'unclear' risk of selective reporting for 78 studies; risk of bias was judged as 'high' in five studies and low in the remainder. Seventy of the included studies presented a 'high' risk of bias in other areas, for example, in relation to sample size, baseline imbalances between groups, or other methodological shortfalls. We could not rule out potential researcher allegiance, since treatment originators were involved in the evaluation of their own intervention in many of the included studies.

3.3. Efficacy

Results of the meta-analyses are summarized in Tables 3 and 4. The strongest evidence of effect was for the studies broadly categorized as CBT-T, and EMDR. Meta-analyses of specific manualized CBT-Ts found that CPT; CT; and PE had the strongest evidence of effect. There was also some evidence supporting the effect of NET (a variant of CBT-T); CBT without a trauma focus; PCT; Group CBT-T and guided internet-based CBT. There was emerging evidence to support the effect of single-session CBT; RTM; VRE (all variants of CBT-T); as well as Written Exposure Therapy; combined group and individual CBT-T; and couples CBT-T. There was insufficient evidence to support the efficacy of BEP (a variant of CBT-T); Supportive Counselling; Group Interpersonal Therapy; Group Stabilizing Treatment; Group Supportive Counselling; Group Interpersonal Therapy; OEI; Psychodynamic Therapy; Relaxation Training; or Psychoeducation.

3.4. Sensitivity analyses

Four of the meta-analyses included 10 or more studies (CBT-T versus waitlist/usual care/minimal attention; PE versus waitlist/usual care/minimal attention; EMDR versus waitlist/usual care/minimal attention; and EMDR versus CBT-T). Sensitivity analyses that removed studies with high risk of bias in three or more domains gave similar SMDs and confidence intervals. Sensitivity analyses that removed studies with a usual care control group found that SMDs and confidence intervals in the analyses of CBT-T and PE, but evidence of improved effect in the case of EMDR.

3.5. Heterogeneity

There was evidence of substantial clinical heterogeneity across studies in terms of the inclusion and exclusion criteria of the studies; the populations from which the samples were drawn; the nature and duration of therapy; the qualifications and experience of therapists; the predominant trauma type; the mean age of participants; and the proportion of female versus male participants. Considerable statistical heterogeneity was also evident in many of the pooled comparisons. This resulted in regular use of a random-effects model.

3.6. Publication bias

All of the included studies were published. There was evidence of some publication bias, demonstrated by a funnel plot using data from the comparison of CBT-T versus waitlist/usual care/minimal attention.

4. Discussion

4.1. Main findings

In agreement with previous reviews and in continued support of existing treatment guidelines (American Psychological Association, 2017; Australian Centre for Posttraumatic Mental Health, 2007; National Collaborating Centre for Mental Health, 2005; US Department of Veterans Affairs, 2017), there was robust evidence for the clinically important effect of the therapies broadly defined as CBT-T, as well as EMDR. A substantial increase in the number of RCTs published in recent years resulted in a greater level of confidence in these findings. This review went further, and we conducted meta-analyses of specific manualized therapies. By applying pre-determined definitions of clinically important effect, we found that the CBT-Ts with the strongest evidence were PE, CPT and CT. There was also some evidence in support of NET; and emerging evidence in support of other CBT-Ts, namely, single-session CBT-T; RTM; VRE; and WRT. There was

Table 2. Risk assessment.

	Random sequence generation	Allocation concealment	Incomplete outcome data assessment	Blinding of outcome	Selective reporting	Other sources of bias	Total no. high risk
Acarturk et al. (2016)	Low	Low	Low	Low	Low	Low	0
Adenauer et al. (2011)	Low	Low	Low	Low	High	High	2
Ahmadi, Hazrati, Ahmadizadeh, and Noohi (2015)	Unclear	Unclear	High	Unclear	Unclear	High	2
Akbarian et al. (2015)	Low	High	Low	Low	Unclear	High	2
Asukai, Saito, Tsuruta, Kishimoto, and Nishikawa (2010)	Low	Low	Low	Low	Unclear	High	1
Basoglu et al. (2005)	Low	Low	Low	Low	Unclear	High	1
Basoglu, Salcioglu, and Livanou (2007)	Low	Low	High	High	Unclear	High	3
Beck, Coffey, Foy, Keane, and Blanchard (2009)	Unclear	Unclear	High	Low	Unclear	High	2
Bichescu, Neuner, Schauer, and Elbert (2007)	High	Unclear	Low	Low	Unclear	High	2
Blanchard et al. (2003)	High	Unclear	Low	Low	Unclear	Low	1
Bradshaw, McDonald, Grace, Detwiler, and Austin (2014)	Unclear	Unclear	Low	High	Unclear	High	2
Brom, Kleber, and Defares (1989)	Unclear	Unclear	High	Unclear	Unclear	High	2
Bryant, Moulds, Guthrie, Dang, and Nixon (2003)	Low	Unclear	Low	Low	Low	High	1
Bryant et al. (2011)	Low	Low	Low	Low	Unclear	High	1
Buhmann, Nordentoft, Ekstroem, Carlsson, and Mortensen (2016)	Low	Low	Unclear	Low	Low	Low	0
Butollo, Karl, König, and Rosner (2016)	Unclear	Unclear	Low	Low	Unclear	High	1
Capezzani et al. (2013)	Unclear	Unclear	Low	Low	Unclear	High	1
Carletto et al. (2016)	Low	Low	High	Low	Low	Low	1
Carlson, Chemtob, Rusnak, Hedlund, and Muraoka (1998)	Unclear	Unclear	High	Unclear	Unclear	Low	1
Castillo et al. (2016)	Unclear	Unclear	Low	Low	Unclear	High	1
Chard (2005)	Unclear	Unclear	Low	Low	Unclear	High	1
Cloitre, Koenen, Cohen, and Han (2002)	Unclear	Unclear	Low	Low	High	Low	1
Cloitre et al. (2010)	Unclear	Low	Low	Low	Low	Low	0
Devilly, Spence, and Rapee (1998)	Unclear	Unclear	High	Low	Unclear	Low	1
Devilly and Spence (1999)	High	Unclear	High	Unclear	Unclear	High	3
Dorrepaal et al. (2012)	Unclear	Low	Low	Low	High	High	2
Duffy, Gillespie, and Clark (2007)	Low	Low	Low	Unclear	Low	High	1
Dunne, Kenardy, and Sterling (2012)	Unclear	Unclear	Low	Unclear	Unclear	High	1
Echeburua, De Corral, Zubizarreta, and Sarasua (1997)	Unclear	Unclear	Low	Unclear	Unclear	High	1
Ehlers, Clark, Hackmann, McManus, and Fennell (2005)	Low	Low	High	Low	Unclear	High	2
Ehlers et al. (2003)	Unclear	Unclear	Low	Low	Unclear	High	2
Ehlers et al. (2014)	Unclear	Low	Low	Low	Low	Low	0
Falsetti, Resnick, and Davis (2008)	Unclear	Unclear	Low	Low	High	High	2
Fecteau and Nicki (1999)	Low	Unclear	High	Unclear	Unclear	High	2
Feske (2008)	Unclear	Unclear	Low	Unclear	Unclear	High	1
Foa, Rothbaum, Riggs, and Murdock (1991)	Unclear	Unclear	High	Low	Unclear	High	2
Foa et al. (1999)	Unclear	Unclear	Low	Low	Unclear	High	1
Foa et al. (2005)	Low	Low	Low	Low	Unclear	Low	0
Foa et al. (2018)	Low	Low	Low	Low	Low	Low	0
Fonzo et al. (2017)	Low	Unclear	Low	Unclear	Low	Low	0
Forbes et al. (2012)	Unclear	Low	Low	Unclear	Unclear	High	1
Ford, Steinberg, and Zhang (2011)	Low	Low	Low	Low	Unclear	High	1
Ford, Chang, Levine, and Zhang (2013)	Low	Low	High	Low	Unclear	High	2
Galovski, Blain, Mott, Elwood, and Houle (2012)	Unclear	Unclear	Low	Low	Unclear	Low	0
Gamito et al. (2010)	Unclear	Unclear	Unclear	Unclear	High	High	2
Gersons, Carlier, Lamberts, and Van der Kolk (2000)	Unclear	Unclear	Low	Low	Unclear	Low	0
Gray, Budden-Potts, and Bourke (2017)	Low	Low	Unclear	Unclear	Unclear	Unclear	0
Hensel-Dittmann et al. (2011)	Low	Low	Low	Low	Unclear	Low	0
Hinton et al. (2005)	Low	Unclear	Low	Low	Unclear	High	1
Hinton, Hofmann, Rivera, Otto, and Pollack (2011)	Unclear	Unclear	Low	Unclear	Unclear	High	1
Hogberg et al. (2007)	Low	Unclear	High	Low	Unclear	High	2
Hollifield, Sinclair-Lian, Warner, and Hammerschlag (2007)	Low	Low	Low	Low	Unclear	High	1
Ironson, Freund, Strauss, and Williams (2002)	Unclear	Unclear	Low	High	Unclear	High	2
Ivarsson et al. (2014)	Low	Unclear	Low	Low	Low	High	1

(*Continued*)

Table 2. (Continued).

	Random sequence generation	Allocation concealment	Incomplete outcome data assessment	Blinding of outcome	Selective reporting	Other sources of bias	Total no. high risk
Jacob, Neuner, Maedl, Schaal, and Elbert (2014)	Low	Low	Low	Low	Unclear	High	1
Jensen (1994)	Unclear	Unclear	High	Unclear	Unclear	High	2
Johnson, Zlotnick, and Perez (2011)	Low	Unclear	Low	High	Unclear	Low	1
Johnson, Johnson, Perez, Palmieri, and Zlotnick (2016)	Low	Low	Low	Low	Unclear	Low	0
Karatzias et al. (2011)	Low	Low	Low	Low	Unclear	High	1
Keane, Fairbank, Caddell, and Zimering (1989)	Unclear	Unclear	Unclear	High	Unclear	High	2
Krupnick et al. (2008)	Unclear	Unclear	Low	Unclear	Unclear	High	1
Kubany, Hill, and Owens (2003)	Unclear	Unclear	Low	Low	Unclear	High	1
Kubany et al. (2004)	Unclear	Unclear	Low	Low	Low	High	1
Laugharne et al. (2016)	Low	Low	Low	Low	Unclear	High	1
Lee, Gavriel, Drummond, Richards, and Greenwald (2002)	Unclear	Unclear	Low	Low	Unclear	High	1
Lewis et al. (2017)	Low	Low	Low	Low	Low	High	1
Littleton et al. (2016)	Low	Unclear	Low	High	Low	Low	1
Litz, Engel, Bryant, and Papa (2007)	Unclear	Unclear	High	Low	Low	High	2
Marcus, Marquis, and Sakai (1997)	Unclear	Unclear	Unclear	High	Unclear	High	2
Markowitz et al. (2015)	Low	Low	Low	Low	Low	High	1
Marks, Lovell, Noshirvani, Livanou, and Thrasher (1998)	Unclear	Unclear	Low	Low	Unclear	Low	0
McDonagh et al. (2005)	Unclear	Unclear	Low	Low	Unclear	Low	0
McLay et al. (2011)	Low	Low	Unclear	High	Unclear	High	2
McLay et al. (2017)	Low	Unclear	Low	Low	Low	Low	0
Monson et al. (2012)	Low	Low	Low	Low	Low	Low	0
Monson et al. (2006)	Low	Low	Low	Low	Unclear	Low	0
Morath et al. (2014)	Low	Low	Unclear	Low	Low	Low	0
Mueser et al. (2008)	Low	Low	Low	Low	Unclear	High	1
Nacasch et al. (2011)	Low	Unclear	Low	Low	Low	High	1
Neuner et al. (2010)	Low	Unclear	Low	Low	Low	High	1
Neuner et al. (2008)	Unclear	Unclear	Low	Low	Unclear	Low	0
Neuner, Schauer, Klaschik, Karunakara, and Elbert (2004)	Unclear	Unclear	Low	Low	Unclear	High	1
Nijdam, Gersons, Reitsma, de Jongh, and Olff (2012)	Unclear	Low	Low	Low	Low	Low	0
Pacella et al. (2012)	Low	Unclear	Low	Low	Unclear	Low	0
Paunovic (2011)	Unclear	Unclear	Low	High	Unclear	High	2
Peniston and Kulkosky (1991)	Unclear	Unclear	Unclear	Low	Unclear	Unclear	0
Power et al. (2002)	Low	Low	High	Low	Unclear	Low	1
Rauch et al. (2015)	Unclear	Unclear	Low	Low	Unclear	High	1
Ready, Gerardi, Backscheider, Mascaro, and Rothbaum (2010)	Unclear	Unclear	Unclear	Low	Unclear	High	1
Reger et al. (2016)	Low	Low	Low	Low	Unclear	Low	0
Resick et al. (2015)	Unclear	Unclear	Low	Low	Unclear	High	1
Resick, Nishith, Weaver, Astin, and Feuer (2002)	Unclear	Unclear	Low	Low	Unclear	Low	0
Resick et al. (2017)	Low	Unclear	Low	Low	Low	Low	0
Rothbaum (1997)	Unclear	Unclear	High	Low	Unclear	High	2
Rothbaum, Astin, and Marsteller (2005)	Unclear	Unclear	High	Low	Unclear	Low	1
Sautter, Glynn, Cretu, Senturk, and Vaught (2015)	Unclear	Unclear	Low	Low	Unclear	Low	0
Scheck, Schaeffer, and Gillette (1998)	Low	Low	High	Unclear	Unclear	High	2
Schnurr et al. (2003)	High	Unclear	Low	Low	Low	Low	1
Schnurr et al. (2007)	Low	Low	Low	Low	Low	Low	0
Schnyder, Müller, Maercker, and Wittmann (2011)	Low	Unclear	Low	Low	Unclear	Unclear	0
Sloan, Marx, Bovin, Feinstein, and Gallagher (2012)	Low	Low	Unclear	Low	Unclear	Low	0
Sloan, Marx, Lee, and Resick (2018)	Low	Low	Low	Low	Low	Low	0
Spence et al. (2011)	Low	Unclear	High	High	Low	Unclear	2
Stenmark, Catani, Neuner, Elbert, and Holen (2013)	Unclear	Unclear	Low	High	Low	High	2
Suris, Link-Malcolm, Chard, Ahn, and North (2013)	Unclear	Unclear	Low	Low	Low	High	1
Taylor et al. (2003)	Unclear	Unclear	Low	Low	Unclear	Low	0
Tylee, Gray, Glatt, and Bourke (2017)	Unclear	Unclear	Unclear	Low	Unclear	High	1
Vaughan et al. (1994)	Unclear	Unclear	Low	Low	Unclear	Low	0
Wells, Walton, Lovell, and Proctor (2015)	Low	Low	Low	Low	Unclear	High	1
Wells and Sembi (2004)	Low	Low	High	High	Unclear	High	3
Yehuda et al. (2014)	Unclear	Unclear	High	Unclear	Unclear	Unclear	1
Zang, Hunt, and Cox (2014)	Unclear	Unclear	Low	Low	Low	High	1
Zang, Hunt, and Cox (2013)	Low	Unclear	Low	Low	Low	High	1
Zlotnick et al. (1997)	Unclear	Unclear	High	Low	Low	High	2

Table 3. Meta-analytic results.

	Severity of PTSD symptoms post-treatment	GRADE judgement for quality of evidence
1) CBT with a trauma focus versus wait list or treatment as usual.	CBT with a trauma focus showed a positive effect when compared with wait list or treatment as usual [k = 51; *N* = 1380; SMD −1.32 CI −1.57 to −1.08].	Moderate quality
2) Brief Eclectic Psychotherapy versus wait list or treatment as usual.	Brief Eclectic Psychotherapy showed no benefit when compared with wait list or treatment as usual [k = 2; *N* = 72; SMD −0.38 CI −0.85 to 0.09].	Very low quality
3) Cognitive Processing Therapy versus wait list or treatment as usual.	Cognitive Processing Therapy showed a positive effect when compared with wait list or treatment as usual [k = 4; *N* = 298; SMD −1.03 CI −1.45 to −0.61].	Low quality
4) Cognitive Therapy versus wait list or treatment as usual.	Cognitive Therapy showed a positive effect when compared with wait list or treatment as usual [k = 4; *N* = 189; SMD −1.33 CI −1.80 to −0.86].	Low quality
5) Narrative Exposure Therapy (NET) versus wait list or treatment as usual.	Narrative Exposure Therapy (NET) showed a positive effect when compared with wait list or treatment as usual [k = 8; *N* = 241; SMD −1.06 CI −1.61 to −0.52].	Low quality
6) Prolonged Exposure versus wait list or treatment as usual.	Prolonged exposure (PE) showed a positive effect when compared with wait list or treatment as usual [k = 12; *N* = 772; SMD −1.59 CI −2.05 to −1.13].	Low quality
7) Single Session CBT with a trauma focus versus wait list or treatment as usual.	Single Session CBT with a trauma focus showed a positive effect when compared with wait list or treatment as usual [k = 2; *N* = 90; SMD −0.57 CI −1.00 to −0.15].	Very low quality
8) Reconsolidation of traumatic memories (RTM) versus wait list or treatment as usual	RTM showed a positive effect when compared with wait list or treatment as usual [k = 2; *N* = 96; SMD −2.35 CI −2.89 to −1.82].	Very low quality
9) EMDR versus wait list or treatment as usual	EMDR showed a positive effect when compared with wait list or treatment as usual [k = 11; *N* = 415; SMD −1.23 CI −1.69 to −0.76].	Low quality
10) Non-trauma focused CBT versus wait list or treatment as usual	CBT without a trauma focus showed a positive effect when compared with wait list or treatment as usual [k = 7; *N* = 318; SMD −1.06 CI −1.39 to −0.73].	Low quality
11) Supportive counselling versus waitlist or treatment as usual	There was no evidence of a difference between supportive counselling and wait list or treatment as usual [k = 2; *N* = 72; SMD −0.43 CI −0.90 to 0.04].	Very low quality
12) Present centred therapy versus waitlist or treatment as usual	Present centred therapy showed a positive effect when compared with waitlist of treatment as usual [k = 2; *N* = 138; SMD −0.97 CI −1.33 to −0.62].	Very low quality
13) Psychodynamic therapy versus treatment as usual	Psychodynamic therapy showed no benefit when compared with wait list or treatment as usual [k = 1; *N* = 52; SMD −0.41; CI −0.96 to 0.14].	Very low quality
14) Written exposure therapy versus treatment as usual	Written exposure therapy showed a positive effect when compared with waitlist of treatment as usual [k = 1; *N* = 44; SMD −3.39; CI −4.43 to −2.44].	Very low quality
15) Virtual Reality Therapy versus wait list or treatment as usual	Virtual Reality Therapy showed a positive effect when compared with wait list or treatment as usual [k = 3; *N* = 104; SMD −0.43 CI −0.83 to −0.03].	Very low quality
16) Observed and experimental integration (OEI) versus wait list or treatment as usual	OEI showed a positive effect when compared with wait list or treatment as usual [k = 1; *N* = 10; SMD −2.86 CI −4.90 to −0.83].	Very low quality
17) Relaxation Training versus wait list or treatment as usual	Relaxation training showed no benefit when compared with wait list or treatment as usual [k = 1; *N* = 53; SMD −0.10; CI −0.65 to 0.46].	Very low quality
18) Group CBT with a trauma focus versus wait list or treatment as usual	Group CBT with a trauma focus showed a positive effect when compared with wait list or treatment as usual [k = 7; *N* = 313; SMD −1.02 CI −1.26 to −0.78].	Moderate quality
19) Group and individual CBT with a trauma focus versus wait list or treatment as usual	Group and individual CBT with a trauma focus showed a positive effect when compared with wait list or treatment as usual [k = 1; *N* = 55; SMD −2.32 CI −3.01 to −1.62].	Very low quality
20) Group stabilizing treatment versus wait list or treatment as usual	Group stabilizing treatment showed no benefit when compared with wait list or treatment as usual [k = 1; *N* = 71; SMD −0.11; CI −0.36 to 0.57].	Very low quality
21) Group interpersonal therapy (IPT) versus wait list or treatment as usual	Group IPT showed a positive effect when compared with waitlist or treatment as usual [k = 1; *N* = 48; SMD −1.19; CI −1.84 to −0.54].	Very low quality
22) Couples CBT with a trauma focus vs waitlist or treatment as usual	Couples CBT with a trauma focus showed a positive effect when compared with waitlist or treatment as usual [k = 1; *N* = 40; SMD −1.12; CI −1.79 to −0.45].	Very low quality
23) Guided internet-based trauma focused CBT versus waitlist/usual care	Guided internet-based CBT with a trauma focus showed a positive effect when compared with wait list or treatment as usual [k = 3; *N* = 145; SMD −1.08 CI −1.80 to −0.37].	Very low quality

insufficient evidence to support the efficacy of BEP. Although CBT-Ts and EMDR demonstrated the strongest evidence of effect, there was also evidence supporting the effect of CBT without a trauma focus; PCT; Group CBT-T; and guided internet-based CBT, as well as emerging evidence in support of combined group and individual CBT with a trauma focus; couples CBT with a trauma focus. There was insufficient evidence to support Group therapies without a trauma focus; OEI; Psychodynamic Therapy; Relaxation Training; or psychoeducation.

The comparison of effect sizes across meta-analyses was not straightforward. Although we can draw conclusions in relation to the treatments most strongly supported by the evidence-base, this does not equate to evidence that other interventions were ineffective. Some comparisons may have lacked sufficient statistical power to demonstrate clinically important effect. On occasion, therapies were delivered to act as an active control and may not have been optimally effective. As an example, supportive counselling often barred discussion of the trauma, which diverges from standard practice. There were many more RCTs of CBT-T and EMDR than those without a trauma-focus, and a greater number of studies of therapies delivered on an individual basis than those delivered to couples or groups. Although it is unlikely new studies will substantially alter the

Table 4. Meta-analytic results.

	Severity of PTSD symptoms post-treatment	GRADE judgement for quality of evidence
1) CBT with a trauma focus versus CBT without a trauma focus	There was no evidence of a difference between CBT with a trauma focus versus CBT without a trauma focus [k = 5; *N* = 185; SMD −0.10 CI −0.19 to 0.39].	Low quality
2) CBT with a trauma focus versus Present Centred Therapy	CBT with a trauma focus showed a positive effect when compared with present centred therapy [k = 4; *N* = 433; SMD −0.45 CI −0.81 to −0.09].	Low quality
3) CBT with a trauma focus versus supportive counselling	CBT with a trauma focus showed a positive effect when compared with supportive counselling [k = 8; *N* = 434; SMD −0.63 CI −1.04 to −0.21].	Low quality
4) CBT with a trauma focus versus psychodynamic therapy	There was no evidence of a difference between CBT with a trauma focus and psychodynamic therapy [k = 1; *N* = 56; SMD −0.03 CI −0.56 to 0.49].	Very low quality
5) CBT with a trauma focus versus Interpersonal Therapy (IPT)	CBT-T showed a positive effect when compared with IPT [k = 1; *N* = 66; SMD −0.48; CI −0.98 to 0.01].	Very low quality
6) CBT without a trauma focus versus PCT	There was no evidence of a difference between CBT without a trauma focus and PCT [k = 1; *N* = 101; SMD −0.04; CI −0.43 to 0.35].	Very low quality
7) CBT with a trauma focus versus dialogical exposure therapy (DET)	CBT with a trauma focus showed a positive effect when compared with dialogical exposure therapy [k = 1; *N* = 138; SMD −0.39; CI −0.73 to −0.05].	Very low quality
8) Cognitive processing therapy (CPT) versus prolonged exposure (PE)	There was no evidence of a difference between cognitive processing therapy and prolonged exposure [k = 1; *N* = 124; SMD −0.18; CI −0.53 to 0.17].	Very low quality
9) EMDR versus CBT with a trauma focus	There was no evidence of a difference between CBT with a trauma focus and EMDR [k = 10; *N* = 387; SMD −0.17 CI −0.55 to 0.21].	Low quality
10) EMDR versus supportive counselling	EMDR showed a positive effect when compared with supportive counselling [k = 1; *N* = 57; SMD −0.75 CI −1.29 to −0.21].	Very low quality
11) EMDR versus EFT	There was no evidence of a difference between EMDR and EFT [k = 1; *N* = 46; SMD = 0.08; CI −0.50 to 0.65].	Very low quality
12) EMDR versus Relaxation Training	There was no evidence of a difference between EMDR and Relaxation Training [k = 4; *N* = 117; SMD = −0.23; CI −0.59 to 0.14].	Very low quality
13) EMDR versus REM Desensitization	There was no evidence of a difference between EMDR and REM Desensitization [k = 1; *N* = 21; SMD = 0.06; CI −0.80 to 0.91].	Very low quality
14) CBT without a trauma focus versus supportive counselling	CBT without a trauma focus showed a positive effect when compared with supportive counselling [k = 1; *N* = 25; SMD −1.22 CI −2.09 to −0.35].	Very low quality
15) CBT with a trauma focus versus psychoeducation	There was no evidence of a difference between CBT-T and psychoeducation [k = 1; *N* = 27; SMD = −0.19; CI −0.95 to 0.57].	Very low quality
16) Written exposure therapy versus CBT with a trauma focus	There was no evidence of a difference between WED and CBT with a trauma focus [k = 1; *N* = 126; SMD 0.13; CI −0.21 to 0.48].	Very low quality
17) CBT with a trauma focus versus relaxation training	Individual CBT with a trauma focus showed a positive effect when compared with relaxation training [k = 5; *N* = 203; SMD −0.49; CI −0.79 to −0.20].	Low quality
18) Supportive counselling versus psychoeducation	There was no evidence of a difference between supportive counselling and psychoeducation [k = 1; *N* = 25; SMD 0.13; CI −0.92 to 0.65].	Low quality
19) Interpersonal therapy versus relaxation training	There was no evidence of a difference between IPT and relaxation training [k = 1; *N* = 60; SMD −0.15; CI −0.67 to 0.38].	Very low quality
20) Virtual reality therapy versus control exposure	There was no evidence of a difference between virtual reality therapy and control exposure [k = 2; *N* = 177; SMD 0.01; CI −0.68 to 0.71].	Low quality
21) Virtual reality therapy and present centred therapy	There was no evidence of a difference between virtual reality therapy and present centred therapy [k = 1; *N* = 9; SMD −0.51; CI −1.86 to 0.84].	Very low quality
22) Group CBT with a trauma focus versus group present centred therapy	Group CBT with a trauma focus showed a positive effect when compared with group present centred therapy [k = 2; *N* = 333; SMD −0.44; CI −0.63 to −0.24].	Low quality
23) Group CBT with a trauma focus versus individual CBT with a trauma focus	Individual CBT with a trauma focus showed a positive effect when compared with group CBT with a trauma focus [k = 1; *N* = 268; SMD 0.35; CI 0.11 to 0.59].	Very low quality
24) Group CBT without a trauma focus versus group supportive counselling	There was no evidence of a difference between group CBT without a trauma focus and group supportive counselling [k = 1; *N* = 72; SMD −0.02; CI −0.48 to 0.44].	Very low quality
25) Couples CBT without a trauma focus vs couples psychoeducation	Couples CBT without a trauma focus showed a positive effect when compared with couples psychoeducation [k = 1; *N* = 43; SMD −1.37; CI −2.04 to −0.70].	Very low quality
26) Internet-based trauma focused CBT versus internet-based psychoeducation	Internet-based CBT with a trauma focus showed no benefit when compared with internet-based psychoeducation [k = 1; *N* = 87; SMD 0.11 CI −0.31 to 0.53].	Very low quality
27) Internet-based trauma focused CBT versus internet-based CBT without a trauma focus	Internet-based CBT with a trauma focus showed no benefit when compared with internet-based CBT without a trauma focus [k = 1; *N* = 31; SMD 0.40 CI −1.12 to 0.31].	Very low quality

estimated pooled-effect of CBT-T or EMDR, it is probable that further research will modify the evidence base for therapies currently represented by fewer studies. Although not as strong as the evidence for CBT-T and EMDR, emerging evidence for interventions such as guided internet-based CBT and PCT advances the field by providing a greater choice of evidence-based therapies.

4.2. Strengths and limitations

The review followed Cochrane guidelines for the identification of relevant studies; data extraction and synthesis; risk of bias assessment; and interpretation of findings (Higgins & Green, 2011). The review moves the field forward, by estimating the effect of specific manualized therapies when available data allowed, rather than grouping similar approaches.

Despite the many strengths of the review, there were inevitable limitations. The small number of studies evaluating interventions delivered to a group or to couples precluded analyses of these therapies, as was previously the case for therapies delivered on an individual basis. All included studies were published, resulting in the possibility of publication bias. A funnel plot constructed from the meta-analysis of CBT-T versus waitlist or usual care found some evidence of publication bias, indicating that the currently available evidence may overestimate the effect of CBT-T. Several studies reported incomplete data and although authors were contacted, it was not always possible to obtain missing information, resulting in the exclusion of otherwise eligible studies. The majority of studies included in the review excluded individuals with comorbidities of substance dependence, psychosis, and severe depression; we are not, therefore, able to draw any conclusions beyond the efficacy of psychological therapies for relatively simple presentations of PTSD. Waitlist and treatment as usual were included as a single comparison group in meta-analyses, giving a more conservative estimate of effect than reviews that have separated the two. It is acknowledged that usual care, especially in more recent studies, may have included evidence-based therapies. This said, sensitivity analyses, which excluded studies with a usual care control group from comparisons with more than ten studies, revealed little difference in the outcome in two of three eligible analyses. The methodological quality of included studies varied considerably, and risk of bias was high/unclear in several domains of many studies. However, sensitivity analyses removing studies with high risk of bias in at least three or more domains revealed little influence. Most of the trials to date have been conducted on DSM-IV PTSD. We are not therefore able to draw conclusions regarding the performance of therapies on the additional cluster of symptoms (alterations in mood and cognitions) that was introduced by DSM-5. Data on the competence of the therapists and the number of therapy sessions was not extracted from the included studies and we cannot therefore comment on these as factor that may have impacted efficacy. Sample sizes were often small; however, the pooled comparisons included data from 8171 participants.

4.3. Clinical implications

The psychological therapies with the strongest evidence of effect should be those prioritized for clinical use when available and acceptable to the patient. It is, however, unlikely that any given therapy is universally appropriate for all individuals with PTSD. There is a need to consider predictors of outcome that may indicate the suitability of particular therapies for specific subgroups of patients. We should also consider the skills and therapeutic style of the therapist, given the likelihood that some are better at delivering certain types of therapy than others. Since there is evidence for the effect of numerous psychological therapies, the evidence-base should be used to guide shared decision-making between patient and clinician. There is a need for detailed assessment; followed by discussion surrounding the evidence; resulting in the co-production of treatment plans that consider patient-preference (National Institute for Health and Care Excellence [NICE], 2018). Although the strongest evidence of effect was for CBT-T and EMDR, there was also evidence in support of CBT without a trauma focus and PCT. This indicates a role for these therapies as alternatives to trauma-focused intervention, if the latter are not available; if patient preference dictates; or if exposure work is contra-indicated, for example, if an individual is unable to tolerate the treatment.

Despite the current review giving a good indication of the therapies most strongly supported by the current evidence-base, these are not always widely available or accessible. There is growing evidence in support of group and internet-based therapies, which are potential avenues for widening access to low-cost treatment and disseminating evidence-based therapies more efficiently. At least a proportion of individuals are likely to respond to these minimally intensive treatments and require no further intervention, which fits well with the principles of prudent healthcare. It is hoped that future work will identify the characteristics of those unlikely to respond to less intensive interventions, allowing a more stratified or personalized approach to treatment. Work is needed to develop optimal clinical pathways that deliver appropriate evidence-based therapies in the most efficient way possible, whilst ensuring the acceptability of the approach to patients. There are additional factors to take into account when considering clinical implications, including rates of attrition from treatment; adverse events; the acceptability of treatment approaches; and cost-effectiveness. Considering these factors was beyond the scope of this review, but they should inform clinical practice.

4.4. Research implications

Although we report effect sizes across a range of therapies, further high-quality head-to-head RCTs of the most effective interventions are necessary to determine comparative efficacy among participants drawn from the same population. We know little about the predictors of outcome and acceptability of psychological therapies, and a greater understanding would enable targeted recommendation of particular

treatments to specific sub-groups of patients. PTSD is a highly heterogeneous condition (DiMauro, Carter, Folk, & Kashdan, 2014, Murphy, Ross, Busuttil, Greenberg, & Armour, 2019) and work is needed to develop more personalized approaches. We do not have a sufficient understanding of the efficacy of current therapies for those with a diagnosis of ICD-11 complex PTSD (Dorrepaal et al., 2013, 2014; Karatzias et al., 2019). Further research is needed to evaluate existing therapies among those with complex PTSD, and to modify or develop new therapies, as appropriate. Work is also needed to determine the efficacy of therapies in addressing the DSM-5 symptom-cluster related to mood and cognition. Therapies delivered in a group format and to couples have shown promise, but there are currently an insufficient number of studies to conduct meta-analyses beyond those grouping interventions into broad categories. There is a need for established standards for the reporting of psychological therapy trials to ensure that methods are transparent and any risk of bias clear. This would also ensure a clearer definition of control groups. In many studies, it was unclear what constituted usual care and what intervention, if any, was permitted in wait-list control groups. We know very little about the acceptability of psychological therapies for PTSD and more work should focus on patient preference.

Acknowledgments

We would like to acknowledge the input and support of the Cochrane Collaboration and the International Society for Traumatic Stress Studies (ISTSS).

Disclosure statement

CL, JB and NR are the authors of one of the included RCTs.

Funding

This work was unfunded.

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