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

Catrin Lewis, Neil P. Roberts, Martin Andrew, Elise Starling and Jonathan I. Bisson

*National Centre for Mental Health (NCMH), Division of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, Cardiff, UK; †Directorate of Psychology and Psychological Therapies, Cardiff & Vale University Health Board, Cardiff, UK; ‡Cardiff Traumatic Stress Service, Cardiff & Vale University Health Board, Cardiff, UK

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.

CONTACT Catrin Lewis LewisCE7@Cardiff.ac.uk Division of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, Hadyn Ellis Building, Maindy Road, Cardiff CF24 4HQ, UK

Work conducted at the Division of Psychological Medicine and Clinical Neurosciences, Cardiff University School of Medicine, Hadyn Ellis Building, Maindy Road, Cardiff CF24 4HQ, UK

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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 blindness (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 I² 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.

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 detention (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.

Figure 1. Study flow diagram.
| 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, Hozati, 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 PE (CBT-T) TAU |                |                |                | General Population | Various | 79           | Unknown             |
| Asukai, Saito, Tsuruta, Kishimoto, and Nishikawa (2010) | 24  | Japan        | PE (CBT-T) WL |                |                |                | General Population | Various | 88           | Unknown             |
| Basoglu, Salicoglu, Livano, Kalender, and Acar (2005) | 59  | Turkey       | Single-session CBT-T WL |                |                |                | General Population | Earthquake | 85          | Unknown             |
| Basoglu, Salicoglu, and Livano (2007) | 31  | Turkey       | Single-session CBT-T MC/RA |                |                |                | General Population | Earthquake | 93          | Unknown             |
| 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 OEI WL |                |                |                | General Population | Road Traffic Accident | 73        | Unknown      | Unknown             |
| Bradshaw, McDonald, Grace, Detwiler, and Austin (2014) | 10  | Canada       | CBT-T SC WL OEI WL |                |                |                | General Population | Road Traffic Accident | 70        | 0           | Unknown             |
| Brom, Kleber, and Defaæs (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             |
| Bryant et al. (2011)                 | 28  | Thailand     | CBT-T SC |                |                |                | General Population | Terrorist Attack | 96        | 84%         | Unknown             |
| Buhmann, Nordentoft, Ekstroem, Carlson, and Mortensen (2016) | 138 | Denmark      | CBT-T WL |                |                |                | Refugees Organized Violence | 41       | Unknown      | Unknown             |
| Buttollo, Karl, König, and Rosner (2016) | 148 | Germany      | CPT (CBT-T) DET |                |                |                | General Population | Various   | 66          | Unknown             |
| Capezzani et al. (2013)              | 21  | Italy        | EMDR CBT-T |                |                |                | General Population | Cancer    | 90          | Unknown             |
| Carletto et al. (2016)               | 50  | Italy        | EMDR Relaxation training |                |                |                | General Population | Multiple Sclerosis | 81        | Unknown      | Unknown             |
| Carlson, Chemboto, 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          | CBT-T WL |                |                |                | Military Personnel/Veterans Child Sexual Abuse | 100      | 44%         | Unknown             |
| Cloitre, Koenen, Cohen, and Han (2002) | 58  | USA          | CBT-T WL |                |                |                | Military Personnel/Veterans Child Abuse | 100      | 24%         | 52                  |
| Cloitre et al. (2010)                | 71  | USA          | CBT-T CBT without a trauma focus WL |                |                |                | 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)
| 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          | TAU                   | General Population      | Various            | Child Abuse       | 100      | Unknown     | Unknown              |
| Dorrepaal et al. (2012)      | 71  | Netherlands   | Group Stabilizing Treatment |                 |                       |                          | General Population   | Child Abuse       | 100      | Unknown     | Unknown              |
| Duffy, Gillespie, and Clark  | 58  | UK            | CT (CBT-T)                  | WL             |                       | General Population      | Various            | Unknown           | 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            | Unknown           | 50       | 23%         | 35                   |
| Ehlers et al. (2003)         | 57  | UK            | CT (CBT-T)                  | MC/RA          | SC                    | General Population      | Road Traffic Accident | Unknown           | 58.7     | 23%         | 26                   |
| Ehlers et al. (2014)         | 91  | USA           | Group CBT-T                 | WL             |                       | General Population      | Various            | Unknown           | 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      | Road Traffic Accident | 100     | 29%         | 90%                  |
| Foa, Rothbaum, Riggs, and Murdock (1991) | 45  | USA           | PE (CBT-T)                  | CBT without a trauma focus | Supportive counselling | General Population      | Road Traffic Accident | 65       | Unknown     | Unknown              |
| Foa et al. (1999)            | 66  | USA           | PE (CBT-T)                  | CBT without a trauma focus | Supportive counselling | General Population      | Road Traffic Accident | 65       | Unknown     | Unknown              |
| Foa et al. (2005)            | 179 | USA           | PE (CBT-T)                  | WL             | PCT                   | General Population      | Military Personnel/Veterans | 100      | 17%         | 34%                  |
| Foa et al. (2018)            | 256 | USA           | PE (CBT-T)                  | WC             | MC/RA                 | General Population      | Military Trauma       | 12       | 100%        | 66%                  |
| Fonzo et al. (2017)          | 66  | USA           | PE (CBT-T)                  | WC             |                       | General Population      | Various             | 65       | Unknown     | Unknown              |
| Forbes et al. (2012)         | 59  | Australia     | CBT (CBT-T)                 | WC             |                       | General Population      | Military Trauma       | 4        | 36%         | 66%                  |
| Ford, Steinberg, and Zhang (2011) | 146 | USA           | CBT without a trauma focus | WC             |                       | 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)                 | WC             |                       | General Population      | Various             | 69       | Unknown     | Unknown              |
| Gamito et al. (2010)         | 10  | Portugal      | VRE (CBT-T)                 | WC             |                       | General Population      | Military Trauma       | 0        | Unknown     | Unknown              |
| Gersons, Carlier, Lamberts, and Van der Kolk (2000) | 42  | Netherlands   | BEP (CBT-T)                 | WC             | Control exposure       | General Population      | Military Trauma       | 0        | Unknown     | Unknown              |
| Gray, Budden-Potts, and Bourke (2017) | 74  | USA           | RTM (CBT-T)                 | WC             |                       | General Population      | Military Trauma       | 0        | Unknown     | Unknown              |
| Hensel-Dittmann et al. (2011) | 28  | Germany       | NET (CBT-T)                 | WC             |                       | Asylum Seekers          | Organized Violence    | Unknown           | Unknown     | Unknown              |
| Hinton et al. (2005)         | 40  | USA           | CBT-T                       | WC             |                       | Refugees                | Genocide             | 60       | Unknown     | Unknown              |
| Hinton, Hofmann, Rivera, Otto, and Pollack (2011) | 24  | USA           | Group CBT-T                 | WC             |                       | General Population      | Various             | 100      | Unknown     | Unknown              |
| 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,                | 55  | USA     | Group trauma-  | WL             |                |                | General Population  | Various          | 68       | Unknown      | 40%                  |
| Warner, and Hammerschlag (2007)           |     |         | focused CBT    |                |                |                |                     |                   |          |              |                      |
| Ironson, Freund, Strauss, and Williams    | 22  | USA     | EMDR           | PE (CBT-T)     |                |                | General Population  | Various          | 77       | Unknown      | Unknown              |
| (2002)                                    |     |         |                |                |                |                |                     |                   |          |              |                      |
| Ivarsson et al. (2014)                    | 62  | Sweden  | I-CBT          | WL             |                |                | General Population  | Various          | 82       | 8%           | 65%                  |
| Jacob, Neuner, Maedl, Schaal, and Elbert  | 76  | Rwanda  | NET (CBT-T)    | WL             |                |                | General Population  | Genocide Survivors| 92       | Unknown      | Unknown              |
| (2014)                                    |     |         |                |                |                |                |                     |                   |          |              |                      |
| Jensen (1994)                             | 25  | USA     | EMDR           | WL             |                |                | Military Personnel  | Military Trauma   | 0        | 68           | Unknown              |
| Johnson, Zlotnick, and Perez (2011)       | 70  | USA     | CBT without    | TAU            |                |                | General Population  | Intimate Partner  | 100      | 73           | 7%                   |
| Johnson, Johnson, Perez, Palermi, and     | 60  | USA     | a trauma       | TAU            |                |                |                     | Violence          | 100      | 77           | 5%                   |
| Zlotnick (2016)                           |     |         | focus          |                |                |                |                     |                   |          |              |                      |
| Karatzias et al. (2011)                   | 46  | UK      | EMDR           | EFT            |                |                | General Population  | Various          | 57       | 37           | 47%                  |
| Keane, Fairbank, Caddell, and             | 24  | USA     | CBT-T          | WL             |                |                | Military Personnel  | Military Trauma   | 0        | Unknown      | Unknown              |
| Zmering (1989)                            |     |         |                |                |                |                |                     |                   |          |              |                      |
| 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  | Various           | 100      | Unknown      | Unknown              |
| Laughame et al. (2016)                    | 20  | Australia | EMDR          | PE (CBT-T)     |                |                | General Population  | Various           | 70       | Unknown      | Unknown              |
| Lee, Gavriel, Drummond, Richards, and     | 24  | Australia | CBT-T          | EMDR           |                |                |                     | Various           | 46       | Unknown      | Unknown              |
| Greenwald (2002)                          |     |         |                |                |                |                |                     |                   |          |              |                      |
| Lewis et al. (2017)                       | 42  | UK      | I-CBT          | WL             |                |                | General Population  | Various          | 57       | 19           | 62%                  |
| Littleton, Grills, Kline, Schoemann, &    | 87  | USA     | I-CBT          | I-Psychoeducation|            |                | General Population  | Rape             | 100      | Unknown      | Unknown              |
| Dodd (2016)                               |     |         |                |                |                |                |                     |                   |          |              |                      |
| Litz, Engel, Bryant, and Papa (2007)      | 45  | USA     | I-CBT          | I-SC           |                |                | Military Personnel  | 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)     | Cognitive      | Relaxation      | General Population  | Various           | 70       | 21           | Unknown              |
| Marks, Lovell, Nochirvani, Livanou, and   | 87  | UK      | PE (CBT-T)     | Cognitive      | Restructuring  | Therapy         | General Population  | Various           | 36       | 54           | Unknown              |
| Thrasrer (1998)                           |     |         | Cognitive      | Restructuring  |               | Therapy         |                     |                   |          |              |                      |
| McDonagh et al. (2005)                    | 74  | USA     | PE (CBT-T)     | PCT            |                |                | General Population  | Child Sexual Abuse | 100      | 17           | Unknown              |
| McIay et al. (2011)                       | 20  | USA     | VRE (CBT-T)    | TAU            |                |                | General Population  | Military Personnel  | 100      | 17           | Unknown              |
| McIay et al. (2017)                       | 81  | USA     | VRE (CBT-T)    | Control exposure therapy | TAU | | General Population  | Military Personnel  | 100      | 17           | Unknown              |
| Monson et al. (2012)                      | 20  | USA     | Couples CBT-   | WL             |                |                | General Population  | Various           | 25       | 40           | Unknown              |
| Monson et al. (2006)                      | 60  | USA     | CPT (CBT-T)    | WL             |                |                | General Population  | Military Personnel  | 100      | Unknown      | Unknown              |
| 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 Violence    | 32       | Unknown      | Unknown              |
| Mueser et al. (2008)        | 108 | USA         | CBT-T          | TAU            |                |                | General Population | Various     | 79           | Unknown              |
| Nacach 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, Klischik,  | 43  | Uganda      | NET (CBT-T)    | SC             | Psychoeducation|                | Refugees   | War                   | 60       | 28           | Unknown              |
| Karunakara, and Elbert       |     |             |                |                |                |                |            |                      |          |              |                      |
| Nijdam, Gersons, Reitsma,   | 140 | Netherlands | BEP (CBT-T)    | EMDR           |                |                | General Population | Various     | 56           | Unknown              |
| de Jongh, and Off (2012)    |     |             |                |                |                |                |            |                      |          |              |                      |
| Pacella et al. (2012)       | 66  | USA         | PE (CBT-T)     | MC/RA          |                |                | General Population | HIV Diagnosis | 37          | Unknown              |
| Paunovic (2011)             | 29  | Sweden      | CBT-T          | WL             |                |                | General Population | Crime       | 63           | 74 Unknown            |
| Peniston and Kulkosky (1991)| 29  | USA         | CBT-T          | TAU            |                |                | Military Personnel/Veterans | Military Trauma | Unknown   | Unknown              |
| Power et al. (2002)         | 105 | UK          | EMDR           | CBT-T          | WL             |                | Military Personnel/Veterans | Various     | 42           | Unknown              |
| Rauch et al. (2015)         | 36  | USA         | PE (CBT-T)     | PCT            |                |                | Military Personnel/Veterans | Military Trauma | 9           | Unknown              |
| Ready, Gerardi, Bacshneider,| 11  | USA         | VRE (CBT-T)    | PCT            |                |                | Military Personnel/Veterans | Military Trauma | Unknown   | Unknown              |
| Mascaro, and Rothbaum (2010)|     |             |                |                |                |                |            |                      |          |              |                      |
| Reger et al. (2016)         | 162 | USA         | VRE (CBT-T)    | PE (CBT-T)     | WL             |                | Military Personnel/Veterans | Military Trauma | 4           | Active duty          |
| Resick et al. (2015)        | 108 | USA         | Group CBT-T    | PE (CBT-T)     |                |                | MILitary Personnel/Veterans | Military Trauma | 8           | 0 Unknown            |
| Resick, Nishith, Weaver,    | 171 | USA         | CPT (CBT-T)    | PE (CBT-T)     | Minimal Attention|               | MILitary Personnel/Veterans | Military Trauma | 100         | 38 Unknown           |
| Astin, and Feuer (2002)     |     |             |                |                |                |                |            |                      |          |              |                      |
| Resick et al. (2017)        | 268 | USA         | CPT (CBT-T)    | Group CBT-T    |                |                | Military Personnel/Veterans | Military Trauma | 9           | 100 Unknown          |
| Rothbaum (1997)             | 18  | USA         | EMDR           | PE (CBT-T)     | WL             |                | General Population | Sexual Assault | 100         | 19 Unknown           |
| Rothbaum, Astin, and        | 60  | USA         | EMDR           | PE (CBT-T)     | EMDR           | WL             | General Population | Rape         | 100         | Unknown              |
| Marsteller (2005)           |     |             |                |                |                |                |            |                      |          |              |                      |
| Sautter, Glynn, Cretu,      | 57  | USA         | Couples CBT    | Couples CBT    | without a trauma focus | Psychoeducation | Military Personnel/Veterans | Military Trauma | 1.75        | 12 Unknown           |
| Senturk, and Vaught (2015)  |     |             |                |                |                |                |            |                      |          |              |                      |
| Scheck, Schaefer, and       | 60  | USA         | EMDR           | SC             |                |                | General Population | Various      | 100         | Unknown              |
| Gillette (1998)             |     |             |                |                |                |                |            |                      |          |              |                      |
| 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)     | Group PCT      |                |                | Military Personnel/Veterans | Military Trauma | 100         | 38 Unknown           |
| Schnyder, Müller, Maercker, | 30  | Switzerland | BEP (CBT-T)    | MC/RA          |                |                | General Population | Various      | 46.7         | Unknown              |
| and Wittmann (2011)         |     |             |                |                |                |                |            |                      |          |              |                      |
| 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          |
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                    |
| Suri, 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, Giatt, 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
| Study                          | 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             | Unclear             | 2                  |
| Akbarian et al. (2015)        | Low                         | High                   | Low                               | Low                 | Unclear             | High                 | 2                  |
| Asukai, Saito, Tsuruta, Kishimoto, and Nishikawa (2010) | Low         | High                   | Low                               | Unclear             | High                | High                 | 1                  |
| Basoglu et al. (2005)         | Low                         | Low                    | Low                               | High                | High                | Low                  | 1                  |
| Basoglu, Salcioglu, and Livanou (2007) | Low     | Low                    | High                               | Unclear             | 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                        | Low                    | Unclear                           | Low                 | Unclear             | High                 | 1                  |
| Bradshaw, McDonald, Grace, Detwiler, and Austin (2014) | Unclear | Unclear | Low                               | Unclear             | High                | High                 | 2                  |
| Brom, Kleber, and Defares (1989) | Unclear | Unclear | High                               | Unclear             | Unclear             | Unclear             | 2                  |
| Bryant, Moulds, Guthrie, Dang, and Nixon (2003) | Low     | Unclear | Low                               | Low                 | Low                 | High                 | 1                  |
| Bryant et al. (2011)          | Low                         | Low                    | Low                               | Low                 | Low                 | Unclear             | 1                  |
| Buhmann, Nordenstorf, Ekstroem, Carlsson, and Mortensen (2016) | Low     | Low                    | Unclear                           | Low                 | Low                 | Low                  | 0                  |
| Butollo, Karl, Konig, and Rosner (2016) | Unclear | Unclear | Low                               | Unclear             | High                | High                 | 1                  |
| Capezzani et al. (2013)       | Unclear                     | Low                    | Low                               | Low                 | Low                 | High                 | 1                  |
| Carletto et al. (2016)        | Low                         | High                   | High                              | Low                 | Low                 | Low                  | 1                  |
| Carlson, Chemtob, Rusnak, Hedlund, and Muraoka (1998) | Unclear | Unclear | High                               | Unclear             | Unclear             | Unclear             | 1                  |
| Castillic et al. (2016)       | Unclear                     | Low                    | Low                               | Low                 | Low                 | Unclear             | 1                  |
| Chard (2005)                  | Unclear                     | Low                    | Low                               | Unclear             | High                | High                 | 1                  |
| Ciotiere, Koenen, Cohen, and Han (2002) | Unclear | Low                    | Low                               | Low                 | Low                 | Low                  | 1                  |
| Ciotiere et al. (2010)        | Unclear                     | Low                    | Low                               | Low                 | Low                 | Low                  | 0                  |
| Devilly, Spence, and Rapee (1998) | Low     | Unclear | High                               | Low                 | Low                 | High                 | 1                  |
| Devilly and Spence (1999)     | High                        | Unclear                | High                              | Unclear             | Unclear             | High                 | 3                  |
| Dorrepaal et al. (2012)       | Unclear                     | Low                    | Low                               | Low                 | Low                 | High                 | 2                  |
| Duffy, Gillespie, and Clark (2007) | Low       | Low                    | Unclear                           | Low                 | Low                 | High                 | 1                  |
| Dunne, Kenardy, and Sterling (2012) | Unclear | Unclear | Low                               | Unclear             | Unclear             | Unclear             | 1                  |
| Echeburua, De Corral, Zubizarreta, and Sarasua (1997) | Unclear | Unclear | Low                               | Unclear             | High                | Unclear             | 1                  |
| Ehlers, Clark, Hackmann, McManus, and Fennell (2005) | Low     | Low                    | High                              | Low                 | Low                 | Unclear             | 2                  |
| Ehlers et al. (2003)          | Unclear                     | Unclear                | Low                               | Low                 | Low                 | Unclear             | 2                  |
| Ehlers et al. (2014)          | Unclear                     | Low                    | Low                               | Low                 | Low                 | Unclear             | 0                  |
| Falsetti, Resnick, and Davis (2008) | Unclear | Unclear | Low                               | Low                 | High                | Low                  | 2                  |
| Fecteau and Nicki (1999)      | Low                         | Unclear                | Low                               | High                | Unclear             | High                 | 2                  |
| Feske (2008)                  | Low                         | Unclear                | Low                               | Unclear             | Unclear             | Unclear             | 1                  |
| Foa, Rothbaum, Riggs, and Murdock (1991) | Unclear | Unclear | Low                               | Low                 | Low                 | Unclear             | 2                  |
| Foa et al. (1999)             | Unclear                     | Unclear                | Low                               | Low                 | Low                 | Unclear             | 1                  |
| Foa et al. (2005)             | Low                         | Low                    | Low                               | Low                 | Low                 | Low                  | 0                  |
| Foa et al. (2018)             | Low                         | Low                    | Low                               | Low                 | Low                 | Low                  | 0                  |
| Fonzo et al. (2017)           | Low                         | Unclear                | Low                               | Unclear             | Unclear             | Low                  | 0                  |
| Forbes et al. (2012)          | Unclear                     | Low                    | Low                               | Unclear             | Unclear             | Unclear             | 1                  |
| Ford, Steinberg, and Zhang (2011) | Low     | Low                    | Low                               | Low                 | Low                 | Unclear             | 1                  |
| Ford, Chang, Levine, and Zhang (2013) | Low     | Low                    | High                              | Low                 | Low                 | Low                  | 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) | Low     | Low                    | Unclear                           | Low                 | Low                 | Unclear             | 0                  |
| Gray, Budden-Potts, and Bourke (2017) | Low    | Low                    | Unclear                           | Unclear             | Unclear             | Unclear             | 0                  |
| Hensel-Dittmann et al. (2011) | Low                         | Low                    | Low                               | Unclear             | Unclear             | High                 | 1                  |
| Hinton et al. (2005)          | Low                         | Unclear                | Low                               | Unclear             | Unclear             | High                 | 1                  |
| Hinton, Hofmann, Rivera, Otto, and Pollack (2011) | Unclear | Unclear | Low                               | Unclear             | Low                 | Low                  | 1                  |
| Hogberg et al. (2007)         | Low                         | Unclear                | High                              | Low                 | High                | Unclear             | 2                  |
| Hollifield, Sinclair-Lian, Warner, and Hammerschlag (2007) | Low     | Low                    | Low                               | Low                 | Unclear             | Unclear             | 1                  |
| Ironson, Freund, Strauss, and Williams (2002) | Unclear | Unclear | Low                               | High                | Unclear             | High                 | 2                  |
| Ivarsson et al. (2014)        | Low                         | Unclear                | Low                               | Low                 | Low                 | Low                  | 1                  |
Table 2. (Continued).

| Study                                      | 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 (2019)                              | Unclear                     | Unclear                | High                              | Unclear             | Unclear             | High                 | 2                   |
| Johnson, Zlotnick, and Perez (2011)         | Low                         | Unclear                | Low                               | Low                 | Unclear             | Low                  | 1                   |
| Johnson, Johnson, Perez, Palmieri, and Zlotnick (2016) | Low                       | Low                    | Low                               | Low                 | Unclear             | Low                  | 0                   |
| Karatzias et al. (2011)                     | Low                         | Low                    | Low                               | Unclear             | High                | High                 | 1                   |
| Keane, Fairbank, Caddell, and Zimering (1989) | Unclear                     | Unclear                | Unclear                           | High                | Unclear             | High                 | 2                   |
| Krupnick et al. (2008)                      | Unclear                     | Unclear                | Low                               | Unclear             | High                | 1                   |
| Kubany, Hill, and Owens (2003)              | Unclear                     | Unclear                | Low                               | Unclear             | High                | 1                   |
| Kubany et al. (2004)                        | Unclear                     | Unclear                | Low                               | Unclear             | High                | 1                   |
| Laughrane et al. (2016)                     | Low                         | Low                    | Low                               | Unclear             | High                | 1                   |
| Lee, Gavriel, Drummond, Richards, and Greenwald (2002) | Low                       | Low                    | Low                               | High                | 1                   |
| Lewis et al. (2017)                         | Low                         | Low                    | Low                               | Low                 | High                | 1                   |
| Littleton et al. (2016)                     | Low                         | Unclear                | Low                               | High                | Low                 | 1                   |
| Litz, Engel, Bryant, and Papa (2007)        | Unclear                     | Unclear                | High                              | Low                 | Low                 | 2                   |
| Marcus, Marquis, and Sakai (1997)           | Unclear                     | Unclear                | High                              | Low                 | High                | 2                   |
| Markowitz et al. (2015)                     | Low                         | Low                    | Low                               | Low                 | High                | 1                   |
| Marks, Lovell, Noshirvani, Livanou, and Thrasher (1998) | Unclear                 | Unclear                | Low                               | Unclear             | Low                 | 0                   |
| McDonagh et al. (2005)                      | Unclear                     | Unclear                | Low                               | Unclear             | Low                 | 0                   |
| McClay et al. (2011)                        | Low                         | Low                    | Unclear                           | High                | Unclear             | Low                  | 2                   |
| McClay et al. (2017)                        | Low                         | Unclear                | Low                               | Low                 | Low                 | 0                   |
| Monson et al. (2012)                        | Low                         | Low                    | Low                               | Low                 | Unclear             | Low                  | 0                   |
| Monson et al. (2006)                        | Low                         | Low                    | Low                               | Low                 | Unclear             | Low                  | 0                   |
| Morath et al. (2014)                        | Low                         | Low                    | Unclear                           | Low                 | Low                 | 0                   |
| Mueser et al. (2008)                        | Low                         | Low                    | Low                               | Unclear             | High                | 1                   |
| Nacach et al. (2011)                        | Low                         | Unclear                | Low                               | Unclear             | High                | 1                   |
| Neuner et al. (2010)                        | Low                         | Unclear                | Low                               | Unclear             | Low                 | 1                   |
| Neuner et al. (2008)                        | Unclear                     | Unclear                | Low                               | Unclear             | Low                 | 0                   |
| Neuner, Schauer, Klaschik, Karunakara, and Elbert (2004) | Unclear                 | Unclear                | Low                               | Low                 | Low                 | 1                   |
| Njëdam, Gersons, Reitsma, de Jongh, and Off (2012) | Unclear                 | Unclear                | Low                               | Low                 | Low                 | 0                   |
| Pacella et al. (2012)                       | Low                         | Unclear                | Low                               | Unclear             | Low                 | 0                   |
| Paunovic (2011)                             | Unclear                     | Unclear                | Low                               | High                | Unclear             | Low                  | 2                   |
| Peniston and Kulkosky (1991)                | Unclear                     | Unclear                | Unclear                           | Low                 | Unclear             | 0                   |
| Power et al. (2002)                         | Low                         | Low                    | High                              | Unclear             | Low                 | 1                   |
| Rauch et al. (2015)                         | Unclear                     | Unclear                | Low                               | Unclear             | High                | 1                   |
| Ready, Gerardi, Backscheidere, Mascaro, and Rothbaum (2010) | Unclear                 | Unclear                | Unclear                           | Low                 | Unclear             | 1                   |
| Reger et al. (2016)                         | Low                         | Low                    | Low                               | Unclear             | Low                 | 0                   |
| Resick et al. (2015)                        | Unclear                     | Unclear                | Low                               | Unclear             | High                | 1                   |
| Resick, Nishith, Weaver, Astin, and Feuer (2002) | Low                       | Low                    | Low                               | Unclear             | Low                 | 0                   |
| Resick et al. (2017)                        | Low                         | Unclear                | Low                               | Low                 | Low                 | 0                   |
| Rothbaum (1992)                             | Low                         | Unclear                | High                              | Unclear             | Low                 | 2                   |
| Rothbaum, Astin, and Marsteller (2005)       | Unclear                     | Unclear                | High                              | Unclear             | Low                 | 1                   |
| Sautter, Gunn, Cretu, Senturk, and Vaught (2015) | Unclear                 | Unclear                | Low                               | Unclear             | Low                 | 0                   |
| Scheek, Schaefter, and Gillette (1998)       | Low                         | Low                    | High                              | Unclear             | High                | 2                   |
| Schnurr et al. (2003)                       | High                        | Unclear                | Low                               | Low                 | Low                 | 1                   |
| Schnurr et al. (2007)                       | Low                         | Low                    | Low                               | Low                 | Unclear             | 0                   |
| Schnyder, Muller, Maercker, and Wittmann (2011) | Low                       | Unclear                | Unclear                           | Unclear             | Low                 | 0                   |
| Slat, Carraro, Fein, Schaller, and Gallagher (2012) | Low                      | Low                    | Unclear                           | Low                 | Unclear             | 0                   |
| Sloan, Marx, Bovin, Feinstein, and Gallagher (2012) | Low                      | Low                    | Unclear                           | Low                 | Unclear             | 0                   |
| Sloan, Marx, Lee, and Resick (2018)          | Low                         | Low                    | Low                               | Low                 | Low                 | 0                   |
| Spence et al. (2011)                        | Low                         | Unclear                | High                              | Unclear             | Low                 | 2                   |
| Sternmark, Catani, Neuner, Elbert, and Hohen (2013) | Unclear                 | Unclear                | Low                               | Unclear             | Low                 | 2                   |
| Suris, Link-Malcolm, Chard, Ahn, and North (2013) | Unclear                 | Unclear                | Low                               | Low                 | Unclear             | 1                   |
| Taylor et al. (2003)                        | Unclear                     | Unclear                | Low                               | Unclear             | Low                 | 0                   |
| Tylee, Gray, Glatt, and Bourke (2017)        | Unclear                     | Unclear                | Unclear                           | Low                 | Unclear             | 1                   |
| Vaughan et al. (1994)                       | Unclear                     | Unclear                | Unclear                           | Low                 | Low                 | 0                   |
| Wells, Walton, Lovell, and Proctor (2015)    | Low                         | Low                    | Low                               | Unclear             | High                | 1                   |
| Wells and Sembi (2004)                       | Low                         | Low                    | High                              | Unclear             | High                | 3                   |
| Yehuda et al. (2014)                        | Unclear                     | Unclear                | High                              | Unclear             | Unclear             | 1                   |
| Zang, Hunt, and Cox (2014)                  | Unclear                     | Unclear                | Low                               | Low                 | Low                 | 1                   |
| Zang, Hunt, and Cox (2013)                  | Low                         | Unclear                | Low                               | Low                 | High                | 1                   |
| Zlotnick et al. (1997)                      | Unclear                     | Unclear                | High                              | Unclear             | Low                 | 2                   |
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

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**Table 3. Meta-analytic results.**

| Comparison | Effect Size | Grade |
|------------|-------------|-------|
| 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低 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]. | Very 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 = −1.39 CI = −2.05 to −1.13]. | Very 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]. | Very 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 waitlist or 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 = −0.65 to 0.46]. | 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 wait list 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 versus wait list or treatment as usual | Couples CBT with a trauma focus showed a positive effect when compared with wait list 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 |
Table 4. Meta-analytic results.

| Study Design | Effect Size | GRADE judgement for quality of evidence |
|--------------|-------------|----------------------------------------|
| CBT with a trauma focus versus CBT without a trauma focus | N/A | Low quality |
| CBT with a trauma focus versus Present Centred Therapy | N/A | Very low quality |
| CBT with a trauma focus versus supportive counselling | N/A | Very low quality |
| CBT with a trauma focus versus psychodynamic therapy | N/A | Very low quality |
| CBT with a trauma focus versus Interpersonal Therapy (IPT) | N/A | Very low quality |
| CBT without a trauma focus versus PCT | N/A | Very low quality |
| CBT with a trauma focus versus diagnostic exposure therapy (DET) | N/A | Very low quality |
| Cognitive processing therapy (CPT) versus prolonged exposure (PE) | N/A | Very low quality |
| EMDR versus CBT with a trauma focus | N/A | Low quality |
| EMDR versus supportive counselling | N/A | Very low quality |
| EMDR versus CBT without a trauma focus | N/A | Very low quality |
| EMDR versus Relaxation Training | N/A | Very low quality |
| EMDR versus REM Desensitization | N/A | Very low quality |
| CBT without a trauma focus versus supportive counselling | N/A | Very low quality |
| CBT with a trauma focus versus psychoeducation | N/A | Very low quality |
| Written exposure therapy versus CBT with a trauma focus | N/A | Very low quality |
| CBT with a trauma focus versus relaxation training | N/A | Low quality |
| Supportive counselling versus psychoeducation | N/A | Low quality |
| Interpersonal therapy versus relaxation training | N/A | Very low quality |
| Virtual reality therapy versus control exposure | N/A | Low quality |
| Virtual reality therapy and present centred therapy | N/A | Low quality |
| Group CBT with a trauma focus versus group present centred therapy | N/A | Low quality |
| Group CBT with a trauma focus versus individual CBT with a trauma focus | N/A | Very low quality |
| Group CBT without a trauma focus versus group supportive counselling | N/A | Very low quality |
| Couples CBT without a trauma focus versus couples psychoeducation | N/A | Very low quality |
| Internet-based trauma focused CBT versus internet-based psychoeducation | N/A | 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 factors 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 contraindicated, 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 insufficient numbers 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.

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ORCID

Catin Lewis http://orcid.org/0000-0002-3818-9377
Neil P. Roberts http://orcid.org/0000-0002-6277-0102
Jonathan I. Bissow http://orcid.org/0000-0001-5170-1243

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