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Cognitive Processing Therapy for Post-traumatic Stress Disorder: A Systematic Review and Meta-analysis

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CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Abbreviations

BDI	Beck Depression Inventory
BDI-II	Beck Depression Inventory II
CAPS	Clinician-Administered PTSD Scale
CBT	cognitive behavioural therapy
CI	confidence interval
CPT	cognitive processing therapy
CST	childhood sexual trauma
DET	dialogue exposure therapy
DSM-5	Diagnostic and Statistical Manual of Mental Disorders—5th Edition
EBT	evidence-based therapy
EMDR	eye movement desensitization and reprocessing
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IPV	intimate partner violence
ITT	intention-to-treat
MD	mean difference
MeST	memory specificity training
MPSS	Modified PTSD Symptom Scale
PCL	PTSD checklist
PCT	present-centred therapy
PE	prolonged exposure
PSS	PTSD Symptom Scale
PTCI	Post-traumatic Cognitions Inventory
PTSD	post-traumatic stress disorder
QIDS	Quick Inventory of Depressive Symptomatology
QoL	quality of life
RCT	randomized controlled trial
SMD	standard mean difference
STAI	State Anxiety Inventory
VA	US Department of Veterans Affairs
WL/UC	wait-list or usual care (controls)

Executive Summary

Context and Policy Issues

Post-traumatic stress disorder (PTSD) is characterized by symptoms that include intrusive or distressing thoughts, nightmares, and flashbacks derived from past exposure to traumatic events, such as the sudden death of a loved one, a serious accident, a natural disaster, sexual or physical assault, childhood sexual or physical abuse, combat exposure, or torture. The lifetime prevalence of PTSD in Canada (i.e., the proportion of the population who will experience PTSD in their lifetime) has been estimated to be 9.2%, with higher rates in the armed forces population.

Psychological treatments, including cognitive behavioural therapy (CBT), are evidence-based therapies (EBTs) for the management of PTSD. There are different types of CBT for PTSD, including cognitive processing therapy (CPT). CPT is a manualized therapy that provides a person with the skills to handle distressing thoughts and regain control in his or her life. Although the CPT protocol consists of 12 sessions of 90 minutes each, additional sessions or changes in the duration of each session may be allowed at the discretion of patients and clinicians. CPT can be conducted in an individual setting, in a group setting, or in a combination of the two.

To help guide decisions about the choice of behavioural therapy for the treatment of PTSD — and the place of CPT in therapy — this study systematically reviews the clinical effectiveness of CPT offered in individual or group settings for adults with PTSD. Equity issues, patient preferences, and implementation and cost considerations are also examined.

Research Question

What is the clinical effectiveness of CPT for adults with PTSD?

Contextual Questions

1. What is the evidence regarding the impact of CPT for the treatment of adults with PTSD on health equity and access?
2. What is the evidence regarding patient values and preferences as they relate to CPT for PTSD?
3. What are the implementation considerations regarding CPT for PTSD?
4. What is the cost-effectiveness of CPT for the treatment of adults with PTSD?

Methods

A peer-reviewed literature search was conducted using the following databases: MEDLINE (1946–) with in-process records and daily updates via Ovid; Embase (1974–) via Ovid; PsycINFO (1806–) via Ovid; The Cochrane Library (2015, Issue 9) via Wiley; and PubMed. Grey literature was also searched. No methodological filters were applied to limit retrieval. Where possible, retrieval was limited to the human population. Retrieval was not limited by publication year, but was limited to the English language. Regular alerts were established to update the search until the publication of the final report. Predefined eligibility criteria included randomized controlled trials (RCTs) and comparative non-randomized studies assessing the clinical effectiveness of CPT for the treatment of PTSD. CPT was compared with other active psychological treatments or wait-list or controls receiving support or symptom management.

For the clinical review, two reviewers independently selected studies. Data were extracted by one reviewer using a data extraction form designed a priori and were checked for accuracy and

completeness by a second reviewer. The risk of bias of RCTs was assessed using the Cochrane Risk of Bias tool. The Downs and Black instrument was used to assess the methodological quality of non-randomized studies. One reviewer assessed risk of bias and a second reviewer checked for accuracy. Meta-analysis was used to synthesize data. Following synthesis, two reviewers independently assessed the quality of evidence and confidence in the effect for each outcome using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.

For the contextual questions, two reviewers screened titles and abstracts while one reviewer made the final selection of full-text articles. One reviewer performed data extraction and critical appraisal. Data regarding the patient population, interventions, comparators, outcomes, and study design were extracted into a standardized electronic form. Risk of bias assessment for randomized studies was performed using the Cochrane Risk of Bias tool.[10] The non-randomized, qualitative, and survey studies were not appraised using any specific quality assessment tool. Instead, common criteria for assessing the quality of these study designs were used to identify important strengths and limitations. A narrative synthesis of study findings was conducted.

Summary of Findings

Ten RCTs and six observational studies were included in the clinical review. Studies compared CPT with wait-list or usual care controls receiving support or symptom management (WL/UC), or with other active psychological treatments, such as prolonged exposure (PE) therapy, present-centred therapy (PCT), or memory specificity training (MeST). In general, the quality of the evidence was low to moderate due to imprecision or risk of bias. One additional RCT comparing CPT with dialogue exposure therapy was identified in the final alert; it is summarized, but was not included in the GRADE analysis. Most studies found that CPT was better than WL/UC for improving PTSD symptoms, depression, anxiety, quality of life (QoL), and remission rates. The proportion of patients who completed treatment was similar between CPT and WL/UC controls. It appeared that there was no difference in effectiveness between CPT provided in group versus individual settings.

The effectiveness of CPT compared with PE therapy, PCT, dialogue exposure therapy, or MeST is uncertain. Comparisons between CPT and these interventions were limited to either single studies finding no statistical difference or to small numbers of studies with inconsistent findings. One RCT found that CPT performed better than dialogue exposure therapy for reducing PTSD symptoms.

Based on evidence from a small number of studies, CPT may have some effectiveness for reducing PTSD symptoms, depression, or anxiety in potentially vulnerable groups, such as survivors of interpersonal violence or women who have experienced military or childhood sexual trauma. CPT has been shown to be effective both with and without a translator, and in low-resource settings, including patients with low literacy. Delivery of CPT via telehealth has been shown to have similar effectiveness to in-person treatment. Based on one study, CPT may have the potential to decrease the utilization and cost of mental health services for patients with PTSD.

Conclusions and Implications for Policy-Making

Based on the moderate- to low-quality evidence identified in this review, CPT may be more effective than WL/UC in reducing PTSD, depression, and anxiety in adults. Very low-quality evidence indicates that it is uncertain whether there is any difference between CPT and PE therapy, PCT, or MeST. CPT may have some effectiveness for treating patients from potentially

vulnerable groups, including individuals who have low literacy; who live in low-resource environments; who have experienced military or childhood sexual trauma or intimate partner violence; or who are experiencing continued trauma while receiving CPT. Additionally, CPT delivered via telehealth is likely as effective as CPT delivered face to face.

Context and Policy Issues

Post-traumatic stress disorder (PTSD) is classified as a trauma- and stress-related disorder in the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5).[1] PTSD is characterized by a cluster of four symptoms, including intrusions, avoidance, negative changes in cognitions and mood, and arousal derived from past exposure to traumatic events, such as the sudden death of a loved one, a serious accident, a natural disaster, sexual or physical assault, childhood sexual or physical abuse, combat exposure, and torture.[2] The lifetime prevalence of PTSD in Canada (i.e., the proportion of the population who will experience PTSD in their lifetime) has been estimated to be 9.2%, with one-month prevalence rates (the proportion of the population who has PTSD in a one-month period) of 2.4%.[3] In general, women are more likely than men to develop PTSD after exposure to traumatic events.[4] PTSD is one of the most common mental disorders in the Canadian Armed Forces. From 2002 to 2013, the 12-month prevalence in this population rose from 2.8% to 5.3%.[5] The lifetime prevalence was 11.1%.[5]

Non-pharmacological and pharmacological treatments are available to treat PTSD, with the goal of reducing symptoms and improving functional ability and adaptive coping. Non-pharmacological treatments are based in psychotherapy, and include such treatments as cognitive behavioural therapy (CBT), eye movement desensitization and reprocessing (EMDR), and present-centred therapy (PCT).[6] Emerging treatment options that have been used for other indications include Memory Specificity Training (MeST), which was first designed to treat depression, and Dialogue Exposure Therapy (DET). CBT includes both cognitive processing therapy (CPT), which has a specific protocol to be completed according to a treatment manual, and prolonged exposure (PE). Both of these therapies are recommended by the US Department of Veterans Affairs (VA) and the US Department of Defense (DOD) as first-line psychological treatment options for patients with PTSD.[7] PCT is also a manualized therapy, but without cognitive behavioural or trauma-focused components.[8] Other psychological treatments exist and are also in use. Pharmacological treatments, some in common use, are outside the scope of this review.

CPT provides a person with the skills to handle distressing thoughts and regain control in his or her life through 12 sessions that can be divided into four main parts: learning about PTSD symptoms and how treatment can help; becoming aware of thoughts and feelings; learning skills to challenge thoughts and feelings and to deal with other problems in daily life; and understanding the changes in beliefs that occur after going through trauma.[9] CPT can be conducted in an individual setting, in a group setting, or in a combination of the two.[9] Although the CPT protocol consists of 12 sessions of 90 minutes each, additional sessions or changes in the duration of each session may be allowed at the discretion of patients and clinicians.[9]

The aim of this systematic review is to determine the clinical effectiveness of CPT offered in an individual or group setting for adults with PTSD.

Research Question

What is the clinical effectiveness of CPT for adults with PTSD?

Key Findings

Based on moderate- to low-quality evidence, CPT may be more effective than no treatment (wait-list) controls in reducing the severity of PTSD, depression, and anxiety symptoms in adults with no difference in compliance. CPT may improve quality of life (QoL). No studies were found

that reported remission, discharge from treatment (due to observed benefits at study completion), or release from military service.

Based on very low-quality evidence, it is uncertain if there is any difference between CPT and other active psychological treatments such as PE, PCT, or MeST in improving PTSD symptoms.

Methods

Literature Search Strategy

The literature search was performed by an information specialist using a peer-reviewed search strategy.

Published literature was identified by searching the following bibliographic databases: MEDLINE (1946–) with in-process records and daily updates via Ovid; Embase (1974–) via Ovid; PsycINFO (1806–) via Ovid; The Cochrane Library (2015, Issue 9) via Wiley; and PubMed. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concept was cognitive processing therapy.

No methodological filters were applied to limit retrieval. Where possible, retrieval was limited to the human population. Retrieval was not limited by publication year, but was limited to the English language.

Regular alerts were established to update the search until the publication of the final report. Regular search updates were performed on databases that did not provide alert services. The final alert was February 11, 2016. The search strategy is provided in Appendix 1.

Grey literature (literature that is not commercially published) was identified by searching the CADTH Grey Matters checklist (https://www.cadth.ca/resources/finding-evidence/grey-matters-practical-search-tool-evidence-based-medicine), which includes the websites of regulatory agencies, health technology assessment agencies, clinical guideline repositories, and professional associations. Google and other Internet search engines were used to search for additional Web-based materials. These searches were supplemented by reviewing the bibliographies of key papers and through contacts with appropriate experts.

Selection Criteria and Methods

Studies were considered for inclusion in the systematic review if CPT was the intervention used for treatment of PTSD symptoms in adults (≥ 18 years old). The therapy could be conducted either in group or individual settings. Populations considered were either military personnel or civilian. There was no restriction regarding the type of traumatic event or the duration of symptoms. The comparator could be any active psychological treatment other than CPT or no treatment (wait-list). To be included, studies had to be randomized controlled trials (RCTs) or comparative non-randomized studies having at least two groups. Relevant Health Technology Assessments and systematic reviews were used to identify additional studies for discussion, but not for primary analysis. Table 1 presents the eligibility criteria for included studies.

Table 1: Table of Selection Criteria

Population	Adults with diagnosed PTSD (≥ 18 years) No restrictions based on failed prior treatment or concurrent treatment
Intervention	Cognitive processing therapy offered in group or individual settings
Comparator	Any active psychological treatment (alone or in combination with other treatments) or no treatment (wait-list)
Outcomes	Clinical effectiveness: PTSD symptom decrease (e.g., CAPS/PCL change in score), depression, discharge from treatment due to benefit at study completion, remission (change in diagnosis by DSM or other criteria), improved quality of life, release from service (military) due to lack of treatment response Harms: Treatment dropout rates or non-compliance
Study Designs	RCTs and comparative non-randomized studies (non-RCTs)

CAPS = Clinician-Administered PTSD Scale; DSM = *Diagnostic and Statistical Manual of Mental Disorders*; PCL = PTSD checklist; PTSD = post-traumatic stress disorder; QoL = quality of life; RCT = randomized controlled trial.

Exclusion Criteria

Studies were excluded if the population consisted of children or adolescents; if there was no comparator (single treatment group); if the comparator was a pharmacological therapy; or if the studies investigated the effect of CPT in patients not diagnosed with PTSD. Studies comparing individual components of CPT were excluded. Guidelines, systematic reviews, and studies reported as conference abstracts were used to search for potential included studies, but were excluded from the analysis. Multiple publications of the same study were excluded unless they provided additional outcome information of interest.

Screening and Selecting Studies for Inclusion

Two reviewers independently screened titles and abstracts relevant to the clinical research question regarding the clinical effectiveness of CPT for PTSD in adults. Full texts of potentially relevant articles were retrieved and independently assessed for possible inclusion based on the pre-determined selection criteria (Table 1). The two reviewers then compared their chosen included and excluded studies; disagreements were discussed until consensus was reached.

Data Extraction Strategy

A data extraction form was designed a priori in an Excel spreadsheet to document and tabulate all relevant information (e.g., study design, eligibility criteria, patient characteristics, setting, and outcomes, such as clinical benefits and harms, as outlined previously) available in the selected studies. Data were extracted by one reviewer using the data extraction form and checked for accuracy by a second reviewer. The continuous outcomes of interest were change in PTSD symptoms measured by instruments, such as the patient's psychological distress (as measured by the PTSD checklist [PCL] or the Clinician-Administered PTSD Scale [CAPS]), the severity of depression as measured by the Beck Depression Inventory II (BDI-II), and health-related QoL. The dichotomous outcomes of interest included the proportion of PTSD cases at baseline that become non-cases after treatment (remission), the proportion of patients who completed or dropped out of treatment, and the proportion of patients dismissed from military service. An attempt was made to obtain any missing information by contacting the authors of included studies.

Risk of Bias Assessment

Risk of bias of the RCTs was assessed using the Cochrane Risk of Bias tool.[10] The Downs and Black instrument was used to assess the quality of non-RCTs.[11] One reviewer assessed the risk of bias of each study, and a second reviewer checked for accuracy. The risk of bias was then used as part of information in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process to assess the level of evidence of the outcomes across studies.

Data Analysis Methods

In the absence of clinical, methodological, and statistical heterogeneity, meta-analysis was used to synthesize data using Review Manager 5.3. The measures of effect for dichotomous data were expressed as a risk ratio with 95% confidence intervals (CIs). To aid interpretation, the risk ratio was converted to natural frequencies (e.g., 1 per 100). The measures of effect for continuous data were expressed as mean differences (MDs) with 95% CIs when similar scales were used, and as standardized mean differences (SMDs) with 95% CIs when different scales were used to measure the effect size of an outcome. Because the SMD is unitless and difficult to understand, it was then converted back to a familiar scale to aid with interpretation. The back-translation was conducted by multiplying the SMD with the standard deviation (SD) of the control group of the study having the lowest risk of bias. The resulting MD was interpreted using the scale of that representative study.[10]

Data were pooled from at least two studies using a fixed-effects model except where heterogeneity was present, in which case a random-effects model was used. Data from RCTs and non-randomized studies were pooled separately. Heterogeneity between studies was checked using both the I^2-test of heterogeneity and the X^2-test of heterogeneity ($P < 0.10$). The I^2 statistic describes the proportion of total variation in study estimates that is due to heterogeneity. Heterogeneity was considered to be low when I^2 was less than 25%, moderate when I^2 was between 25% and 50%, and high when I^2 was ≥ 50%. A fixed-effects model was used for I^2 ≤ 25%. With moderate I^2 statistic (25% to 50%), both the X^2-test and a visual inspection of the forest plot were used to decide between fixed- and random-effects models.

Subgroup analyses were planned based on types of traumatic events, comorbidities, settings (outpatient versus residential; group versus individual), and military service status (veteran versus active).

Data Imputation

Continuous outcome measures at end of treatment or at end of follow-up were expressed as mean change from baseline. When SDs for changes from baseline were not provided, they were conservatively calculated using a correlation of coefficient (r) equal to 0. Sensitivity analysis was conducted with larger correlation of coefficient ($r = 0.5$) on PTSD severity, which did not change the direction of the effect (data not shown).[12]

Quality of the Evidence

Once the evidence was synthesized for each of the outcomes, two reviewers independently assessed the quality of evidence and confidence in the effect for each outcome using the GRADE approach.[10,13] Consensus was reached when there were discrepancies. The reviewers used the GRADE criteria: overall risk of bias, inconsistency, indirectness, imprecision, publication bias, magnitude of effect, dose response, and opposing bias or confounding. The quality of the evidence was assessed at one of four levels: high, moderate, low, or very low. When there was serious or very serious concern with a criterion, the evidence was downgraded accordingly by a level. To assess imprecision for dichotomous outcomes, cut-off thresholds of

< 0.75 to > 1.25 were used as an important effect. For each continuous outcome, the minimal clinically important difference (MCID) was determined based on the clinical experience of an expert.

The results were described using the magnitude or importance of the effect and the quality of the evidence. The quality of evidence was interpreted as:

- High quality: We are very confident that the true effect lies close to that of the estimate of the effect.
- Moderate quality: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
- Low quality: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.
- Very low quality: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

A summary of the findings and the quality of the evidence for the comparisons are presented in the evidence profiles (Table 2 to Table 5).

Results

Quantity of Research Available

The literature search yielded 517 citations. Upon screening titles and abstracts, 62 potentially relevant articles were retrieved for full-text review. One additional relevant report was retrieved from database alerts and included in the analysis. Of the 63 potentially relevant articles, 34 reports representing 16 studies were included in this review. Of those 16 studies, 10[14-23] were RCTs and six[24-29] were non-RCTs. One additional study was identified from the final database alert.[30] As this study was identified after all analyses were complete, its findings have been summarized without inclusion in the main analyses and without inclusion in the GRADE process. The study selection process is outlined in a PRISMA flowchart (Appendix 2). The lists of included and excluded studies are shown in Appendix 3 and Appendix 4, respectively.

Study Characteristics

The characteristics of the included studies with brief definitions of the interventions are summarized in Appendix 5.

Randomized Controlled Trials

All of the RCTs were conducted at outpatient clinics. The number of participants randomized in the trials ranged from 59[16] to 405.[14] The follow-up period ranged from one month[19] to 12 months.[15,21] The mean age of participants ranged from 32 years[20,21] to 54 years.[19] The proportion of males ranged from 0%[14,15,20] to 97%.[16] The type of trauma was heterogeneous among study populations and could be divided into two categories: childhood and adult sexual trauma[14,15,17-20,22] and combat-related trauma.[16,21] Five studies[14,15,17,20,23] had civilian populations and five[16,18,19,21,22] had military populations. The duration of trauma was reported in four studies,[15,17,20,22] and was not reported in six studies.[14,16,18,19,21,23] CPT was given in individual settings,[16-20,22] in group settings,[21,23] or as a combination of both group and individual.[14,15] The included trials compared CPT with WL/UC (a group of terminologies included wait-list, delayed treatment, treatment as usual [education and supportive counselling or non-trauma-focused symptom management], and as-needed individual support),[14-17,19,20] PE,[20] PCT,[18,21,22] and with MeST.[23] The definitions of the interventions and comparators are briefly presented in Appendix 5. The most-reported outcomes were PTSD symptom severity and depression. PTSD symptom

severity was assessed using either clinician-administered scales or self-reported scales. Depression symptoms were assessed using self-reported scales. QoL was reported in two studies.[16,17]

Comparative Non-randomized Controlled Trials

Three studies were chart reviews[24-26] and three were cohort studies.[27-29] Of the six studies, one included civilian women who experienced sexual violence[27] and the rest examined a veteran population who had combat-related trauma.[24-26,28,29] The mean age of participants ranged from 30.6[27] to 61.9 years.[28] The proportion of males ranged from 0[27] to 100.[24,28] The interventions of the studies included CPT provided in a group setting[24,27-29] or in a combination of group and individual settings.[25,26] The comparators were wait-list or usual care (a group of terminologies that included wait-list, trauma-focused therapy, trauma group exposure, and long-term process [psychotherapy]),[24,25,27,28] PE,[26,29] and a combination of EMDR and group CPT.[25] Trauma group exposure may be different than other WL or UC controls, since it involves one of two primary components of PE, trauma-focused in vivo exposure. The definitions of the interventions and comparators are briefly presented in Appendix 5. PTSD symptoms and depression severity were the most common outcomes assessed using self-reported instruments. QoL was reported in one study.[24]

Critical Appraisal of Individual Studies

Randomized Controlled Trials

The method of randomization was reported in five trials,[14,16,17,22,23] which were judged to be at low risk of bias, while five other trials[15,18-21] provided insufficient information about randomization. Eight[14-21] out of 10 trials did not report details of allocation concealment, and were judged to be unclear in terms of the risk of bias. All trials were judged to be at unclear to high risk of bias regarding the blinding of participants and personnel, which are difficult to achieve in psychological therapy. However, blinding of outcome assessment was reported in six trials.[14,16,18,19,21,22] It was unclear whether or not the outcome assessors were blinded in four trials.[15,17,20,23] All trials except one[20] were judged to be at high risk of attrition bias, since the dropout rates were moderate to high (approximately 15% to 30%) and the method for handling of missing data was not reported. One trial[18] had to exclude a large portion (73%) of the study population (data of two therapists) due to inconsistencies in ratings by therapists. Nine out of 10 trials had a small sample size (ranging from 18 to 171 patients) that lacked power and generalizability. The period of follow-up was short, because it was impractical and unethical to have a long follow-up, particularly for the wait-list control group. Follow-up rates were low in most trials. It was difficult to judge differences in the level of competency of therapists between groups, and whether or not they were randomly assigned. However, the majority of the trials had clear objectives and clearly described the methods, validated instruments were used to assess important outcomes, and dropout rates were reported, but the reasons for treatment discontinuation were not clearly described.

Non-randomized Controlled Trials

In non-RCTs, factors such as reporting, external validity, internal validity, and power were considered in the assessment of the risk of bias (Appendix 6). Five[25-29] out of six studies did not clearly report the characteristics of participants at baseline to show whether there were differences between treatment groups. It was impossible to know how participants were selected in each treatment group in those studies. It was also unclear if the outcome assessors were blinded in all studies. None of the studies included power calculations to determine a sufficient sample size to detect a clinical important effect. Two studies[25,28] had small sample sizes (N = 51 and 21, respectively), which was distributed among three treatment groups. There was a high risk of bias due to the lack of treatment adherence and potential differences in

therapist competency in the non-RCTs. In all studies, there was also risk of reporting bias, since only self-reported measures were used. Taken together, all studies were judged to be at high risk of bias.

Data Analysis and Synthesis

Cognitive Processing Therapy Compared with Wait-List or Usual Care

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated by Clinician

Five RCTs[15-17,19,20] with a total of 357 participants used the CAPS to assess the severity of PTSD symptoms at baseline and at end of treatment. The CAPS ranges from 0 to 136, and participants who entered the studies had an average of 75 points at baseline, which is considered severe. Improvement in PTSD symptoms is indicated by a decrease in CAPS scores. The MD in the changes from baseline between CPT and WL/UC was –31.35 (95% confidence interval [CI], –40.84 to –21.86) (Figure 1, Appendix 7). For absolute effects, CAPS scores were lowered by 6 points for WL/UC and by 37.35 points for CPT at the end of treatment (Table 2). The overall quality of evidence was moderate.

Of the five RCTs, four[16,17,19,20] with a total of 302 participants had CPT given in individual settings. The MD in the changes from baseline between CPT and WL/UC was –28.07 (95% CI, –35.23 to –20.92) (Figure 1, Appendix 7). For absolute effects, WL/UC reduced CAPS scores by 7 points, while CPT lowered scores by 35.07 points at the end of treatment (Table 2). The quality of evidence was moderate.

One RCT[15] with a total 55 participants had CPT given in both group and individual settings. Results for group or individual treatment were not reported separately. The MD in the changes from baseline between CPT and WL/UC was –51.12 (95% CI, –69.17 to –33.07) (Figure 1, Appendix 7).

Three RCTs[16,19,20] with a total of 228 participants had results of follow-up for one, three, and nine months. MDs in the changes from baseline between CPT and WL/UC ranged from –13.9 to –31.3 points. Meta-analysis yielded a MD of –22.01 (95% CI, –32.94 to –11.09) (Figure 2). For absolute effects, WL/UC lowered CAPS scores by 6 points, while CPT lowered scores by 28.01 points at the end of follow-up (Table 2). The quality of evidence was low.

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated Using Self-Reported Instruments

Six RCTs[14-17,19,20] with a total of 627 participants used different self-reported instruments to assess the severity of PTSD symptoms at baseline and at end of treatment. Meta-analysis results were expressed as SMD and 95% CI, which was –0.89 (–1.15 to –0.62) (Figure 3). The SMD was back-translated using the SD of the control group in the Monson 2006 study,[19] which assessed the severity of PTSD using the PCL (scale ranged from 17 to 85 points), and participants had an average of 60 points at baseline. The calculated MD of the changes from baseline between CPT and WL/UC was –13.12 (95% CI, –16.95 to –9.14). For absolute effects, WL/UC lowered scores by 5 points, while CPT lowered scores by 18.12 points on the PCL scale at the end of treatment (Table 2). The quality of evidence was moderate.

Of the six RCTs, four[16,17,19,20] had CPT given in an individual setting with a total of 302 participants. Meta-analysis results were expressed as SMD and 95% CI, which was –0.87 (–1.11 to –0.63) (Figure 3). The SMD was back-translated using the SD of the control group in the Monson 2006 study,[19] which assessed the severity of PTSD using the PCL instrument (scale ranged from 17 to 85 points), and participants had an average of 60 points at baseline. On the PCL scale, the MD of the changes from baseline between CPT and WL/UC was –12.82 (95% CI, –16.95 to –9.14). For absolute effects, WL/UC lowered scores by 5 points, while CPT

lowered scores by 17.82 points on the PCL scale at the end of treatment (Table 2). The quality of evidence was moderate.

Two other RCTs[14,15] with a total 325 participants had CPT given in both group and individual settings. Results for group or individual treatment were not reported separately. The SMD was -1.08 (95% CI –1.97 to –0.18) (Figure 3).

Four RCTs[14,16,19,20] had results of follow-up for one, three, six, and nine months with a total of 541 participants. The SMD of the changes from baseline between CPT and WL/UC ranged from –0.6 to –1.2 (Figure 4). Meta-analysis and back-translation to PCL scale yielded an MD of –12.00 (95% CI, –16.48 to –7.52). For absolute effects, WL/UC lowered scores by 8 points, while CPT lowered scores by 20 points on the PCL scale at one month of follow-up (Table 2). The quality of evidence was low.

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated Using Self-Reported Instruments in Observational Studies

Four observational studies[24,25,27,28] with a total population of 285 participants assessed the severity of PTSD symptoms using different self-reported instruments at baseline and at the end of treatment. The SMD was –0.38 (95% CI, –0.62 to –0.15) (Figure 5). The SMD was back-translated to the PCL scale (range 17 to 85) using the Alvarez 2011 study,[24] where participants had 65 points at baseline. The calculated MD of the changes from baseline between CPT and WL/UC was –5.45 (95% CI, –8.88 to –2.15). For absolute effects, WL/UC lowered scores by 4 points, while CPT lowered scores by 9.45 points on the PCL scale at the end of treatment (Table 2). The quality of evidence was very low.

Change in Severity of Post-traumatic Stress Disorder Symptoms in the Military Population Rated by Clinician

Two RCTs[16,19] with a total population of 119 military veterans used the CAPS (scale: 0 to 136) to assess the severity of PTSD symptoms at baseline and at end of treatment. Participants had an average of 75 points at baseline. The MD in the changes from baseline between CPT and WL/UC was –21.15 (95% CI, –31.33 to –10.97) (Figure 6). For absolute effects, WL/UC lowered scores by 5 points, while CPT lowered scores by 26.15 points on the CAPS at the end of treatment (Table 2). The quality of evidence was low.

Those two RCTs[16,19] had results from follow-up at one and three months, respectively. MDs in the changes from baseline between CPT and WL/UC were –14 points in the study by Monson et al.[19] and –18 points in Forbes et al.[16] Meta-analysis yielded a MD of –16.01 (95% CI, –26.71 to –5.31) (Figure 7). For absolute effects, WL/UC lowered scores by 8 points, while CPT lowered scores by 24.01 points on the CAPS at the end of follow-up (Table 2). The quality of evidence was low.

Change in Severity of Post-traumatic Stress Disorder Symptoms in the Civilian Population Rated by Clinician

Three RCTs[15,17,20] with a total population of 238 civilians used the CAPS (scale: 0 to 136) to assess the severity of PTSD symptoms at baseline and at end of treatment. Participants had an average of 73 points at baseline. The MD in the changes from baseline between CPT and WL/UC was –37.66 (95% CI, –47.75 to –27.58) (Figure 8). For absolute effects, WL/UC lowered scores by 7 points, while CPT lowered scores by 44.66 points on the CAPS at the end of treatment (Table 2). The quality of evidence was low.

One RCT[20] had results of follow-up for nine months with a total population of 109 participants. The MD in the changes from baseline between CPT and WL/UC was –31.30 (95% CI, –43.17 to

–19.43) (Figure 9). For absolute effects, WL/UC lowered scores by 0.6 points while CPT lowered scores by 31.9 points on the CAPS at the end of follow-up (Table 2). The quality of evidence was low.

Change in Severity of Post-traumatic Stress Disorder Symptoms in Military Population Rated Using Self-Reported Instruments in Observational Studies

Two observational studies[24,28] with a total population of 213 participants assessed the severity of PTSD symptoms using the PCL (scale: 17 to 85) at baseline and at end of treatment. Participants had an average of 62 points at baseline. The MD of the changes from baseline between CPT and WL/UC was –5.05 (95% CI, –9.30 to –0.80) (Figure 10). For absolute effects, WL/UC lowered scores by 3 points, while CPT lowered scores by 8.05 points on the PCL scale at the end of treatment (Table 2). The quality of evidence was very low.

Change in Severity of Depression Symptoms

Six RCTs[14-17,19,20] with a total of 626 participants used different self-reported instruments to assess the severity of depression symptoms at baseline and at end of treatment. The SMD in the changes from baseline between CPT and WL/UC was –0.76 (95% CI, –0.96 to –0.57) (Figure 11). The SMD was back-translated using the SD of the control group in the Monson 2006 study,[19] which assessed the severity of depression using the BDI-II (scale: 0 to 63), and participants had an average of 27 points at baseline. The calculated MD in the changes from baseline between CPT and WL/UC was –8.85 (95% CI, –12.6 to –6.63). For absolute effects, WL/UC lowered scores by 1.5 points, while CPT lowered scores by 10.35 points on the BDI-II scale at the end of treatment (Table 2). The quality of evidence was moderate.

Of the six RCTs, four[16,17,19,20] had CPT given in individual settings, with a total of 301 participants. The SMD in the changes from baseline between CPT and WL/UC was –0.63 (95% CI, –0.86 to –0.40) (Figure 11). On the BDI-II scale, the calculated MD was –7.33 (95% CI, –10.01 to –4.66). For absolute effects, WL/UC lowered scores by 1.5 points, while CPT lowered scores by 8.83 points on the BDI-II scale at the end of treatment (Table 2). The quality of evidence was low.

Four RCTs[14,16,19,20] with a total of 540 participants had results of follow-up for one, three, six, and nine months. The SMD in the changes from baseline between CPT and WL/UC was –0.54 (–0.81 to –0.26) (Figure 12). On the BDI-II scale, the calculated MD was –7.12 (95% CI, –10.68 to –3.43). For absolute effects, WL/UC lowered scores by 4.6 points, while CPT lowered scores by 11.72 points on the BDI-II scale at one month of follow-up (Table 2). The quality of evidence was low.

Change in Severity of Depression Symptoms in Military Population

Two RCTs[16,19] with a total population of 119 military veterans used the BDI-II (scale: 0 to 63) to assess the severity of depression symptoms at baseline and at the end of treatment. Participants had an average of 26 points at baseline. The MD in the changes from baseline between CPT and WL/UC was –6.49 (95% CI, –11.55 to –1.43) (Figure 13). For absolute effects, WL/UC lowered scores by 2.6 points while CPT lowered scores by 9.09 points on the BDI-II scale at the end of treatment (Table 2). The quality of evidence was low.

The two RCTs[16,19] also had results of follow-up for one and three months, respectively. MDs in the changes from baseline between CPT and WL/UC were –2 points and –6 points after one and three months, respectively. Meta-analysis yielded a MD of –3.61 (95% CI, –8.97 to 1.76) (Figure 14). For absolute effects, WL/UC lowered scores by 5 points, while CPT lowered scores by 8.61 points on the BDI-II scale at the end of follow-up (Table 2). The quality of evidence was low.

Change in Severity of Depression Symptoms in Civilian Population

Four RCTs[14,15,17,20] with a total population of 507 civilians used different self-reported instruments to assess the severity of depression symptoms at baseline and at the end of treatment. The SMD in the changes from baseline between CPT and WL/UC was –0.85 (95% CI, –1.04 to –0.67) (Figure 15). The SMD was back-translated using the standard deviation of the control group in the Galovski 2012 study,[17] which assessed the severity of depression using BDI-II (scale: 0 to 63); participants had an average of 30 points at baseline. The calculated MD was –14.51 (95% CI, –17.75 to –5.29). For absolute effects, WL/UC lowered scores by 7 points, while the CPT lowered scores by 21.51 points on the BDI-II scale at the end of treatment (Table 2). The quality of evidence was moderate.

Two RCTs[14,20] with a total population of 421 civilians had results of follow-up for six and nine months. The SMD in the changes from baseline between CPT and WL/UC was –0.73 (95% CI, –0.93 to –0.53) (Figure 16). The SMD was back-translated using the standard deviation of the control group in the Resick 2002 study,[20] which assessed the severity of depression using the BDI (scale: 0 to 63); participants had an average of 24 points at baseline. The calculated MD was –8.61 (95% CI, –10.96 to –6.25). For absolute effects, WL/UC lowered scores by 0.7 points, while CPT lowered scores by 9.31 points on the BDI scale at nine months of follow-up (Table 2). The quality of evidence was moderate.

Change in Severity of Depression Symptoms Reported from Observational Studies

Three observational studies with a total population of 269 participants used different self-reported instruments to assess the severity of depression symptoms at baseline and at the end of treatment. The SMD in the changes from baseline between CPT and WL/UC was –0.23 (95% CI, –0.47 to 0.01) (Figure 17). The SMD was back-translated using the standard deviation of the control group in the Alvarez 2011 study,[24] which assessed the severity of depression using the BDI (scale: 0 to 63); participants had an average of 26 points at baseline. The calculated MD was –3.22 (95% CI, –6.57 to 0.14). For absolute effects, WL/UC lowered scores by 3.7 points, while CPT reduced scores by 6.92 points on the BDI scale at the end of treatment (Table 2). The quality of evidence was very low.

Change in Severity of Anxiety Symptoms

Three RCTs[14,16,19] with a total population of 389 participants used different self-reported instruments to assess the severity of anxiety symptoms at baseline and at end of treatment. The SMD of the changes from baseline between CPT and WL/UC was –0.76 (95% CI, –0.97 to –0.55) (Figure 18). The SMD was back-translated using the SD of the control group in the Monson 2006 study,[19] which assessed the severity of anxiety using the State-Trait Anxiety Inventory (STAI) (scale: 20 to 80), and participants had an average of 55 points at baseline. The calculated MD was –11.2 (95% CI, –14.3 to –8.11). For absolute effects, WL/UC increased scores by 2.5 points, while CPT lowered scores by 8.7 points on the STAI scale at the end of treatment (Table 2). The quality of evidence was moderate.

These three RCTs[14,16,19] had results of follow-up for one, three, and six months. The SMD of the changes from baseline between CPT and WL/UC was –0.69 (95% CI, –0.88 to –0.49) (Figure 19). Based on the STAI scale, the calculated MD was –11.04 (95% CI, –14.08 to –7.84). For absolute effects, WL/UC lowered scores by 1.4 points, while CPT lowered scores by 12.44 points on the STAI scale at the end of follow-up (Table 2). The quality of evidence was moderate.

Compliance Assessed with Number of People Who Completed Treatment

Six RCTs[14–17,19,20] with a total population of 804 participants reported the number of patients who completed the study at end of treatment. There was no difference between the CPT and WL/UC

groups (73% versus 71%; relative risk [RR] 0.96; 95% CI, 0.85 to 1.10) (Figure 20). The quality of evidence was moderate (Table 2).

Of these six RCTs, four[16,17,19,20] with a total population of 328 participants had CPT given in individual settings. There was also no difference between the CPT and WL/UC groups (73% versus 82%; RR 0.89; 95% CI, 0.79 to 1.00) (Figure 20). The quality of evidence was low (Table 2).

Three RCTs[14,16,19] with a total population of 524 participants reported the number of patients who completed follow-up of one, three, and six months, respectively. There was no difference between the CPT and WL/UC groups (84% versus 72%; RR 1.09; 95% CI, 0.87 to 1.37) (Figure 21). The quality of evidence was low (Table 2).

Quality of Life

Two RCTs[16,17] and one observational study[24] reported QoL as an outcome. In the RCT by Galovski 2012,[17] participants in the CPT group compared with WL control had a greater (six- to 79-fold) improvement in QoL as assessed using the Quality of Life Inventory (QOLI) and the Medical Outcome Study 36-Item Short Form Health Survey (SF-36). In the RCT by Forbes 2012,[16] using the World Health Organization Quality of Life (WHOQOL) scale to assess QoL, CPT was found to improve the psychological, social, and environmental subscales by four-fold, five-fold, and three-fold, respectively, but there was no change on the physical subscale, compared with 'treatment as usual' which varied depending on the care provider. Treatment as usual included education and supportive counselling, non-trauma focused symptom management, or CBT with elements of exposure. However, the observational study by Alvarez 2011[24] did not find any difference in any subscales of the WHOQOL between CPT and psycho-education and patient autobiographical review, although QoL seemed to improve in both groups.

Remission

The BASS 2013 study[14] did not measure remission, as not all patients had a confirmed PTSD diagnosis; rather, it reported the number of participants with probable PTSD before treatment, at the end of treatment, and after six months of follow-up. At baseline, probable PTSD was 60% (94/157) in the CPT group and 83% (205/248) in the individual support group. At the end of treatment, the number dropped to 8% (9/114) in the CPT group and 54% (85/156) in the individual support group. After six months of follow-up, it was 9% (12/138) and 42% (73/175), respectively.

Discharge from Treatment

No studies reported this outcome.

Release from Service (Military)

No studies reported this outcome.

Cognitive Processing Therapy Compared with Prolonged Exposure

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated by Clinicians

One RCT[20] with a total population of 124 participants used the CAPS (scale: 0 to 136) to assess the severity of PTSD symptoms at baseline and at end of treatment; participants had an average of 75 points at baseline. There was no difference between CPT and PE in the changes from baseline at end of treatment (MD –3.97; 95% CI, –16.72 to 8.78) (Figure 22, Appendix 8). For absolute effects, PE reduced scores by 32 points, while CPT reduced scores by 35.97 points on the CAPS at the end of treatment (Table 3). The quality of evidence was very low.

At the nine-month follow-up from the same RCT,[20] there was also no difference in the change in severity of PTSD symptoms between CPT and PE (MD –2.27; 95% CI, –15.54 to 11.00) (Figure 23). For absolute effects, PE reduced scores by 30 points, while CPT reduced scores by 32.27 points on the CAPS at the end of follow-up (Table 3). The quality of evidence was very low.

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated Using a Self-Reported Instrument

One RCT[20] with a total population of 124 participants used the PTSD Symptom Scale (PSS) (scale: 0 to 51) to assess the severity of PTSD symptoms at baseline and at the end of treatment, and participants had an average of 30 points at baseline. There was no difference between CPT and PE in changes from baseline at the end of treatment (MD –3.79; 95% CI, –9.09 to 1.51) (Figure 24). For absolute effects, PE lowered scores by 12 points, while CPT lowered scores by 15.79 points on the PSS at the end of treatment (Table 3). The quality of evidence was very low.

At the nine-month follow-up from the same RCT,[20] there was also no difference in the change in severity of PTSD between CPT and PE (MD –4.71; 95% CI, –10.27 to 0.85) (Figure 25). For absolute effects, PE lowered scores by 12 points, while CPT lowered scores by 16.71 points on the PSS at the end of follow-up (Table 3). The quality of evidence was very low.

Change in Severity of Post-traumatic Stress Disorder Symptoms in Observational Studies Rated Using a Self-Reported Instrument

One observational study[26] with a total population of 263 participants used PCL (scale: 17 to 85) to assess severity of PTSD symptoms at baseline and at end of treatment, and participants had an average of 61 points at baseline. In this study, PE was associated with better improvement than CPT in PTSD severity at end of treatment (MD 12.54; 95% CI, 8.27 to 16.81) (Figure 26). For absolute effects, PE lowered scores by 24 points, while CPT lowered scores by 11.46 points on PCL at the end of treatment (Table 3). The quality of evidence was very low. Another observational study[29] found in its preliminary results that there was no difference between CPT and PE in ther effect on PTSD severity at end of treatment (data not reported in the study).

Change in Severity of Depression Symptoms

One RCT[20] with a total population of 124 participants used the BDI (scale: 0 to 63) to assess the severity of depression symptoms at baseline and at the end of treatment, and participants had an average of 24 points at baseline. There was no difference between CPT and PE in changes from baseline at end of treatment (MD –2.94; 95% CI, –8.17 to 2.29) (Figure 27). For absolute effects, PE lowered scores by 8 points, while CPT lowered scores by 10.94 points on the BDI at the end of treatment (Table 3). The quality of evidence was very low.

At the nine-month follow-up from the same RCT,[20] there was also no difference in the change in severity of depression between CPT and PE (MD –1.91; 95% CI, –7.27 to 3.45) (Figure 28). For absolute effects, PE lowered scores by 7.6 points, while CPT lowered scores by 9.51 points on the BDI at the end of follow-up (Table 3). The quality of evidence was very low.

Compliance Assessed With Number of People Who Completed Treatment

One RCT[20] with a total population of 124 participants reported the number of patients who completed the study at end of treatment. There was no statistically significant difference between CPT and PE (66% versus 65%; RR 1.02; 95% CI, 0.79 to 1.32) (Figure 29). The quality of evidence was very low (Table 3).

Quality of Life

No studies reported this outcome.

Remission
No studies reported this outcome.

Discharge from Treatment
No studies reported this outcome.

2.9 Release from Service (Military)
No studies reported this outcome.

Cognitive Processing Therapy Compared with Present-Centred Therapy

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated by Clinician
Two RCTs[21,22] with a total population of 182 participants used two different instruments to assess the severity of PTSD symptoms. The SMD of the changes from baseline at the end of treatment was –0.59 (95% CI, –1.52 to 0.33) (Figure 30, Appendix 9). The SMD was back-translated using the SD of the Suris 2013 study,[22] which assessed the severity of PTSD using the CAPS (scale: 0 to 136), and participants had an average of 84 points at baseline. The calculated MD was –2.88 (–7.42 to 1.61), which was not statistically significant. For absolute effects, PCT lowered scores by 15 points, while CPT lowered scores by 17.88 points on the CAPS at the end of treatment (Table 4). The quality of evidence was very low.

The two RCTs[21,22] had results of follow-up for six and 12 months. The SMDs were –0.14 and –0.70; the overall SMD was –0.43 (95% CI, –0.97 to 0.11) (Figure 31). Based on CAPS, there was no statistically significant difference, with a calculated MD of –2.08 (95% CI, –4.69 to 0.53). For absolute effects, PCT lowered scores by 22 points, while CPT lowered scores by 24.08 points on the CAPS at the end of follow-up (Table 4). The quality of evidence was very low.

Change in Severity of Post-traumatic Stress Disorder Symptoms Rated Using Self-Reported Instruments
Three RCTs[18,21,22] with a total population of 227 participants used different instruments to assess the severity of PTSD symptoms. The SMD in the changes from baseline at the end of treatment was –1.03 (95% CI, –2.36 to 0.30) (Figure 32). The SMD was back-translated using the SD of the Suris 2013 study,[22] which assessed the severity of PTSD using the PCL (scale: 17 to 85), and participants had an average of 65 points at baseline. The calculated MD was –3.05 (–6.96 to 0.89), which was not statistically significant. For absolute effects, PCT lowered scores by 8 points, while CPT lowered scores by 11.05 points on PCL at the end of treatment (Table 4). The quality of evidence was very low.

The three RCTs[13,21,22] also had results of follow-up for six months, six months, and 12 months, respectively. The SMDs were –0.2, –0.6, and –2.1; the overall SMD was –0.97 (95% CI, –2.13 to 0.18) (Figure 33). Based on the PCL, the calculated MD was –2.86 (95% CI, –6.28 to 0.53), which was not statistically significant. For absolute effects, PCT lowered scores by 9 points, while CPT lowered scores by 11.86 points on the PCL at the end of treatment (Table 4). The quality of evidence was very low.

Change in Severity of Depression Symptoms
Two RCTs[21,22] with a total population of 181 participants used different self-reported instruments to assess the severity of depression symptoms. The SMD of the changes from baseline at the end of treatment was –0.60 (95% CI, –1.28 to 0.08) (Figure 34). The SMD was back-translated using the SD of the Suris 2013 study,[22] which assessed the severity of depression using the Quick Inventory of Depressive Symptomatology (QIDS) (scale: 0 to 27), and participants had an average of 16 points at baseline. The calculated MD was –0.68 (95% CI, –1.45 to 0.09), which was not statistically significant. For absolute effects, PCT lowered scores by 2 points, while CPT lowered scores by 2.68 points on the QIDS scale at the end of treatment (Table 4). The quality of evidence was very low.

The two RCTs[21,22] also had results of follow-up for six and 12 months. The SMDs were –0.2 and –1.8; the overall SMD was –1.01 (95% CI, –2.61 to 0.59) (Figure 35). Based on QIDS, there was no difference between CPT and PCT, with a calculated MD of –1.12 (95% CI, –2.9 to 0.65). PCT lowered scores by 2 points, while CPT lowered scores by 3.12 points on QIDS at the end of follow-up (Table 4). The quality of evidence was very low.

Compliance Assessed With Number of People Who Completed Treatment

Two RCTs[21,22] with a total population of 237 participants reported the number of patients who completed the study at end of treatment. The proportion of patients completing treatment was lower in the CPT group compared with those in the PCT group (66% versus 82%; RR 0.82; 95% CI, 0.71 to 0.95) (Figure 36). The quality of evidence was very low (Table 3).

Quality of Life

No studies reported this outcome.

Remission

No studies reported this outcome.

Discharge from Treatment

No studies reported this outcome.

Release from Service (Military)

No studies reported this outcome.

Cognitive Processing Therapy Compared with Memory Specificity Training

One RCT[23] with 16 participants (eight civilians per group) compared CPT (group) with MeST, which taught individuals how to retrieve specific memories. MeST was first designed to treat depression.[31] The severity of PTSD and depression were assessed using the self-reported instruments, i.e., the Modified PTSD Symptom Scale (MPSS) and BDI-II. There were no differences between groups for the improvement in PTSD and depression symptoms at end of treatment and at three-month follow-up (Figures 37 to 40 of Appendix 10, Table 5). The study also showed no difference in the improvement in global functioning and ability to retrieve specific memories between CPT and MeST. The quality of evidence was very low.

Cognitive Processing Therapy Compared with Eye Movement Desensitization and Reprocessing

No study was found that compared CPT with EMDR.

One observational study[25] with 34 participants (17 military veterans in each group) compared CPT (individual and group) with EMDR plus CPT individual therapy. The outcomes considered in this study were severity of PTSD, depression, and anxiety, which were assessed using self-reported instruments (i.e., the PCL, BDI, and Beck Anxiety Inventory [BAI], respectively). Based on very low-quality evidence, there were no differences between the CPT and the EMDR plus CPT groups for change in severity of PTSD (62.53 ± 9.72 versus 65.82 ± 13.52), change in depression symptoms (25.24 ± 12.81 versus 26.00 ± 13.11), and change in anxiety symptoms (25.88 ± 13.14 versus 23.47 ± 13.42) at end of treatment.

Cognitive Processing Therapy Compared with Dialogue Exposure Therapy

One RCT[30] was identified from the final alert (February 11, 2016) comparing DET with CPT for adult outpatients suffering from PTSD after a variety of traumas. As it was identified after data analyses were complete, its findings are summarized here without inclusion in the main or GRADE analysis. Both treatments achieved similar reductions in PTSD symptoms assessed using a self-reported instrument, the Impact of Event Scale – Revised (IES-R). At pre-treatment

versus post-treatment, the effect sizes (Hedges' *g*) for DET and CPT were 1.14 and 1.57, respectively. The effects were stable after six-month follow-up (1.33 versus 1.50). For overall psychological functioning and trauma-related cognition measured by the Brief Symptom Inventory (BSI) and the Posttraumatic Cognitions Inventory (PTCI), respectively, CPT performed better than DET at the post-treatment assessment (BSI: 0.88 versus 0.64; PTCI: 1.03 versus 0.65). Dropout rates were similar for both treatments (post-treatment: 12.2% for DET and 14.9% for CPT).

Table 2: Comparison 1 —— Cognitive Processing Therapy Compared With Wait-List or Usual Care

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population		Relative Effect (95% CI)	Anticipated Absolute Effects	
							WL/UC	CPT		Risk with WL/UC	Risk difference with CPT relative to WL/UC
Change in severity of PTSD symptoms (assessed by clinician-administered CAPS, scale range from 0 to 136); improvement indicated by decrease; average 75 points at baseline											
357 (5 RCTs) End of treatment Group or individual	Serious[a]	Not serious	Not serious[b]	Not serious	None	⨁⨁⨁◯ MODERATE[a,b]	169	188	-	6 points lower	**31.35 points further reduced** (40.84 lower to 21.86 lower)
302 (4 RCTs) End of treatment Individual	Serious[a]	Not serious	Not serious[b]	Not serious	None	⨁⨁⨁◯ MODERATE[a,b]	142	160	-	7 points lower	**28.07 points further reduced** (35.23 lower to 20.92 lower)
228 (3 RCTs) At longest follow-up (1, 3, and 9 months)	Serious[a]	Not serious	Not serious	Serious[c]	None	⨁⨁◯◯ LOW [a,c]	106	122	-	6 points lower	**22.01 points further reduced** (32.94 lower to 11.09 lower)
Change in severity of PTSD symptoms (assessed by self-reported instrument, PCL, scale range from 17 to 85); improvement indicated by decrease; 60 points at baseline											
627 (6 RCTs) End of treatment Group and individual	Serious[a]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[a]	325	302	-	5 points lower	**13.12 points further reduced** (16.95 lower to 9.14 lower)[d,e]
302 (4 RCTs) End of treatment Individual	Serious[a]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[a]	142	160	-	5 points lower	**12.82 points further reduced** (16.95 lower to 9.14 lower)[d,f]

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population WL/UC	Total Population CPT	Relative Effect (95% CI)	Anticipated Absolute Effects Risk with WL/UC	Anticipated Absolute Effects Risk difference with CPT relative to WL/UC
541 (4 RCTs) At longest follow-up (1, 3, 6, and 9 months)	Serious[a]	Not serious	Not serious	Serious[h]	None	⨁⨁◯◯ LOW[a,h]	281	260	-	8 points lower at 1 month	**12 points further reduced** (16.48 lower to 7.52 lower)[d,g]
Change in severity of PTSD symptoms (assessed by self-reported instrument, PCL, scale range from 17 to 85); improvement indicated by decrease; 65 points at baseline											
285 (4 observational studies) End of treatment	Very serious[k]	Not serious	Not serious	Serious[l]	None	⨁◯◯◯ VERY LOW[k,l]	136	149	-	4 points lower	**5.45 points further reduced** (8.88 lower to 2.15 lower)[i,j]
Change in severity of PTSD symptoms (assessed by CAPS, scale range from 0 to 136); improvement indicated by decrease; average 75 points at baseline											
119 (2 RCTs) End of treatment Military	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	59	60	-	5 points lower	**21.15 points further reduced** (31.33 lower to 10.97 lower)
119 (2 RCTs) At longest follow-up (1 and 3 months) Military	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	59	60	-	8 points lower	**16.01 points further reduced** (26.71 lower to 5.31 lower)
Change in severity of PTSD symptoms (assessed by CAPS, scale range from 0 to 136); improvement indicated by decrease; average 73 points at baseline											
238 (3 RCTs) End of treatment Civilian	Serious[a]	Not serious	Not serious[m]	Serious[n]	None	⨁⨁◯◯ LOW[a,m,n]	110	128	-	7 points lower	**37.66 points further reduced** (47.75 lower to 27.58 lower)
109 (1 RCT) At longest follow-up (9 months) Civilian	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	47	62	-	0.6 points lower	**31.3 points further reduced** (43.17 lower to 19.43 lower)

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population WL/UC	Total Population CPT	Relative Effect (95% CI)	Anticipated Absolute Effects Risk with WL/UC	Anticipated Absolute Effects Risk difference with CPT relative to WL/UC
Change in severity of PTSD symptoms (assessed by self-reported instrument, PCL, scale range from 15 to 85); improvement indicated by decrease; average 62 points at baseline											
213 (2 observational studies) End of treatment Military	Very serious[k]	Not serious	Not serious	Serious[n]	None	⨁◯◯◯ VERY LOW[k,n]	99	114	-	3 points lower	**5.05 points further reduced** (9.3 lower to 0.8 lower)
Change in severity of depression symptoms (assessed by self-reported instrument, BDI-II, scale range from 0 to 63); improvement indicated by decrease; average 27 points at baseline											
626 (6 RCTs) End of treatment Group and Individual	Serious[a]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[a]	325	301	-	1.5 points lower	**8.85 points further reduced** (12.6 lower to 6.63 lower)[d,o]
301 (4 RCTs) End of treatment Individual	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	142	159	-	1.5 points lower	**7.33 points further reduced** (10.01 lower to 4.66 lower)[d,p]
540 (4 RCTs) At longest follow-up (1, 3, 6, and 9 months)	Serious[a]	Not serious	Not serious	Serious[r]	None	⨁⨁◯◯ LOW[a,r]	281	259	-	4.6 points lower at one month	**7.12 points further reduced** (10.68 lower to 3.43 lower)[d,q]
Change in severity of depression symptoms (assessed by self-reported instrument, BDI-II, scale range from 0 to 63); improvement indicated by decrease; average 26 points at baseline											
119 (2 RCTs) End of treatment Military	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	59	60	-	2.6 points lower	**6.49 points further reduced** (11.55 lower to 1.43 lower)

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population WL/UC	Total Population CPT	Relative Effect (95% CI)	Anticipated Absolute Effects Risk with WL/UC	Anticipated Absolute Effects Risk difference with CPT relative to WL/UC
119 (2 RCTs) At longest follow-up (1 and 3 months) Military	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	59	60	-	5 points lower	**3.61 points further reduced** (8.97 lower to 1.76 higher)
Change in severity of depression symptoms (assessed by self-reported instrument, BDI or BDI-II, scale range from 0 to 63); improvement indicated by decrease; 30 points at baseline											
507 (4 RCTs) End of treatment Civilian	Serious[a]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[a]	266	241	-	7 points lower	**14.51 points further reduced (BDI-II)** (17.75 lower to 5.29 lower)[s,t]
421 (2 RCTs) At longest follow-up (6 and 9 months) Civilian	Serious[a]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[a]	222	199	-	0.7 points lower at nine months	**8.61 points further reduced (BDI)** (10.96 lower to 6.25 lower)[u,v]
Change in severity of depression symptoms (assessed by self-reported instrument, BDI, scale range from 0 to 63); improvement indicated by decrease; 26 points at baseline											
269 (3 observational studies) End of treatment	Very serious[k]	Not serious	Not serious	Serious[n]	None	⨁◯◯◯ VERY LOW[k,n]	130	139	-	3.7 points lower	**3.22 points further reduced** (6.57 lower to 0.14 higher)[l,w]
Change in severity of anxiety symptoms (assessed by self-reported instrument, STAI, scale range from 20 to 80); improvement indicated by decrease; 55 points at baseline											
389 (3 RCTs) End of treatment	Serious[y]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[y]	215	174	-	2.5 points higher	**11.2 points further reduced** (14.3 lower to 8.11 lower)[d,x]

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population WL/UC	Total Population CPT	Relative Effect (95% CI)	Anticipated Absolute Effects Risk with WL/UC	Anticipated Absolute Effects Risk difference with CPT relative to WL/UC
432 (3 RCTs) At longest follow-up (1, 3, and 6 months)	Serious[y]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[y]	234	198	-	1.4 points lower at one month	**11.04 points further reduced** (14.08 lower to 7.84 lower)[d,z]
Compliance (assessed with: number of people who completed treatment)											
804 (6 RCTs) End of treatment Group and Individual	Serious[a]	Not serious	Not serious	Not serious	None	⨁⨁⨁◯ MODERATE[a]	309/436 (70.9%)	269/368 (73.1%)	**RR 0.96** (0.85 to 1.10)	**Study population** 71 per 100	**3 more per 100** (7 fewer to 11 more)
328 (4 RCTs) End of treatment Individual	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	126/153 (82.4%)	127/175 (72.6%)	**RR 0.89** (0.79 to 1.00)	**Study population** 82 per 100	**9 fewer per 100** (17 fewer to 0 fewer)
524 (3 RCTs) At longest follow-up (1, 3, and 6 months)	Serious[a]	Serious[aa]	Not serious	Not serious	None	⨁⨁◯◯ LOW[a,aa]	220/307 (71.7%)	183/217 (84.3%)	**RR 1.09** (0.87 to 1.37)	**Study population** 72 per 100	**12 more per 100** (9 fewer to 27 more)

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population WL/UC	Total Population CPT	Relative Effect (95% CI)	Anticipated Absolute Effects Risk with WL/UC	Anticipated Absolute Effects Risk difference with CPT relative to WL/UC
Quality of Life											
133 (2 RCTs) End of treatment	Serious[a]	Not serious	Not serious	Serious[n]	None	⨁⨁◯◯ LOW[a,n]	In the Galovski 2012 study,[17] the change in QoL in the CPT group was many-fold larger than that in the WL group when assessed using QOLI and SF36 instruments. The Forbes 2012 study[16] used WHOQOL to assess QoL and found that CPT improved the psychological, social, and environmental subscales, but not the physical subscale compared with 'treatment as usual'. Treatment as usual included education and supportive counselling, non-trauma focused symptom management, or CBT with elements of exposure. The Alvarez 2011 observational study[24] did not find any difference between CPT and psycho-education and patient autobiographical review when assessed by WHOQOL.				
Remission: The BASS 2013 study[14] did not actually measure remission, but reported the number of participants with probable PTSD. At baseline, probable PTSD was 60% (94/157) in the CPT group and 83% (205/248) in the individual support group. At the end of treatment, the number dropped to 8% (9/114) in the CPT group and to 54% (85/156) in the individual support group. After 6 months of follow-up, it was 9% (12/138) and 42% (73/175), respectively.											
Discharge from treatment: Not measured											
Release from service (military): Not measured											

BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory-II; CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; CPT = cognitive processing therapy; PCL = PTSD checklist; PTSD = post-traumatic stress disorder; STAI = State-Trait Anxiety Inventory; QoL= quality of life; QOLI = Quality of Life Inventory; RCT = randomized controlled trial; RR = relative risk; SF-36 = Short Form 36-Item Health Survey; SMD = standardized mean difference; WHOQOL = World Health Organization Quality of Life scale; WL/UC = wait-list or usual care.

[a] Unclear randomization, allocation concealment, and blinding of outcome assessment; high dropout rates.
[b] Trials included either civilians or veterans; the effect was similar for both populations, although the change difference was higher for civilians.
[c] Few participants; difference ranged from 14 to 31 points; follow-up period was 1, 3 and 9 months.
[d] SMD was back-translated using the Monson 2006 study.
[e] Based on SMD –0.89 (–1.15 to –0.62).
[f] Based on SMD –0.87 (–1.11 to –0.63).
[g] Based on SMD –0.75 (–1.03 to –0.47).
[h] Varied in follow-up periods 1, 3, 6, and 9 months.
[i] SMD was back-translated using the Alvarez study.
[j] Based on SMD –0.38 (–0.62 to –0.15).
[k] Studies lacked external validity and internal validity, according to Downs and Black assessment tool.
[l] Few participants; SMD ranged from 0.3 to 0.7.
[m] The effect was slightly higher than for military personnel, but the trend was not different.
[n] Few participants.
[o] Based on SMD –0.76 (–0.96 to –0.57).
[p] Based on SMD –0.63 (–0.86 to –0.40).
[q] Based on SMD –0.54 (–0.81 to –0.26).
[r] SMD ranged from 0.4 to 1.3; substantial heterogeneity.
[s] SMD was back-translated using the Galovski 2012 study.
[t] Based on SMD –0.85 (–1.04 to –0.67).
[u] SMD was back-translated using the Resick 2002 study.
[v] Based on SMD –0.73 (–0.93 to –0.53).
[w] Based on SMD –0.23 (–0.47 to 0.01).
[x] Based on SMD –0.76 (–0.97 to –0.55).
[y] Unclear allocation concealment, high dropout rates, but outcome assessors were blind.
[z] Based on SMD –0.69 (–0.88 to –0.49).
[aa] High heterogeneity.

Table 3: Comparison 2 — Cognitive Processing Therapy Compared With Prolonged Exposure

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population		Relative Effect (95% CI)	Anticipated Absolute Effects	
							PE	CPT		Risk with PE	Risk difference with CPT relative to PE
Change in severity of PTSD symptoms (assessed by clinician-administered CAPS, scale range from 0 to 136); improvement indicated by decrease; 75 points at baseline											
124 (1 RCT) End of treatment	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	62	62	-	32 points lower	**3.97 points further reduced** (16.72 lower to 8.78 higher)
124 (1 RCT) At longest follow-up (9 months)	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	62	62	-	30 points lower	**2.27 points further reduced** (15.54 lower to 11 higher)
Change in severity of PTSD symptoms (assessed by self-reported instrument PSS, scale range from 0 to 51); improvement indicated by decrease; 30 points at baseline											
124 (1 RCT) End of treatment	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	62	62	-	12 points lower	**3.79 points further reduced** (9.09 lower to 1.51 higher)
124 (1 RCT) At longest follow-up (9 months)	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	62	62	-	12 points lower	**4.71 points further reduced** (10.27 lower to 0.85 higher)
Change in severity of PTSD symptoms (assessed by self-reported instrument, PCL, scale range from 17 to 85); improvement indicated by decrease; 61 points at baseline											
263 (1 observational study) End of treatment	Very serious[c]	Not serious	Not serious	Serious[d]	None	⨁◯◯◯ VERY LOW[c,d]	85	178	-	24 points lower	**12.54 points higher than PE** (8.27 higher to 16.81 higher)
Change in severity of depression symptoms (assessed by self-reported instrument, BDI, scale range from 0 to 63); improvement indicated by decrease; 24 points at baseline											
122 (1 RCT) End of treatment	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	61	61	-	8 points lower	**2.94 points further reduced** (8.17 lower to 2.29 higher)
122 (1 RCT) At longest follow-up (9 months)	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	61	61	-	7.6 points lower	**1.91 points further reduced** (7.27 lower to 3.45 higher)

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population		Relative Effect (95% CI)	Anticipated Absolute Effects	
							PE	CPT		Risk with PE	Risk difference with CPT relative to PE
Compliance (assessed with: number of people who completed treatment)											
124 (1 RCT) End of treatment	Serious[a]	Not serious	Not serious	Very serious[b]	None	⨁◯◯◯ VERY LOW[a,b]	40/62 (64.5%)	41/62 (66.1%)	**RR 1.02** (0.79 to 1.32)	**Study population**	
										65 per 100	**1 more per 100** (14 fewer to 21 more)
Quality of life: Not measured											
Remission: Not measured											
Discharge from treatment: Not measured											
Release from service (military): Not measured											

BDI = Beck Depression Inventory; CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; PCL = PTSD checklist; PSS = PTSD Symptom Scale; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial; RR = relative risk.

[a] Unclear randomization, allocation concealment, and blinding of outcome assessment.

[b] Few participants.

[c] Lacking in external validity and internal validity, according to Downs and Black quality assessment tool.

[d] Few events.

Table 4: Comparison 3 — Cognitive Processing Therapy Compared with Present-Centred Therapy

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population		Relative Effect (95% CI)	Anticipated Absolute Effects	
							PCT	CPT		Risk with PCT	Risk difference with CPT relative to PCT
Change in severity of PTSD symptoms (assessed by clinician-administered CAPS, scale range from 0 to 136); improvement indicated by decrease; 84 points at baseline											
182 (2 RCTs) End of treatment	Serious[c]	Serious[d]	Not serious	Very serious[e]	None	⨁◯◯◯ VERY LOW[c,d,e]	93	89	-	15 points lower	**2.88 points further reduced** (7.42 lower to 1.61 higher)[a,b]
126 (2 RCTs) At longest follow-up (6, and 12 months)	Serious[c]	Serious[d]	Not serious	Very serious[e]	None	⨁◯◯◯ VERY LOW[c,d,e]	62	64	-	22 points lower at 6 months	**2.08 points further reduced** (4.69 lower to 0.53 higher)[a,f]
Change in severity of PTSD symptoms (assessed by self-reported instrument, PCL, scale range from 17 to 85); improvement indicated by decrease; 65 points at baseline											
227 (3 RCTs) End of treatment	Serious[h]	Serious[d]	Not serious	Very serious[j]	None	⨁◯◯◯ VERY LOW[d,h,j]	106	121	-	8 points lower	**3.05 points further reduced** (6.96 lower to 0.89 higher)[a,g]
171 (3 RCTs) At longest follow-up (6, 6, and 12 months)	Serious[h]	Serious[d]	Not serious	Very serious[k]	None	⨁◯◯◯ VERY LOW[d,h,k]	75	96	-	9 points lower at 6 months	**2.86 points further reduced** (6.28 lower to 0.53 higher)[a,j]
Change in severity of depression symptoms (assessed by self-reported instrument, QIDS, scale range from 0 to 27); improvement indicated by decrease; 16 points at baseline											
181 (2 RCTs) End of treatment	Serious[c]	Serious[d]	Not serious	Very serious[m]	None	⨁◯◯◯ VERY LOW[c,d,m]	93	88	-	2 points lower	**0.68 points further reduced** (1.45 lower to 0.09 higher)[a,l]
126 (2 RCTs) At longest follow-up (6 and 12 months)	Serious[c]	Serious[d]	Not serious	Very serious[o]	None	⨁◯◯◯ VERY LOW[c,d,o]	61	65	-	2 points lower at 6 months	**1.12 points further reduced** (2.9 lower to 0.65 higher)[a,n]

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population		Relative Effect (95% CI)	Anticipated Absolute Effects	
							PCT	CPT		Risk with PCT	Risk difference with CPT relative to PCT
Compliance (assessed with: number of people who completed treatment)											
237 (2 RCTs)	Serious[c]	Not serious	Not serious	Very serious[p]	None	⨁◯◯◯ VERY LOW[c,p]	89/109 (81.7%)	85/128 (66.4%)	**RR 0.82** (0.71 to 0.95)	**Study population**	
										82 per 100	**15 fewer per 100** (24 fewer to 4 fewer)
Quality of life: Not measured											
Remission: Not measured											
Discharge from treatment: Not measured											
Release from service (military): Not measured											

CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; CPT = cognitive processing therapy; PCL = PTSD checklist; PCT = present-centred therapy; PTSD = post-traumatic stress disorder; QIDS = Quick Inventory of Depressive Symptomatology; RCT = randomized controlled trial; RR = relative risk; SMD = standardized mean difference.

[a] SMD was back-translated using the Suris 2013 study.

[b] Based on SMD –0.59 (–1.52 to 0.33).

[c] High dropout rates, low follow-up rates, potential selective reporting.

[d] High heterogeneity.

[e] Few participants; SMD varied from –0.13 to –1.07.

[f] Based on SMD –0.43 (–0.97 to 0.11).

[g] Based on SMD –1.03 (–2.36 to 0.30).

[h] Unclear randomization and allocation concealment in Holliday 2014 and Resick 2015; high dropout rates; low follow-up rates.

[i] Few participants; the effect ranged from a greater reduction of –2.35 with CPT to as little as no difference in effect of –0.25 with CPT.

[j] Based on SMD –0.97 (–2.13, 0.18)

[k] Few participants; SMD varied from –0.21 to –2.09.

[l] Based on SMD –0.60 (–1.28 to 0.08).

[m] Few participants, SMD varied from –0.25 to –0.95.

[n] Based on SMD –1.01 (–2.61 to 0.59).

[o] Few participants; SMD varied from –0.19 to –1.83.

[p] Few participants.

Table 5: Comparison 4 — Cognitive Processing Therapy Compared with Memory Specificity Training for Post-traumatic Stress Disorder in Adults

Quality Assessment							Summary of Findings				
Number of Participants (Studies) Follow-Up	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias	Overall Quality of Evidence	Total Population		Relative Effect (95% CI)	Anticipated Absolute Effects	
							MeST	CPT		Risk with MeST	Risk difference with CPT relative to MeST
Change in severity of PTSD symptoms (assessed by self-reported instrument, MPSS, scale range from 0 to 68); improvement indicated by decrease; 59 points at baseline											
16 (1 RCT) End of treatment	Serious[a]	Not serious	Not serious	Very serious[a]	None	⨁◯◯◯ VERY LOW	8	8	-	14.5 points lower	**1.5 points further reduced** (30.14 lower to 27.14 higher)
Change in severity of PTSD symptoms (assessed by self-reported instrument, MPSS, scale range from 0 to 68); improvement indicated by decrease; 59 points at baseline											
16 (1 RCT) At 3-month follow-up	Serious[a]	Not serious	Not serious	Very serious[a]	None	⨁◯◯◯ VERY LOW	8	8	-	30 points lower	**1 points higher than MeST** (29.69 lower to 31.69 higher)
Change in severity of depression symptoms (assessed by self-reported instrument, BDI-II, scale range from 0 to 63); improvement indicated by decrease; 25 points at baseline											
16 (1 RCT) End of treatment	Serious[a]	Not serious	Not serious	Very serious[a]	None	⨁◯◯◯ VERY LOW	8	8	-	5.88 points lower	**3 points further reduced** (22.23 lower to 16.23 higher)
Change in severity of depression symptoms (assessed by self-reported instrument, BDI-II, scale range from 0 to 63); improvement indicated by decrease; 25 points at baseline											
16 (1 RCT) At 3-month follow-up	Serious[a]	Not serious	Not serious	Very serious[a]	None	⨁◯◯◯ VERY LOW	8	8	-	8 points lower	4.25 points lower (22.47 lower to 13.97 higher)
Compliance: Not measured											
Quality of life: Not measured											
Remission: Not measured											
Discharge from treatment: Not measured											
Release from service (military): Not measured											

BDI-II = Beck Depression Inventory-II; CI = confidence interval; CPT = cognitive processing therapy; MeST = memory specific training; MPSS = Modified PTSD Symptom Scale; RCT = randomized controlled trial; PTSD = post-traumatic stress disorder.

[a] Unclear in blinding of outcome assessment; potential selective reporting; very few participants.

Contextual Information

In order to inform the GRADE process beyond a review of clinical effectiveness, a supplementary review was conducted. The review aimed to identify, evaluate, and synthesize evidence relating to cost-effectiveness, health equity and access, patient values and preferences, and implementation considerations of CPT for the treatment of PTSD in adult patients.

Contextual Questions

1. What is the evidence regarding the impact of CPT for the treatment of adults with PTSD on health equity and access?
2. What is the evidence regarding patient values and preferences as they relate to CPT for PTSD?
3. What are the implementation considerations regarding CPT for PTSD?
4. What is the cost-effectiveness of CPT for the treatment of adults with PTSD?

Methods

Selection Criteria and Methods

The systematic literature search conducted for the primary research question was used to identify information related to cost-effectiveness, health equity and access, patient values and preferences, and considerations for implementation of CPT.

In the first level of screening, titles and abstracts were reviewed independently by two reviewers, and the full texts of potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was conducted by a single reviewer based on the inclusion criteria presented in Table 6.

Table 6: Selection Criteria

Population	Adults diagnosed with PTSD
Intervention	Cognitive processing therapy (group or individual)
Comparator	Any active treatment, wait-list control, no treatment
Outcomes	Costs and resource requirements, cost-effectiveness, health equity and access,[a] patient values and preferences (e.g., satisfaction, experiences, beliefs), implementation considerations (e.g., training, policies and standards)
Study Designs	Health technology assessments, systematic reviews or meta-analyses, randomized controlled trials, non-randomized studies, surveys, program evaluations, qualitative studies, and economic evaluations.

PTSD = post-traumatic stress disorder.

[a] Factors such as ethnicity, gender, socioeconomic position, age, and disability can contribute to access to health care and effects on health. For the purpose of this report, health equity is the presence or absence of systematic disparities in one or more aspects of health (or in the social determinants of health) between groups who have different levels of underlying social advantage or disadvantage.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, were duplicate publications, did not present results, or if the study examined CPT and other interventions but did not present results for CPT separately. Additionally, one study[24] was excluded because it was the pilot study of a trial that was selected for inclusion.

Data Extraction and Critical Appraisal

One reviewer performed data extraction and critical appraisal. Data regarding the patient population, interventions, comparators, outcomes, and study design were extracted into a standardized electronic form. The same author also conducted the critical appraisal and risk of bias assessment. Risk of bias for randomized studies was performed using the Cochrane Risk of Bias tool.[10] The non-randomized, qualitative, and survey studies were not appraised using any specific quality assessment tool. Instead, common criteria for assessing the quality of these study designs were used to identify important strengths and limitations. For example, for all included studies, the congruence between the research questions and research design was assessed; for qualitative studies, the believability, credibility, dependability, and transferability of the results were assessed;[32] for survey studies, validity and reliability in the survey instrument(s), sampling procedures, and response rates were assessed; and for other non-randomized studies, other factors that could contribute to biased results, including confounding, were assessed.

Data Synthesis

Due to the anticipated heterogeneity of the results, a narrative synthesis was conducted. For each included study, a descriptive summary is provided, including study design and patient population alongside a summary of the main results as relevant to the research question. Where possible, results relating to the same topic are grouped and summarized together.

Results

Quantity of Research Available

The targeted literature search identified 517 citations, 480 of which were excluded as irrelevant based on title and abstract screening. The full texts of 37 citations were examined for potential inclusion. Thirteen studies were excluded following full-text review: one citation was excluded based on an irrelevant population,[33] three based on an irrelevant intervention,[34-36] four based on study design,[37-40] and five based on outcomes.[41-45] Twenty-four studies were included in the review: 11 were relevant to equity considerations,[14,46-55] two related to patient experiences,[56,57] 10 related to implementation,[58-67] and one related to costing.[29] Within the studies relevant to equity, studies relevant to six categories related to equity were identified: sex and gender;[52] race, ethnicity, language, and culture;[46-49] former military and childhood sexual trauma;[51] intimate partner violence (IPV);[50] resource-poor, low-literacy environments;[14] and access.[53-55] The study selection process is represented in a PRISMA flow diagram in Appendix 11.

Summary of Study and Patient Characteristics

Equity

Eleven studies relevant to equity considerations were reviewed. Four of the included studies were RCTs,[14,53-55] two of which were non-inferiority trials.[53,55] One study was a post-hoc analysis of a randomized trial[52] and one was a subgroup analysis of an RCT.[50] The seven remaining studies were all non-randomized: a cross-sectional study (using qualitative content and thematic analysis),[49] two cohort studies (one using general growth mixture modelling),[46,51] and two program evaluations.[47,48]

The CPT protocols followed the established “manual” length of treatment (12 sessions lasting 90 minutes) in seven studies and[14,46,49,50,53-55] allowed for additional or longer sessions at the discretion of the patients and clinicians in four studies.[47,48,51,52] The cognitive-only model was used in one study;[14] different CPT protocols were compared in one study;[50] and the remaining studies used the full CPT protocol. Five studies examined individual therapy;[46-50,52] two examined a combination of group and individual therapy;[14,51] and three studies compared in-person CPT to CPT delivered via videoconferencing telehealth.[53-55]

The number of patients ranged from 37[49] to 405[14] and eight of the study samples were composed solely or primarily of women.[14,47-52,55]

Additional detail related to the characteristics of the studies examining equity and access are included in Appendix 12, Table A4.

Patient Preference

Two studies[56,57] examined patient preferences and experiences with respect to PTSD treatment. Hundt et al.[56] was a qualitative, descriptive study examining the pathways to therapy and patient decision-making related to PTSD therapy and Schumm et al.[57] used a mixed methods approach to explore veteran satisfaction with a VA PTSD specialty clinic pre-treatment orientation group, and to test differences in treatment preference.

The Hundt[56] study interviewed 23 patients who were primarily men (n = 17) and the Schumm[57] study examined the preferences of 183 veterans who were also primarily men (n = 164). Additional detail is included in Appendix 12, Table A5.

Implementation

Four of the included studies examined factors related to implementing in-patient programs;[58-61] five examined factors related to implementing outpatient programs;[62-65,67] and one examined clinician factors related to providing CPT in both in-patient and outpatient settings.[66]

Cook and various colleagues conducted numerous evaluations of 38 VA sites offering residential programs for people with PTSD.[58-61] Data collection methods included interviews,[58-60] questionnaires,[59,61] observation,[58] and field notes.[58]

All five studies examining the implementation of CPT in outpatient PTSD clinics were conducted in the American VA setting.[62,63,65,67,68] Three were surveys,[62,64,67] one was an implementation evaluation,[63] and one was a cross-sectional, mixed methods study primarily reporting a retrospective database evaluation.[65] The studies reported information gathered from care providers,[62,64,67] clinic administrators,[63] and clinic administrative details.[65]

Garcia et al.[66] examined the relationship between burnout and the use of evidence-based therapies (EBTs) for the treatment of PTSD among Veterans Health Administration (VHA) mental health clinicians. Licensed and unlicensed, trained, non-prescribing VHA providers were surveyed regarding their provision of CPT and PE and factors related to burnout.

Additional information is included in Appendix 12, Table A6.

Costing

Meyers et al.[29] evaluated the one-year cost and health care service utilization associated with a course of PE or CPT in the VA medical centre setting. National VA database data for 70 veterans (75% of whom were men) who had completed PE or CPT for the treatment of PTSD were analyzed. Additional detail is available in Appendix 12, Table A7.

Summary of Critical Appraisal

A detailed summary of the strengths and limitations of each study are presented in Appendix 13.

Equity — Sex and Gender

Although Galovski et al.[52] included patients from a randomized trial, those included were from one group of the study; therefore, the principles of randomization do not extend to the subset. The strengths of the study were the use of validated scales to measure outcomes, similar demographic characteristics between the two groups, and the use of an intention-to-treat (ITT)

analysis. However, the sample was small and due to study exclusions, the results may not be generalizable to those who are on psychotropic medication or those with substance abuse. As many individuals with PTSD have concomitant substance abuse or are on psychotropic medication,[63] this is a major limitation.

Equity — Race, Ethnicity, Language, and Culture

Two of the included studies that examined race and ethnicity had limitations with respect to translating either outcome scales[47] or the CPT manual itself.[49] It is unclear whether the translated version of the PSS used in Schulz et al.[47] has been validated, and it was noted that the Spanish version of the CPT manual used in Marques et al.[49] was both difficult to use and may not be culturally appropriate. Strengths of the qualitative study examining Latino culture and CPT were that coding was audited, coding consensus was reached, and data saturation was achieved.[49]

One of the studies by Schulz et al.,[48] examining Bosnian refugees, contained limited data; thus, it was difficult to extract conclusions. However, a strength was that verbatim transcriptions were presented.[48] It seems likely that the patient population was similar to or the same as the Bosnian portion of the second Schulz study.[47] In the second study examining Bosnian refugees (which included a small number of Afghan refugees as well), limitations include the fact that adherence to the CPT protocol and manual was not enforced, and that the "no-interpreter" group received therapy sessions from the same clinician.[47] The clinician, or any strong or weak adherence to the manual, could have affected the results.

The growth mixture modelling study used validated measures, addressed missing data appropriately, and likely represented a real-world clinician mix (in that those providing therapy had various levels of training in CPT); however, fidelity to the treatment manual was not rated and therapy sessions were not recorded for review.[46]

Equity — Military and Childhood Sexual Trauma

The Walter et al.[51] study used outcome scales that were validated and had high completion rates, but may not have been adequately powered to detect a meaningful difference in all outcomes (particularly those included in this review, as they were secondary outcomes). Additionally, as it took place in an in-patient setting, other psychoeducational treatment did occur, so the treatment effects may not be due solely to CPT.

Equity — Intimate Partner Violence

Strengths of the Iverson et al.[50] study included an ITT analysis and the use of validated scales to measure outcomes of interest. Limitations included that the outcomes were reliant on self-reporting, and the sample size of those with recent IPV was small. Additionally, the participants in the sample were primarily low-income; therefore, the results may not generalize to other populations.

Resource-Poor, Low-Literacy Environment

The Bass et al.[14] RCT reported that randomization occurred, although it was unclear how the sequence was generated or if the allocation was adequately concealed. In this study, losses to follow-up were addressed appropriately, and there was no suggestion that selective outcome reporting occurred. A small number of Congolese villages were included; thus, there may have been bias in selecting participants (psychosocial assistants recruiting patients knew ahead of time whether they would be providing therapy or individual support), and the study authors stated that the outcome measure may not have been validated for PTSD that was comorbid with depression and anxiety. Due to the nature of the interventions, neither patients nor personnel

delivering the CPT were blinded; however, the outcome accessors were blinded to the intervention.

Equity — Access

The three studies related to access were RCTs comparing CPT delivered in person or via videoconferencing telehealth.[53-55] It was clear in two studies[53,54] that randomization occurred (and that the randomization process was adequate); however, it was unclear if the allocation was adequately concealed. Losses to follow-up were adequately addressed in two of the three studies,[53,54] and there was no suggestion that selective outcome reporting occurred in the three studies.[53-55] In the Maiertisch RCT,[53] discontinuation rates were too high to reach statistical power; however, the discontinuation rates were similar in each group.[53]

Due to the nature of the interventions, neither patients nor personnel delivering the CPT were blinded,[53-55] although in two of these studies, outcome assessors were blinded.[54,55] In the Morland 2014[54] study examining rural patients undergoing telehealth or in-person CPT, there was an observer in the room during the videoconference sessions to observe the technology. This may have influenced the sessions.

The Morland 2015 study[55] was poorly reported and it was unclear how randomization occurred, whether allocation was adequately concealed, and whether the outcome assessors were blinded to the intervention. The study was further limited by the fact that the main outcome measure was administered two weeks post-treatment. As this was measured by CAPS, which assesses symptoms over the previous 30 days, administering the scale two weeks after treatment does not accurately reflect therapy progress.

Patient Preference

Some strengths of Hundt et al.'s qualitative study examining patient preferences regarding choosing and initiating evidence-based treatment for PTSD included audio recording of interviews, ending recruitment when data saturation was reached (this was defined a priori), and reporting statements verbatim.[56] As the study setting was a VA PTSD clinic, the results may or may not be generalizable beyond the setting, as VA clinics are highly structured.

The mixed methods study used both quantitative and qualitative methods to answer the appropriate questions, resulting in a more complete picture of the outcomes.[57] However, Schumm et al.[69] did not include family members in their interviews, despite the fact that the study authors state that family members are often involved in decisions to seek treatment; and as the sample was primarily male, the results may not be applicable to women.

Implementation — In-Patient Clinics

One of the main strengths of the studies regarding the implementation of CPT in in-patient clinics is that they were all part of a "suite" of studies that examined many aspects of CPT in VA centres, using multiple methods.[58-61] Some strengths of these studies included the use of triangulation of the data,[61] the reporting of statements verbatim,[58] discussion of ratings until consensus was reached,[58] recording of interviews,[59,60] standardization of interviews,[59] standardization of coding,[60] the authors' search for deviant cases,[60] and the use of data analysis software.[59]

One of the primary limitations of the in-patient implementation studies is the setting: the VA in-patient clinic is quite standardized. Therefore, not only may the results not be transferrable to an outpatient setting, but they may also not transfer to a non-VA clinic in the United States.[58-61] Other limitations include the reliance on self-reporting (providers may be reluctant to report

negative aspects of their programs)[59,60] and lack of clarity regarding whether or not the outcome measures were validated.[60]

Implementation — Outpatient Clinics

Four of the studies examining the implementation of CPT in outpatient clinics took place in the American VA clinic setting.[62-65] As this setting is highly structured (and similar between clinics), it is unclear if results are generalizable to other settings. Two of the studies were relatively small (six clinics in the Watts study[65] and 128 care providers in the Finley study[62]), making it unclear if the results were generalizable or representative of the larger VA setting. The two surveys[62,64] had similar main limitations: the respondents self-selected, and the cross-sectional design does not allow for the identification of trends or for determining the direction of associations.

Strengths of the studies included assuring the anonymity of survey responses[62,67] and the independent coding of interviews; for the Hamblen study,[63] a strength was that the semi-structured interviews were re-examined holistically as well as coded, which provided further insights into program models.[63] The Raza study[64] had a relatively large sample size, with a diverse sample of clinicians interviewed, making it more likely to be applicable to other settings.

There was a low (< 35%) response rate to the survey in the Borah study.[67] Due to the lack of demographic information collected (to ensure anonymity), it was unclear if it was a representative sample of providers.

Implementation — In-Patient and Outpatient Clinics

The survey regarding clinician burnout[66] had some main limitations: the respondents self-selected, and the cross-sectional design does not allow for the identification of trends or for determining the direction of associations. The strengths included using validated outcome measures and taking measures to assure anonymity of responses.

Costing

The study that examined the potential cost-savings of CPT was not a full economic evaluation but rather a clinical study that included costing information.[29] Main strengths included a diverse clinical sample and the consideration of mental health, primary care, and emergency department costs. However, the sample was small, and non-medical costs, such as work absenteeism, were not included; thus, a full picture of the societal costs was not included. Additionally, as it examined a VA sample, it is unclear if findings are generalizable beyond the structured American VA setting.

Summary of Findings

Equity — Sex and Gender

Galovski et al. evaluated the treatment response trajectory for male (n = 22) and female (n = 47) survivors of interpersonal assault in a group of patients who were participants in one arm of a larger RCT. Men and women entered the study with similar levels of trauma, PTSD, and depression.[52] At study completion, there were no gender differences with respect to dropouts (eight men and 11 women; $P = 0.261$), the length of treatment (11.43 sessions for men and 10.58 sessions for women; $P = 0.55$), and treatment success. The authors concluded that CPT was likely equally amenable to both men and women, but that further study may be necessary regarding the treatment of male survivors of sexual trauma, because this population was underrepresented.

Equity — Race, Ethnicity, Language, and Culture

In an evaluation of the differences and similarities among Spanish-speaking Latino, English-speaking Latino, and non-Latino individuals with PTSD, authors examined a subset (those who

filled out their "stuck point" logs) of community mental health clients who were enrolled in a larger implementation trial for CPT.[49] Marques et al.[49] found that "stuck points" (defined as assimilated and over-accommodated beliefs) differed with respect to the groups; power- and control-related stuck points were more common among English- than Spanish-speaking Latinos, and non-Latinos were less likely than their Latino counterparts to self-blame when the abuse was perpetrated by family members. Religious beliefs were found to be important, particularly among Latino patients. Authors suggested that CPT providers should be mindful and curious about their clients' cultural and religious backgrounds, as understanding these can aid in identifying important stuck points during the CPT process, and may help to bridge cultural and environmental differences between therapist and client.

Two citations reported on efforts to adapt CPT for Bosnian refugees[48] or both Bosnian and Afghan refugees in the United States.[47] Materials were translated into Serbo–Croatian, but not into Farsi, and patients usually received treatment from an English-speaking care provider through an interpreter. CPT sessions were generally between 60 and 120 minutes.[47,48] Patients and providers reported that CPT was generally well adapted for both Bosnian[47,48] and Afghan patients.[47] The treatment was generally well received by Bosnian clients; the degree of acceptance was not reported for Afghan clients.[48] For both Bosnian and Afghan refugees, the CPT was effective both for patients who did and did not receive therapy through an interpreter and the authors indicated that treatment effect sizes were similar to CPT studies with non-translated or translator therapy (effect size from baseline using Hedge's *g* for small sample sizes: 2.6 in this study; the effect size ranges from 0.62 to 2.7 in non-translator studies).[47]

Schumm et al.[46] used a general growth mixture modelling model (a method that can be applied to test the existence of categorically distinct trajectories of change in outcomes over time) to examine the effect of certain variables on the outcomes and success of CPT treatment for PTSD. Modelling showed that among US military veterans with a diagnosis of PTSD, age, ethnicity, and having combat trauma affected the success of CPT. Those who were older, not Caucasian, and whose "worst trauma" was combat trauma tended to both enter and end treatment with worse PTSD symptoms, and CPT tended to have less of an effect on these patients. The authors highlighted that there are important patient characteristics that can influence the outcomes of CPT for PTSD.

Equity — Military and Childhood Sexual Trauma

Walter et al. conducted a cohort study of 110 female veterans who were admitted to a PTSD rehabilitation program.[51] CPT consisted of two group and two individual sessions per week for seven weeks, with additional individual sessions available as needed. Participants were those with military sexual trauma (MST) and those with both MST and childhood sexual trauma (CST). CPT effectively reduced the symptoms of PTSD in both groups; however, the authors suggested that the results should be replicated before making definitive conclusions.

Equity — Intimate Partner Violence

In a secondary analysis of an RCT examining CPT for the treatment of PTSD, Iverson et al.[50] examined 150 female patients who had or had not experienced IPV. Those who had experienced more recent IPV (n = 23) were less likely to begin treatment for PTSD than those who had experienced it further in the past (n = 48) or who had not experienced it at all (n = 79). Race was also a predictor: recent IPV and African-American race were independent predictors of failure to start treatment among women. However, IPV did not seem to influence whether or not CPT was successful. Authors suggested further research into how IPV influences PTSD treatment.

Equity — Resource-Poor, Low-Literacy Environment

In a randomized trial, Bass et al. examined adapted CPT (one individual session and 11 group sessions) versus individual support for female survivors of sexual violence in the Congo.[14] The CPT model used was the cognitive-only model because the authors found that it had similar efficacy to the full therapy. Sixteen study villages (402 individuals) were randomized to either CPT or individual support services. Participants in both groups (CPT n = 157; control n = 248) had improvements in PTSD symptoms, depression, and anxiety; however, those receiving CPT had more improvement ($P < 0.001$). The effects were maintained for six months. In the resource-poor, low-literacy environment with ongoing trauma, CPT was effective in reducing PTSD symptoms for women who participated.

Equity — Access

Three randomized trials examining the delivery of CPT via videoconference versus in-person treatment were identified.[40,53,55] In the two non-inferiority trials comparing CPT delivered via telemedicine or in person, PTSD symptoms were reduced from baseline regardless of treatment group, and the success of PTSD treatment delivered via telehealth was not found to be inferior to in-person treatment.[54,55] Additionally, there were no differences in dropout rates between groups, and no difference were reported in ratings of the therapeutic alliance in either study.[40,55]

In the trial comparing telemental health versus in-person delivery of CPT to veterans of the Iraq and Afghanistan conflict, there were a large number of dropouts (no difference between groups); thus, no definitive conclusions could be made. However, the results trended toward the equivalence of telehealth and in-person care for the reduction of PTSD symptoms and the strength of the therapeutic alliance.[53] Further detail is included in Appendix 14, Table A10.

Patient Preference

Two studies were identified examining patient preferences for and experiences with PTSD therapy, including barriers, facilitators, and satisfaction.[56,57]

In the Hundt et al.[56] study using qualitative interviews with PTSD patients who had completed at least eight sessions of PE or CPT, most patients were ambivalent about receiving EBT.[56] Authors found that the most common barriers to accessing EBT were anxiety avoidance, skepticism regarding the treatment rationale, and lack of knowledge about treatment. The most common facilitators were buying into the rationale of the treatment, believing that prior treatments had given them the skills to handle the EBT, prior knowledge of the therapy, specific therapist behaviours that encouraged the therapy, seeing treatment success in other veterans, and desperation for relief from symptoms. Mental health providers were able to provide the most knowledge regarding therapy options, but witnessing other veterans' success generally provided the final push toward EBT.

Using a mixed methods approach to explore veteran satisfaction with a VA PTSD specialty clinic and pre-treatment orientation group, Schumm et al. found that a mostly male sample of 183 veterans indicated a preference toward receiving a combination of medication and therapy.[57] Fifty-one per cent of participants endorsed CPT as their first choice for the therapy component of their treatment (compared with cognitive behavioural conjoint therapy: 20.4%; PE: 18.5%; PCT, nightmare resolution, or virtual reality exposure therapy: < 7%) and the orientation group was found to be a good strategy for introducing treatment options.

Implementation — Residential Programs

Cook and various colleagues conducted numerous evaluations of VA residential programs for PTSD.[58-61] Prior to being studied, VA psychologists, social workers, psychiatrists, and nurses with advanced degrees from 38 sites were trained in delivering both PE and CPT. Following the

introduction of training to the VA centres, program evaluations were conducted. Data collection as part of these evaluations included surveys[59,61] and qualitative interviews.[58-60] Barriers to the adoption of CPT were identified as:

- Insufficient time for training, or short training sessions provided to master the delivery of CPT[58]
- Long duration of time required for the delivery of CPT[58]
- Provider autonomy (due to the fact that it is a manualized treatment)[58]

Factors associated with successful implementation of CPT were identified as:

- Positive view of CPT by clinicians and directors[61]
- Provider belief in CPT (i.e., CPT having a robust research base; CPT's ability to be delivered in a group format; the belief that CPT maximized patient benefit)[60]
- Having a champion for CPT (i.e., a specific colleague or group of colleagues within a program or facility were often identified as contributing to successful implementation)[60]
- Having dedicated time and resources available to aid in the implementation of CPT (i.e., clinicians identified that the time to implement the procedures was important in allowing them to feel confident that they could deliver CPT effectively)[60]
- Having top-down buy-in for implementation of CPT — clinicians needed to feel supported by their directors in order to deliver the therapy effectively.[60,61]

In general, there was a relationship between increased implementation of CPT and increased level of provider training in CPT.[59] The first training in CPT occurred in 2007, and by 2010, almost 70% of VA programs had implemented CPT as either a full or partial protocol (examples of partial protocols include tailoring the number of sessions, adding or removing modules, adjusting the order of modules, or lengthening the number of sessions). Cook et al. noted that, as it generally takes an average of 17 years to implement knowledge generated by RCTs, they considered the implementation of CPT to be an "expedited transfer of knowledge from research to clinical service."[59]

Implementation — Outpatient Clinics

In addition to residential PTSD treatment, the US VA system also offers outpatient therapy. Five studies examining the implementation of CPT in outpatient PTSD clinics in the VA system were identified.[62-65,67] Data collection as part of these evaluations took the form of surveys,[62,64,67] semi-structured interviews,[63] and a retrospective database evaluation.[65]

CPT uptake and implementation was associated with:

- Having staff with a cognitive behavioural orientation[62]
- Perceived effectiveness of CPT (which was positively associated with adherence to the manual and the number of hours of delivery of CPT)[62]

Care providers were more likely to suggest CPT as an option for their patients if the client had high literacy (which also may have an impact on equity, not just implementation).[64] The delivery of evidence-based PTSD care was found to be quite low in patients who were newly diagnosed (authors speculated that VA had not yet had success in promoting evidence-based treatments).[65] Preparatory groups were found to improve readiness for PTSD treatment.[63]

In the Borah survey[67] of providers who had undergone multi-day training workshops regarding CPT or PE and of therapists who had subsequently seen patients with PTSD, 80.9% of CPT-trained and 70% of PE-trained therapists used the new therapy; however, "supportive therapy" was the most commonly used therapy. Challenges to providing CPT included the time required to provide the therapy, patient interest, and "other" (other reasons not provided). Suggested

supports to improve therapy uptake included a change in existing clinic structure (in order to provide more time for CPT provision), at-work training in CPT, and on-site supervision for CPT.[67]

Implementation — In-Patient and Outpatient Clinics

In a survey of both in-patient and outpatient providers who delivered CPT for PTSD within the VA system, the amount of time spent on CPT was not found to be associated with provider burnout.[66] This was considered an important finding due to the concern regarding exposure-based therapies having the potential to be associated with provider burnout (due to vicarious exposure).[66]

Costing

In a database review of health care costs in the one-year period following PE or CPT therapy in veterans, the estimated cost of providing CPT was US$2,082.42 per patient and the cost of providing PE was $2,267.58.[29] Although the results were not split, in the one year following completion of either PE or CPT, those EBT options were found to be associated with a significant reduction in mental health costs [$t(69) = 3.84$; $P < 0.001$] from $3,215.70 (SD = $2,710.50) to $1,860.00 (SD = $2,105.20) per patient. Veterans who completed either type of EBT reduced their utilization of mental health services by 32%. Primary care use was reduced (but not statistically significant); emergency department use remained the same. The authors concluded that compared with pre-treatment utilization and costs, the completion of PE and CPT for the treatment of PTSD could significantly reduce mental health service utilization and costs.

Discussion

Summary of Evidence

Ten RCTs and six observational studies with a total of 1,865 participants were included in this review. The “GRADE profile” table for each of the four comparisons was created based on available data. One additional RCT was identified in the final alert, and is summarized, but was not included in the GRADE analysis.

CPT compared with WL/UC

Based on moderate- to low-quality evidence, CPT may be more effective in improving PTSD symptoms as assessed by CAPS or a self-reported instrument such as PCL. The change in CAPS total severity score achieved with CPT exceeded the minimal clinically important difference, which is ≥ 15 points, at the end of treatment and at the longest follow-up, for CPT offered in both group and individual settings.[70] CPT also achieved the minimum threshold of a 10-point change in PCL score for a clinically meaningful improvement of PTSD symptoms, at end of treatment and at the longest follow-up in both treatment settings.[71] The beneficial effects of CPT were sustained at different time points of follow-up. Although formal testing for subgroup interactions was not conducted, it appeared that there was no difference in effectiveness between CPT provided in group or individual settings. Also, the effect of CPT on the improvement of PTSD symptoms appeared to be greater in the civilian population than in the military population, and was larger in RCTs than in observational studies.

Based on moderate- to low-quality evidence, CPT improved depression symptoms at end of treatment and at end of up to nine months’ follow-up. The change in BDI-II score achieved with CPT exceeded the MCID, which is estimated to be a 17.5% reduction in scores.[69] The change in BDI-II scores appeared to be similar between group and individual settings, higher in the civilian population than in the military population, and higher in RCTs than in observational studies.

Based on evidence of moderate quality, CPT also improved anxiety symptoms — a 25% decrease in STAI scores was reported at the end of treatment, and a 23% decrease was reported at up to six months' follow-up.

Based on moderate- to low-quality evidence, about 20% to 30% of participants dropped out of treatment. There was no difference between CPT and WL/UC in the proportion of patients who completed treatment and follow-up.

There was low-quality evidence that CPT improved QoL and remission rates.

CPT compared with PE

Based on very low-quality evidence, it was uncertain whether there was any difference between the effectiveness of CPT and PE in improving PTSD and depression symptoms, and in the number of participants who completed treatment.

CPT compared with PCT

Based on very low-quality evidence, it was uncertain whether there was any difference between the effectiveness of CPT and PCT in improving PTSD and depression symptoms. However, more patients completed treatment with PCT than with CPT.

CPT compared with MeST

Based on very low-quality evidence, it was uncertain whether there was any difference between the effectiveness of CPT and MeST in improving PTSD symptoms, depression symptoms, global functioning, and ability to retrieve specific memory.

CPT compared with DET

Both treatments produced similar reductions in PTSD symptoms and dropout rates. CPT performed better than DET on overall psychological functioning and trauma-related cognitions. The quality of the evidence was not assessed.

Twenty-four studies were included to address contextual questions related to the use of CPT for the treatment of PTSD; 11 were relevant to equity considerations,[14,46-55] two related to patient preference,[56,57] 10 related to implementation,[58-67] and one related to costing.[29]

Equity

Based on evidence from a small number of studies, CPT may have some effectiveness for treating some potentially vulnerable groups. It was found to be equally effective in both male and female survivors of IPV and potentially effective for women who have experienced military and CST. Women who have had recent experience with IPV seemed less likely to start CPT treatment; however, once they did start treatment, CPT seemed to be as effective for these women as it was for those who had not experienced IPV. CPT is likely also effective for those with lower income and social status.

Religious beliefs may be important in exploring ‘’stuck points” during CPT, and discussions of culture and religion may be helpful to the therapeutic alliance. Being older and not Caucasian may be associated with starting and ending CPT with worse PTSD symptoms. CPT has been shown to be effective both with and without a translator for refugees who have undergone trauma, and has been shown to be effective in low-resource settings that include patients with low literacy and who are experiencing ongoing trauma.

With respect to access, CPT delivered via telehealth was shown to be similar in effectiveness to in-person treatment.

The results in this review do not present a complete picture of the potential equity considerations that may be important to the delivery of CPT. For example, no literature was identified that examined the potential implications of sexual orientation or physical disability on the outcomes of CPT for the treatment of PTSD. Patients from other vulnerable groups may react in different ways to CPT. Furthermore, for many equity categories, only one study or a limited number of studies were identified; thus, the results should be interpreted with the limitations of this review in mind.

Patient Preference

Based on two studies, it is unclear whether CPT is a preferred treatment for patients. Patients may be ambivalent toward choosing a treatment, although seeing others succeed in treatment may be a predictor of choosing a treatment type (CPT included). One study did find that the majority (51%) of patients chose CPT as a first-choice therapy option in a mixed treatment (therapy plus medication) approach; patients indicated a preference for the mixed approach.

Implementation

It is unclear whether factors that contributed to barriers or to uptake of CPT adoption that were identified in the literature are transferrable to a setting other than the American VA system. However, contributors to uptake include clinician and provider confidence in their training on CPT, belief that CPT is evidence-based, and adequate time for both the implementation and provision of CPT, as it requires fairly lengthy sessions. Provider autonomy may be threatened due to the manualized nature of the therapy; thus, care should likely be taken in order to emphasize clinicians' ability to sway from CPT protocol if they deem it necessary.

Cost

Based on a single study, CPT may have the potential to decrease the utilization and cost of mental health services for patients with PTSD.

All results should be considered within the context of the limitations of this review.

Limitations

This review considered the evidence of both RCTs and observational studies to determine the effectiveness of CPT provided in group settings, in individual settings, or in a combination of the two. Several factors limit the generalizability of the review. Most studies included participants who were either civilians or military veterans. Participants were mostly outpatients. One study involved active duty soldiers with deployment-related trauma.[21] In this study, loss to follow-up was high (up to 50%), likely due to deployment or retirement from active duty.[21] For the types of trauma, all studies were limited to sexual assault and military-related traumatic events, and may not be generalizable to trauma from different causes, such as natural disasters or non-military service (e.g., firefighters, police officers, or paramedics). Most studies were from the US and the results may not be generalizable to other countries.

Blinding of outcome assessors was unclear in many studies. There are more studies comparing CPT with WL control or treatment as usual than comparing CPT with PE, PCT, or MeST. The overall quality of evidence of CPT compared with those active treatments was very low; therefore, the effectiveness of this group of therapies as compared with CPT is unclear. Many studies excluded participants with comorbidities, substance abuse, uncontrolled psychosis, or

who were unstable with medication therapy. Those populations may be more difficult to treat; therefore, the results of this review may have limited generalizability to these groups.

Although there are limited long-term follow-up data, current evidence suggests that the benefits of CPT could be maintained after treatment for up to 12 months. The effects of CPT were greater in RCTs than in observational studies. Therefore, there is limited understanding of whether the beneficial effects of CPT could still be observed when the treatment is applied to participants in the real world, where confounding factors are not controlled. The aim of evidence-based psychotherapy for PTSD is to reduce symptoms and improve functional ability and adaptive coping. Studies reported improvement in PTSD symptoms but — while this is not necessarily the goal of treatment — there is no clear evidence that patients no longer met the diagnostic threshold for PTSD after CPT treatment. One study reported the proportion of patients with probable PTSD after treatment, but did not report the number of people who were free of PTSD.[14] Most studies reported dropout rates that ranged from 20% to 30%, but the reasons for dropout were not clearly documented, suggesting that adverse effects, along with other factors, might be contributing to dropout. However, adverse effects were not reported in any study and, while available information on patient preferences suggests that many endorse CPT as their first choice of therapy, the tolerability of treatment remains uncertain.

The overall quality of evidence was moderate to low in the comparison between CPT and WL/UC. The quality of evidence was very low in the comparisons of CPT with PE, PCT, and MeST. Most studies had severe risk of bias associated with blinding of participants and therapists, since a placebo- or sham-controlled design is impossible in psychological therapy studies. We were unable to detect publication bias using a funnel plot due to the small number of studies. Despite a rigorous literature search, including hand-search and grey literature search (in addition to searches of main databases), the potential for missing studies cannot be ruled out. The term “CPT” might be masked by the more general term “CBT,” and such studies might be overlooked when screening titles and abstracts. However, two reviewers independently screened the search results for included studies, and the list of the included studies was reviewed by a clinical expert to ensure that all studies on CPT had been captured from the literature search. Finally, in this review, the grouping of WL or delayed treatment together with treatment as usual may not be accurate, because the latter could offer better therapeutic benefit than the former. However, patients in the WL group did periodically receive telephone contact and consultation, which might have some effect in psychological therapy.

There are various CPT protocols available to therapists; it remains unclear which components of CPT treatment have the greatest potential for PTSD symptom reduction. There is some evidence from dismantling studies[72] that have compared CPT with the individual cognitive and written account components. While all three groups showed an improvement in PTSD symptoms, there were some differences during the course of treatment, with the cognitive component reporting greater improvement than written accounts. While the current review is not intended to address the question of effectiveness of individual components of treatment, this may be of interest to clinicians wanting to focus on elements that may be more effective.

For questions related to equity, access, implementation, and costs, there are several limitations in the body of literature identified and reviewed, as well as the review itself.

None of the identified studies addressing these questions included Canadian patients in a Canadian setting. All but one study[14] examined PTSD treatment in the United States; and of the American studies, three were conducted outside of the VA context.[46-48] It is unclear how generalizable data from the American veterans’ health system is to the Canadian context,

although there was evidence suggesting that CPT is effective across types of trauma, gender, and ethnic origin. While the Congolese study setting[14] seems vastly different from a Canadian setting, it is possible that the results would generalize to Canadians with PTSD who had low literacy and/or were experiencing continued trauma while undergoing CPT.

A limited number of randomized studies were identified. While this is a limitation of the body of literature as a whole — in that it is unclear in most studies whether or not there were fundamental differences in the samples that could contribute to the results beyond the factor or intervention being studied — the more diverse, less rigidly controlled samples are likely more indicative of the real-world population with PTSD. Still, many of the studies excluded those with comorbid substance abuse disorders, which are common in those with PTSD.

In this review, a structured tool was not used to facilitate critical appraisal of non-randomized trials, qualitative studies, or surveys. Strengths and limitations are summarized based on common criteria used to assess study quality for these types of designs. Therefore, it is possible that some strengths and limitations were not identified.

Conclusions and Implications for Decision- or Policy-Making

Based on the moderate- to low-quality evidence identified in this review, CPT may be more effective than WL or UC in reducing the severity of PTSD, depression, and anxiety symptoms in adults. While most studies demonstrated a reduction in symptoms relative to WL/UC, they were found to be at risk of bias based on unclear allocation concealment, incomplete outcome data, and other potential biases, and there were some concerns about imprecision. Very low-quality evidence indicates that it is uncertain whether there is any difference between CPT and PE, CPT and PCT, or CPT and MeST. CPT may have some effectiveness for treating patients from potentially vulnerable groups, including individuals who have low literacy, live in low-resource environments, have experienced military sexual trauma, CST, or IPV, or are experiencing continued trauma while receiving CPT. Additionally, CPT delivered via telehealth is likely as effective as CPT delivered face to face. This is an important finding for the delivery of care to patients in rural and remote settings.

Well-designed trials including larger populations, appropriate methods of randomization, allocation concealment, blinding of outcome assessors, and long-term follow-up are needed. More studies should also be conducted to compare CPT with other active psychological treatments. Future studies should capture outcomes such as QoL, adverse events, remission, number of people discharged from treatment, and military personnel who could return to or are released from service. Further research should also explore the potential effectiveness of the combination of CPT with other psychological therapies or with medication. This is especially important considering the finding that patients may have a preference for a mixed treatment approach.

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Appendix 1: Literature Search Strategy

OVERVIEW	
Interface:	Ovid
Databases:	EBM Reviews — Cochrane Central Register of Controlled Trials July 2015 Embase 1974 to 2015 August 27 Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations Ovid MEDLINE(R) Daily Ovid MEDLINE(R) 1946 to Present PsycINFO 1806 to August Week 4 2015 **Note:** Subject headings have been customized for each database. Duplicates between databases were removed in Ovid.
Date of Search:	August 28, 2015
Alerts:	Monthly search updates began August 28, 2015 and ran until February 11, 2016
Study Types:	No methodological filters were used to limit search results
Limits:	No date limit English language only

SYNTAX GUIDE	
*	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
ADJ#	Adjacency within # number of words (in any order)
.ti	Title
.ab	Abstract
.kw	Author keyword (Embase)
.id	Key concepts (PsycInfo)
.pt	Publication type

MULTI-DATABASE STRATEGY	
#	**Searches**
1	(Cognit* adj3 Process* adj3 Therap*).ti,ab,kw,id.
2	1 not conference abstract.pt.
3	remove duplicates from 2
4	limit 3 to english language

OTHER DATABASES		
PubMed	A limited PubMed search was performed to capture records not found in MEDLINE. Same MeSH, keywords, limits, and study types used as per MEDLINE search, with appropriate syntax used.	
Cochrane Library Issue 9, 2015	Same MeSH, keywords, and date limits used as per MEDLINE search, excluding study types and Human restrictions. Syntax adjusted for Cochrane Library databases.	

Grey Literature

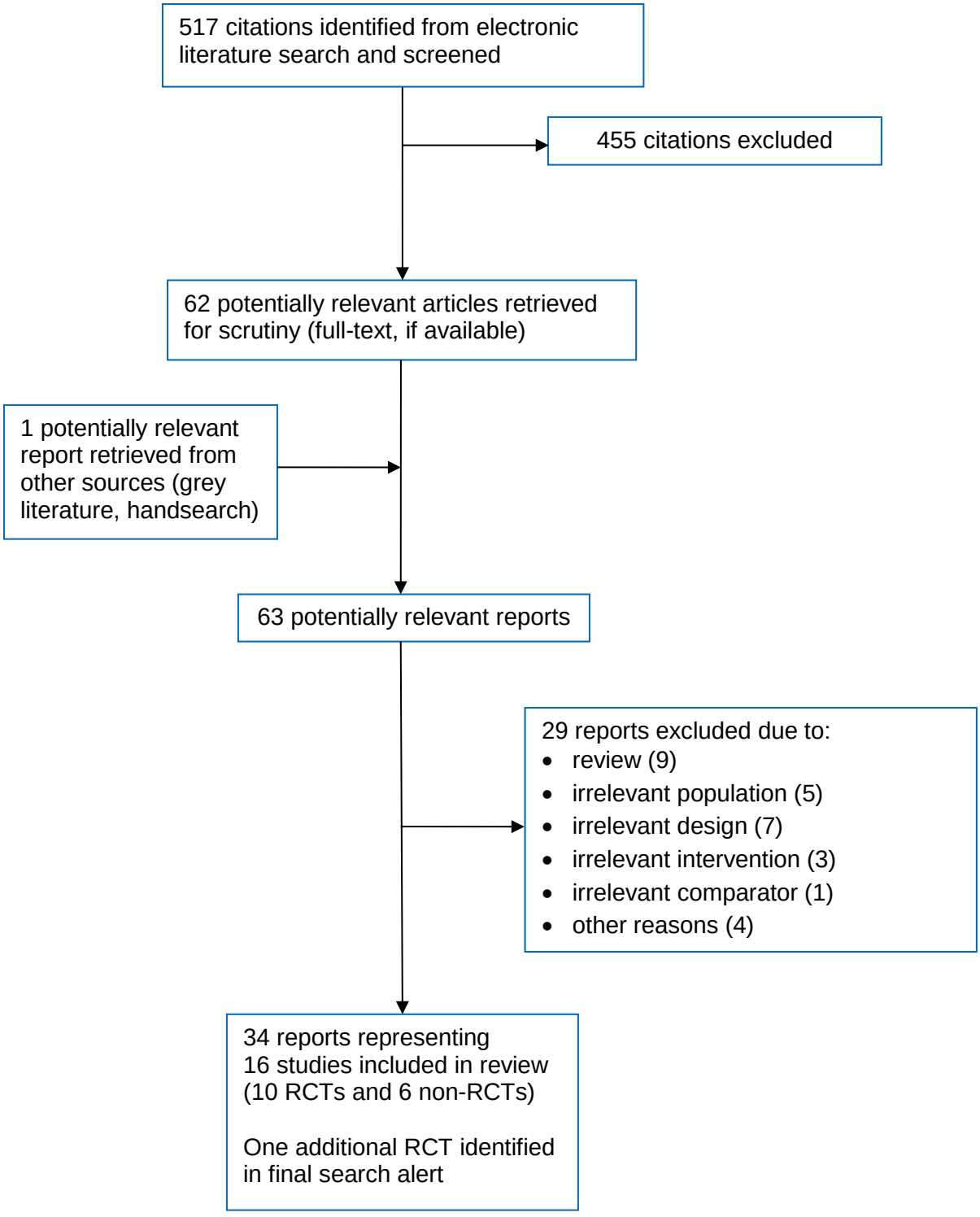
Dates for Search:	August 2015
Keywords:	Included terms for cognitive processing therapy
Limits:	English language only

Relevant websites from the following sections of the CADTH grey literature checklist, "Grey matters: a practical tool for searching health-related grey literature" (https://www.cadth.ca/grey-matters) were searched:

- Background
- Clinical Practice Guidelines
- Clinical Trial Listing
- Databases (free)
- Health Economics
- Health Technology Assessment Agencies
- Internet Search
- Miscellaneous: Mental health
- Open Access Journals
- Statistics and/or Prevalences.

Organizations: Canadian Psychiatric Association, Canadian Academy of Geriatric Psychiatry

Appendix 2: Selection of Included Studies



RCT = randomized controlled trial.

Appendix 3: List of Included Studies

Randomized Controlled Trials

1. Bass JK, Annan J, McIvor MS, Kaysen D, Griffiths S, Cetinoglu T, et al. Controlled trial of psychotherapy for Congolese survivors of sexual violence. N Engl J Med. 2013 Jun 6;368(23):2182-91.

   Related articles:

   Hall BJ, Bolton PA, Annan J, Kaysen D, Robinette K, Cetinoglu T, et al. The effect of cognitive therapy on structural social capital: results from a randomized controlled trial among sexual violence survivors in the Democratic Republic of the Congo. Am J Public Health. 2014 Sep;104(9):1680-6.

   Bass JK, Annan J, Murray SM, Kaysen D, Griffiths S, Cetinoglu T, et al. "Controlled trial of psychotherapy for Congolese survivors of sexual violence": Erratum. The New England Journal of Medicine. 2014;370(26):2547

2. Butollo W, Karl R, König J, Rosner R. A Randomized Controlled Clinical Trial of Dialogical Exposure Therapy versus Cognitive Processing Therapy for Adult Outpatients Suffering from PTSD after Type I Trauma in Adulthood. Psychother Psychosom. 2016;85(1):16-26.

3. Chard KM. An evaluation of cognitive processing therapy for the treatment of posttraumatic stress disorder related to childhood sexual abuse. J Consult Clin Psychol. 2005 Oct;73(5):965-71.

   Related articles:

   Owens GP, Pike JL, Chard KM. Treatment effects of cognitive processing therapy on cognitive distortions of female child sexual abuse survivors. Behav Ther. 2001;32(3):413-24.

4. Forbes D, Lloyd D, Nixon RD, Elliott P, Varker T, Perry D, et al. A multisite randomized controlled effectiveness trial of cognitive processing therapy for military-related posttraumatic stress disorder. J Anxiety Disord. 2012 Apr;26(3):442-52.

   Related articles:

   Lloyd D, Nixon RD, Varker T, Elliott P, Perry D, Bryant RA, et al. Comorbidity in the prediction of cognitive processing therapy treatment outcomes for combat-related posttraumatic stress disorder. J Anxiety Disord. 2014 Mar;28(2):237-40.

5. Galovski TE, Blain LM, Mott JM, Elwood L, Houle T. Manualized therapy for PTSD: flexing the structure of cognitive processing therapy. J Consult Clin Psychol. 2012 Dec;80(6):968-81.

6. Holliday R, Link-Malcolm J, Morris EE, Suris A. Effects of cognitive processing therapy on PTSD-related negative cognitions in veterans with military sexual trauma. Mil Med. 2014 Oct;179(10):1077-82.

7. Maxwell K, Callahan JL, Holtz P, Janis BM, Gerber MM, Connor DR. Comparative study of group treatments for posttraumatic stress disorder. Psychotherapy (Chic). 2015 Sep 21.

8. Monson CM, Schnurr PP, Resick PA, Friedman MJ, Young-Xu Y, Stevens SP. Cognitive processing therapy for veterans with military-related posttraumatic stress disorder. J Consult Clin Psychol. 2006 Oct;74(5):898-907.

   Related articles:

   Monson CM, Macdonald A, Vorstenbosch V, Shnaider P, Goldstein ES, Ferrier-Auerbach AG, et al. Changes in social adjustment with cognitive processing therapy: effects of treatment and association with PTSD symptom change. J Trauma Stress. 2012 Oct;25(5):519-26.

   Macdonald A, Monson CM, Doron-Lamarca S, Resick PA, Palfai TP. Identifying patterns of symptom change during a randomized controlled trial of cognitive processing therapy for military-related posttraumatic stress disorder. J Trauma Stress. 2011 Jun;24(3):268-76.

Price JL, MacDonald HZ, Adair KC, Koerner N, Monson CM. Changing beliefs about trauma: a qualitative study of cognitive processing therapy. Behav Cogn Psychother. 2014 Dec 16;1-12.

9. Resick PA, Nishith P, Weaver TL, Astin MC, Feuer CA. A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. J Consult Clin Psychol. 2002 Aug;70(4):867-79.

   Related articles:

   Gutner CA, Casement MD, Stavitsky GK, Resick PA. Change in sleep symptoms across cognitive processing therapy and prolonged exposure: a longitudinal perspective. Behav Res Ther. 2013 Dec;51(12):817-22.

   Gradus JL, Suvak MK, Wisco BE, Marx BP, Resick PA. Treatment of posttraumatic stress disorder reduces suicidal ideation. Depress Anxiety. 2013 Oct;30(10):1046-53.

   Nishith P, Nixon RD, Resick PA. Resolution of trauma-related guilt following treatment of PTSD in female rape victims: a result of cognitive processing therapy targeting comorbid depression? J Affect Disord. 2005 Jun;86(2-3):259-65.

   Resick PA, Nishith P, Griffin MG. How well does cognitive-behavioral therapy treat symptoms of complex PTSD? An examination of child sexual abuse survivors within a clinical trial. CNS Spectr. 2003;8(5):351-5.

   Nishith P, Resick PA, Griffin MG. Pattern of change in prolonged exposure and cognitive-processing therapy for female rape victims with posttraumatic stress disorder. J Consult Clin Psychol. 2002 Aug;70(4):880-6.

   Wachen JS, Jimenez S, Smith K, Resick PA. Long-term functional outcomes of women receiving cognitive processing therapy and prolonged exposure. Psychol Trauma. 2014;6(Suppl 1):S58-S65.

   Gallagher MW, Resick PA. mechanisms of change in cognitive processing therapy and prolonged exposure therapy for PTSD: preliminary evidence for the differential effects of hopelessness and habituation. Cognit Ther Res. 2012 Dec;36(6).

   Galovski TE, Monson C, Bruce SE, Resick PA. Does cognitive-behavioral therapy for PTSD improve perceived health and sleep impairment? J Trauma Stress. 2009 Jun;22(3):197-204.

   Resick PA, Williams LF, Suvak MK, Monson CM, Gradus JL. Long-term outcomes of cognitive-behavioral treatments for posttraumatic stress disorder among female rape survivors. J Consult Clin Psychol. 2012 Apr;80(2):201-10.

   Rizvi SL, Vogt DS, Resick PA. Cognitive and affective predictors of treatment outcome in cognitive processing therapy and prolonged exposure for posttraumatic stress disorder. Behav Res Ther. 2009 Sep;47(9):737-43.

   Lester K, Resick PA, Young-Xu Y, Artz C. Impact of race on early treatment termination and outcomes in posttraumatic stress disorder treatment. J Consult Clin Psychol. 2010 Aug;78(4):480-9.

10. Resick PA, Wachen JS, Mintz J, Young-McCaughan S, Roache JD, Borah AM, et al. A randomized clinical trial of group cognitive processing therapy compared with group present-centered therapy for PTSD among active duty military personnel. J Consult Clin Psychol. 2015 May 4.

11. Suris A, Link-Malcolm J, Chard K, Ahn C, North C. A randomized clinical trial of cognitive processing therapy for veterans with PTSD related to military sexual trauma. J Trauma Stress. 2013 Feb;26(1):28-37.

Comparative Non-randomized Studies

1. Alvarez J, McLean C, Harris AH, Rosen CS, Ruzek JI, Kimerling R. The comparative effectiveness of cognitive processing therapy for male veterans treated in a VHA posttraumatic stress disorder residential rehabilitation program. J Consult Clin Psychol. 2011 Oct;79(5):590-9.
2. Graca JJ, Palmer GA, Occhietti KE. Psychotherapeutic interventions for symptom reduction in veterans with PTSD: an observational study in a residential clinical setting. J Loss Trauma. 2014;19(6):558-67.
3. Jeffreys MD, Reinfeld C, Nair PV, Garcia HA, Mata-Galan E, Rentz TO. Evaluating treatment of posttraumatic stress disorder with cognitive processing therapy and prolonged exposure therapy in a VHA specialty clinic. J Anxiety Disord. 2014 Jan;28(1):108-14.
4. Resick PA, Schnicke MK. Cognitive processing therapy for sexual assault victims. J Consult Clin Psychol. 1992 Oct;60(5):748-56.
5. Williams W, Graham DP, McCurry K, Sanders A, Eiseman J, Chiu PH, et al. Group psychotherapy's impact on trust in veterans with PTSD: a pilot study. Bull Menninger Clin. 2014;78(4):335-48.
6. Meyers LL, Strom TQ, Leskela J, Thuras P, Kehle-Forbes SM, Curry KT. Service utilization following participation in cognitive processing therapy or prolonged exposure therapy for post-traumatic stress disorder. Mil Med. 2013 Jan;178(1):95-9.

Appendix 4: List of Excluded Studies

Table A1: Excluded Studies

Studies	Reason for exclusion
1. Basharpoor S, Narimani M, Gamari-Give H, Abolgasemi A, Molavi P. Effect of cognitive processing therapy and holographic reprocessing on reduction of posttraumatic cognitions in students exposed to trauma. Iran J Psychiatry. 2011; 6(4):138-44.	Children and adolescents
2. Bolton P, Bass JK, Zangana GA, Kamal T, Murray SM, Kaysen D, et al. A randomized controlled trial of mental health interventions for survivors of systematic violence in Kurdistan, Northern Iraq. BMC Psychiatry. 2014;14(1):360.	Patients diagnosed with depression, not PTSD
3. Chard KM, Ricksecker EG, Healy ET, Karlin BE, Resick PA. Dissemination and experience with cognitive processing therapy. J Rehabil Res Dev. 2012;49(5):667-78.	Irrelevant population and outcomes
4. Chard KM, Schumm JA, McIlvain SM, Bailey GW, Parkinson RB. Exploring the efficacy of a residential treatment program incorporating cognitive processing therapy-cognitive for veterans with PTSD and traumatic brain injury. J Trauma Stress. 2011 Jun;24(3):347-51.	Irrelevant design (single arm)
5. Christensen SS, Frostholm L, Ornbol E, Schroder A. Changes in illness perceptions mediated the effect of cognitive behavioural therapy in severe functional somatic syndromes. J Psychosom Res. 2015 Apr;78(4):363-70.	Irrelevant intervention (CBT, not CPT)
6. Dossa NI, Hatem M. Cognitive-behavioral therapy versus other PTSD psychotherapies as treatment for women victims of war-related violence: a systematic review. ScientificWorldJournal. 2012;2012:181847.	Review
7. Fortney JC, Pyne JM, Kimbrell TA, Hudson TJ, Robinson DE, Schneider R, et al. "Telemedicine-based collaborative care for posttraumatic stress disorder: a randomized clinical trial": Correction. JAMA Psychiatry. 2015;72(1):96.	Erratum (correction)
8. Haagen JF, Smid GE, Knipscheer JW, Kleber RJ. The efficacy of recommended treatments for veterans with PTSD: a metaregression analysis. Clin Psychol Rev. 2015 Aug;40:184-94.	Review
9. Hedman E, Mortberg E, Hesser H, Clark DM, Lekander M, Andersson E, et al. Mediators in psychological treatment of social anxiety disorder: individual cognitive therapy compared to cognitive behavioral group therapy. Behav Res Ther. 2013 Oct;51(10):696-705.	Irrelevant intervention
10. Hemmy AO, Dickstein BD, Chard KM. Do scores on the Beck Depression Inventory-II predict outcome in cognitive processing therapy? Psychol Trauma. 2015 May 25.	Irrelevant design (single-arm)
11. Hundt NE, Mott JM, Miles SR, Arney J, Cully JA, Stanley MA. Veterans' perspectives on initiating evidence-based psychotherapy for posttraumatic stress disorder. Psychol Trauma. 2015 Apr 27.	Irrelevant design (qualitative)
12. Iverson KM, King MW, Cunningham KC, Resick PA. Rape survivors' trauma-related beliefs before and after cognitive processing therapy: associations with PTSD and depression symptoms. Behav Res Ther. 2015 Mar;66:49-55.	Irrelevant design (one-arm)

Studies	Reason for exclusion
13. Jayawickreme N, Cahill SP, Riggs DS, Rauch SA, Resick PA, Rothbaum BO, et al. Primum non nocere (first do no harm): symptom worsening and improvement in female assault victims after prolonged exposure for PTSD. Depress Anxiety. 2014 May;31(5):412-9.	Using data from four previous studies
14. Jonas DE, Cusack K, Forneris CA, Wilkins TM, Sonis J, Middleton JC, et al. Psychological and pharmacological treatments for adults with posttraumatic stress disorder (PTSD). Rockville (MD): Agency for Healthcare Research and Quality (US); 2013 Apr. (AHRQ Comparative Effectiveness Reviews).	Review
15. Kehle-Forbes SM, Meis LA, Spoont MR, Polusny MA. Treatment initiation and dropout from prolonged exposure and cognitive processing therapy in a VA outpatient clinic. Psychol Trauma. 2015 Jun 29.	Irrelevant design
16. Lenz S, Bruijn B, Serman NS, Bailey L. Effectiveness of cognitive processing therapy for treating posttraumatic stress disorder. J Ment Health Couns. 2014;36(4):360-76.	Review
17. Mott JM, Mondragon S, Hundt NE, Beason-Smith M, Grady RH, Teng EJ. Characteristics of U.S. veterans who begin and complete prolonged exposure and cognitive processing therapy for PTSD. J Trauma Stress. 2014 Jun;27(3):265-73.	Irrelevant outcomes (look at characteristics)
18. Nishith P, Weaver TL, Resick PA, Uhlmansiek MH. General memory functioning at pre- and posttreatment in female rape victims with posttraumatic stress disorder. In: Williams LM, editor. Trauma & memory. Thousand Oaks (CA): Sage Publications, Inc; US; 1999. p. 47-55.	Irrelevant intervention (CPT and PE together)
19. Nixon RD. Cognitive processing therapy versus supportive counseling for acute stress disorder following assault: a randomized pilot trial. Behav Ther. 2012 Dec;43(4):825-36.	Patients diagnosed with acute stress disorders, not PTSD
20. Nixon RDV. Using cognitive processing therapy for assault victims with acute stress disorder. In: Einstein DA, editor. Innovations and advances in cognitive behaviour therapy. Bowen Hills, QLD, Australia: Australian Academic Press; Australia; 2007. p. 185-96.	Irrelevant population
21. Regehr C, Alaggia R, Dennis J, Pitts A, Saini M. Interventions to reduce distress in adult victims of rape and sexual violence: a systematic review. Res Soc Work Pract. 2013;23(3):257-65.	Review
22. Rothbaum BO, Meadows EA, Resick P, Foy DW. Cognitive-behavioral therapy. In: Foa EB, editor. Effective treatments for PTSD: Practice guidelines from the International Society for Traumatic Stress Studies. New York: Guilford Press; US; 2000. p. 60-83.	Review
23. Schnurr PP, Chard KM, Ruzek JI, Chow BK, Shih MC, Resick PA, et al. Design of VA Cooperative Study #591: CERV-PTSD, comparative effectiveness research in veterans with PTSD. Contemp Clin Trials. 2015 Mar;41:75-84.	Protocol of an RCT
24. Schulz PM, Resick PA, Huber LC, Griffin MG. The effectiveness of cognitive processing therapy for PTSD with refugees in a community setting. Cogn Behav Pract. 2006;13(4):322-31.	Irrelevant design (single-arm)
25. Sloan DM, Bovin MJ, Schnurr PP. Review of group treatment for PTSD. J Rehabil Res Dev. 2012;49(5):689-702.	Review

Studies	Reason for exclusion
26. Steenkamp MM, Litz BT, Hoge CW, Marmar CR. Psychotherapy for military-related PTSD: a review of randomized clinical trials. JAMA. 2015 Aug 4;314(5):489-500.	Review
27. Vickerman KA, Margolin G. Rape treatment outcome research: empirical findings and state of the literature. Clin Psychol Rev. 2009 Jul;29(5):431-48.	Review
28. Voelkel E, Pukay-Martin ND, Walter KH, Chard KM. Effectiveness of cognitive processing therapy for male and female U.S. veterans with and without military sexual trauma. J Trauma Stress. 2015 Jun;28(3):174-82.	Irrelevant design (one-arm)
29. Walter KH, Dickstein BD, Barnes SM, Chard KM. Comparing effectiveness of CPT to CPT-C among U.S. Veterans in an interdisciplinary residential PTSD/TBI treatment program. J Trauma Stress. 2014 Aug;27(4):438-45.	Irrelevant comparator

CBT = cognitive behavioural therapy; CPT = cognitive processing therapy; PE = prolonged exposure; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial.

Appendix 5: Characteristics of Included Studies

Table A2: Summary of Study Characteristics

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Reported Outcomes (Outcome Measures)
RCT									
Bass et al. 2013, Democratic Republic of Congo[14]	Local psychosocial assistant offices	405 (100) / 270 (67) / 313 (77)	6	35.4 (18.3)	0/100	Sexual violence (civilian)	Not reported	CPT (G + I) IS	PTSD symptoms (HTQ), combined depression and anxiety symptoms (HSCL-25), functional impairment score, probable PTSD, probable depression or anxiety

Intervention Definitions:
1. CPT (G + I): 1 individual session (1 hour) plus 11 sessions with 6 to 8 women per group (2 hours each). In the group format, the cognitive-only model (without trauma narrative) was used. Outside the therapy, participants had access to psychosocial assistants if needed.

2. IS: Psychosocial assistants provided support services to individuals as needed, including economic, medical, and legal referrals.

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Reported Outcomes (Outcome Measures)
Chard 2005, USA[15]	Local mental health facilities	71 (100) / 55 (77) / not fully reported	3, 12 (no data from control group)	32.8 (8.9)	0/100	Childhood sexual abuse (civilian)	6.4 (2.8)	CPT-SA (G + I) WL/DT	PTSD symptoms (CAPS-SX, MPSS), depression (BDI-II), dissociation (DES-II)
Intervention Definitions: 1. CPT-SA (G + I): The treatment included 17 weeks of manual-based group and individual therapy, with 90-minute group sessions each week and 60-minute individual sessions for the first 9 weeks and the 17th week. 2. WL/DT: Telephone call (5 to 10 minutes) once a week was provided to participants to assess their current emotional state and to give support and brief counselling if there was a crisis. If a symptom was severe, participants were referred to immediate therapy and were included in the dropout list.									
Forbes et al., 2012, Australia[16]	Clinics	59 (100) / 47 (80) / 41 (69)	3	53.4 (19.3)	97/3	Military-related	Not reported	CPT (I) TAU	PTSD symptoms (CAPS, PCL, PTCI), depression (BDI-II), anxiety (STAI), anger (DAR7), alcohol use and abuse (AUDIT), relationships (ADAS), and quality of life (WHOQOL-BREF)

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Study (Author, Year, Country)
Intervention Definitions: 1. CPT (I): 12-session manualized treatment; 90 minutes for session 1 and 1 hour for sessions 2 to 12; all sessions were videotaped. 2. TAU: Depending the orientation of therapists, treatment could be psycho-education and supportive counselling, non-trauma-focused symptom management interventions, or CBT with element of exposure. TAU sessions were not video recorded for external validation.									
Galovski et al., 2012, USA[17]	Clinics	100 (100) / 74 (74) / 64 (64)	3	39.8 (11.7)	31/69	Sexual or physical assault (civilian)	3 months to 52.7 years (mean 228.8 months; SD = 191.7)	M-CPT (I) WL/DT	PTSD symptoms (CAPS, PDS), depression (BDI-II), guilt (TRGI), distress (TRGI), quality of life (QOLI, SF-36)
Intervention Definitions: 1. M-CPT (I): Treatment consisted of 18 sessions; the first 12 sessions were the same as those in the original CPT. Participants could complete treatment after session 4. Treatment was terminated when PDS ≤ 20 and BDI-II ≤ 18. 2. WL/DL: Symptoms of PTSD and depression were monitored daily through telephone calls; three phone interviews to assess PTSD symptom using CAPS; weekly completion of PDS and BDI-II. No cognitive therapy or other trauma-focused intervention was provided.									
Holliday et al., 2014, USA[18]	Clinics	121 (100) / 45 (37) / 45 (37)[a]	2, 6	41.9 (9.7)	24/76 (of n = 45 who completed treatment)	Military sexual trauma	Not reported	CPT (I) PCT	Trauma-related negative cognitions (PTCI) for PTSD symptoms

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Study (Author, Year, Country)
Intervention Definitions: 1. CPT (I): Not provided. 2. PCT: Not provided.									
Maxwell et al., 2015, USA[23]	Clinics	18 (100) / 16 (89) / 16 (89)	3	Not reported	19/81	Mixed (civilian)	Not reported	CPT (G) MeST	PTSD symptoms (MPSS), depression (BDI-II), overgeneral memory (AMT), global functioning (GAF)
Intervention Definitions: 1. CPT (G): 12 biweekly 90-minute sessions for 6 weeks. 2. MeST: Group treatment consisted of 6 weekly 90-minute sessions directed toward teaching individuals how to retrieve specific memories. It was first designed to treat depression.									
Monson et al., 2006, USA[19]	Medical centres	60 (100) / 51 (85) / 49 (82)	1	54.0 (6.3)	90/10	Military-related	Not reported	CPT (I) WL/DT	PTSD symptoms (CAPS, PCL), depression (BDI-II), anxiety (STAI)
Intervention Definitions: 1. CPT (I): Treatment consisted of 12 sessions, twice weekly for 6 weeks, and 1 month follow-up. 2. WL/DT: Treatment was delayed for 10 weeks. Details during waiting period were not provided.									

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Study (Author, Year, Country)
Resick et al., 2002, USA[20]	Clinics	171 (100) / 121 (71) / not reported	3, 9	32.0 (9.9)	0/100	Rape (civilian)	At least 3 months	CPT (I) PE MA	PTSD symptoms (CAPS, PSS), depression (BDI), guilt (TRGI)
Intervention Definitions: 1. CPT (I): 12 sessions, twice weekly for 6 weeks; total 13 hours. 2. PE: Twice weekly for a total of 13 hours of treatment completed within 6 weeks. Treatment consists of 4 components: education-rationale, breathing retraining, behavioural exposures, and imaginal exposures. 3. MA: Minimal attention for 6 weeks; participants were called every 2 weeks and were encouraged to call if they wanted to talk to a therapist. If any participant called more than once in the first 2 weeks or more than 4 times over the 6-week period and showed signs of suicidal ideation or intent, they were referred to hospitalization and considered as dropouts from MA condition.								
Resick et al., 2015, USA[21]	Military-based clinics	108 (100) / 86 (80) / 56 (52)	6, 12	32.1 (10.8)	93/7	Active duty soldiers with deployment-related trauma	Not reported	CPT-C (G) PCT	PTSD symptoms (PCL-S, PSS-I), depression (BDI-II)
Intervention Definitions: 1. CPT-C (G): 12 of 90-minute group sessions, twice weekly for 6 weeks. Cognitive therapy focused on why patients believe the index event occurred, how that event affected their beliefs, and how to differentiate thoughts from facts. 2. PCT: 12 of 90-minute group sessions, twice weekly for 6 weeks. Treatment focused on problem solving and PTSD symptom management, without including discussion of traumatic events.									
Suris et al., 2013, USA[22]	VA medical centre	129 (100) / 88 (68) / 72 (56)	2, 4, 6	46.1 (8.6)	15/85	Military sexual trauma	At least 3 months	CPT (I) PCT	PTSD symptoms (CAPS, PCL), depression (QIDS)

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Study (Author, Year, Country)
Intervention Definitions: 1. CPT (I): Manualized CBT, 12 sessions, once or twice weekly. 2. PCT: Manualized therapy for treatment of PTSD, without the cognitive behavioural or trauma-focused components of CPT; 12 sessions, once or twice weekly.									
Non-RCT									
Alvarez et al., 2011, USA[24]	Residential rehabilitation centre	Retrospective chart review (n = 197)	0	55.2 (9.2)	100/0	Military-related	Not reported	CPT (G) TAU	PTSD symptoms (PCL), depression (BDI), quality of life (WHOQOL-BREF), coping (Brief COPE), psychological distress (SCL-6)
Intervention Definitions: 1. CPT (G): 14 sessions; manualized, trauma-focused form of CBT for PTSD. The 2 initial sessions focused on gathering information. 2. TAU: 15-session, trauma-focused therapy, based on lifespan development model, incorporating elements of CBT. Treatment consisted of psycho-education about PTSD in the first session, and reviewing veteran's autobiography in a developmental context in most of the remaining sessions. One session of therapist-guided and in-session exposure to the trauma memory per individual was given in the final sessions.									
Graca et al., 2014, USA[25]	Residential clinic	Retrospective chart review (n = 51)	0	47.5 (12.9)	92/8	Mixed (military)	Not reported	CPT (G + I) EMDR + CPT (G) TGE	PTSD symptoms (PCL-C), depression (BDI-II), anxiety (BAI)

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Study (Author, Year, Country)
Intervention Definitions: 1. CPT (G + I): 20 CPT group sessions (1.5-hour group CPT, 3 to 4 times each week) and 11 individual CPT sessions. 2. EMDR + CPT (G): Treatment was not clearly described. 3. TGE: Treatment was not clearly described. TGE would be considered as usual care.									
Jeffreys et al., 2014, USA[26]	Veterans Health Administration clinic	Retrospective chart review (n = 263)	0	51.0 (13.9)	98/2	Military-related	Not reported	CPT (G + I) PE	PTSD symptoms (PCL)
Intervention Definitions: 1. CPT (G + I): 12 sessions (60-minute individual, 90-minute group therapy) focused on safety, trust, power and control, esteem, and intimacy. 2. PE: 10 to 15 weekly 90-minute sessions delivered in individual format, consisting of psycho-education, breathing retraining, in vivo exposures, and imaginal exposures.									
Meyers et al., 2013, USA[29]	VA medical centre	Cohort (n = 70)	0	48.1 (14.3)	75/25	Military-related	Not reported	CPT (G) PE	PTSD symptoms (PCL-M), depression (BDI-II)
Intervention Definitions: 1. CPT (G): Treatment was not clearly described. 2. PE: Treatment was not clearly described.									
Resick and Schnicke, 1992, USA[27]	Clinic	Cohort (n = 39)	3, 6 (no data from control group)	30.6 (7.3)	0/100	Sexual assault (civilian)	6.4 (6.9)	CPT (G) WL/DT	PTSD symptoms (SCL-90-R-PTSD subscales), depression (SCL-90-R-depression subscales)

Study (Author, Year, Country)	Setting	Participants At Pre-treatment/ Post-treatment/ Follow-Up, n (%)	Period of Follow-Up, Month(s)	Mean (SD) Age, Years	Male/Female, %	Type of Trauma	Mean (SD) Onset of Trauma, Years	Interventions	Study (Author, Year, Country)
Resick and Schnicke, 1992, USA[27]	Clinic	Cohort (n = 39)	3, 6 (no data from control group)	30.6 (7.3)	0/100	Sexual assault (civilian)	6.4 (6.9)	CPT (G) WL/DT	PTSD symptoms (SCL-90-R-PTSD subscales), depression (SCL-90-R-depression subscales)
Intervention Definitions: 1. CPT (G): 12 sessions, 90 minutes each. 2. WL/DT: At least 12 weeks of waiting, and eventually received treatment, but the related data were not included in the analyses.									
Williams et al., 2014, USA[28]	Clinic	Cohort (n = 21)	0	61.9 (1.8)	100/0	Military-related	Not reported	CPT (G) LTP Control	PTSD symptoms (PCL-M)
Intervention Definitions: 1. CPT (G): 12 sessions of supported, manualized CBT with elements of exposure treatment. The treatment focused on safety, trust, emotional power and control, self-esteem, and intimacy. 2. LTP: Treatment consisted of weekly 90-minute sessions of psychodynamic psychotherapy emphasizing improving relationships with other people and family members, learning how to cope and deal with PTSD symptoms, and learning how to regulate and contain emotions. 3. Control: Treatment with medication. Note: In our meta-analysis, LTP was considered as usual care, and data from the control group were excluded.									

ADAS = Abbreviated Dyadic Adjustment Scale; AMT = autobiographical memory task; AUDIT = Alcohol Use disorders Identification Test; BAI = Beck Anxiety Inventory; BDI-II = Beck Depression Inventory-II; CAPS = Clinician-Administered PTSD Scale; CAPS-SX = Clinician-Administered PTSD Scale for DSM-IV: One-Week Symptom Status Version; CBT = cognitive behavioural therapy; CPT = cognitive processing therapy; CPT-C = cognitive-only version of CPT; CPT-SA = CPT for sexual abuse survivors; DAR7 = Dimensions of Anger Reactions; DES-II = Dissociative Experiences Scale-II; G = group; EMDR = eye movement desensitization and reprocessing; GAF = Global Assessment of Functioning; HSCL-25 = Hopkins Symptom Checklist; HTQ = Harvard Trauma Questionnaire; I = individual; IS = individual support; LTP = long-term process; MA = minimal attention; M-CPT = modified CPT; MeST = memory specificity training; MPSS = Modified PTSD Symptom Scale; PBRS = Personal Beliefs and Reactions Scale; PCL = PTSD Checklist; PCL-C = PCL-civilian version; PCL-M = PCL-military version; PCL-S = stressor-specific version of PCL; PCT = present-centred therapy; PDS = Posttraumatic Stress Distress Scale; PE = prolonged exposure; PTCI = Posttraumatic Cognitions Inventory; PSS = PTSD Symptom Scale; PTSD = post-traumatic stress disorder; QIDS = Quick Inventory of Depressive Symptomatology; QOLI = Quality of Life Inventory; SCL-90-R = Symptom Checklist-90-Revised; SD = standard deviation; SF-36 = Medical Outcomes Study 36-Item Short Form Health Survey; STAI = State-Trait Anxiety Inventory; TAU = treatment as usual; TGE = trauma group exposure; TRGI = Trauma-Related Guilt Inventory; VA = Veterans Affairs; WAS = World Assumptions Scale; WL/DT = wait-list or delayed treatment; WHOQOL-BREF = World Health Organization Quality of Life scale, short form.

[a] Data from two therapists (n = 76 participants) were excluded due to irregularities.

Appendix 6: Quality Assessment of Non-Randomized Controlled Trials

Table A3: Summary of Critical Appraisal

First Author, Publication Year, Country, Design	Strengths	Limitations
Alvarez et al., 2011[24] USA Retrospective chart review (N = 197)	*Reporting* • The objective was clearly described • The main outcome measures were clearly described • The baseline characteristics of the patients included in the study were clearly described • Actual probability values were reported	*Reporting* • Important adverse events were not reported *External validity* • The participants might not be representative of the entire population from which they were recruited *Internal validity — bias* • It was unclear if there was an attempt to blind those measuring the main outcomes of the intervention • It was unclear if follow-up was the same for all participants *Internal validity — confounding (selection bias)* • Patients in different intervention groups were not recruited from the same population • Patients in different intervention groups were not recruited over the same period of time • Patients were not randomized to intervention groups *Power* • A power calculation was not reported for the primary outcome • The study did not have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%
Graca et al., 2014[25] USA Retrospective chart review (N = 51)	*Reporting* • The objective was clearly described • Actual probability values were reported	*Reporting* • The main outcome measures were not clearly described • The baseline characteristics of the patients included in the study were not clearly described • Important adverse events were not reported *External validity* • The participants might not be representative of the entire population from which they were recruited *Internal validity — bias* • It was unclear if there was an attempt to blind those measuring the main outcomes of the intervention

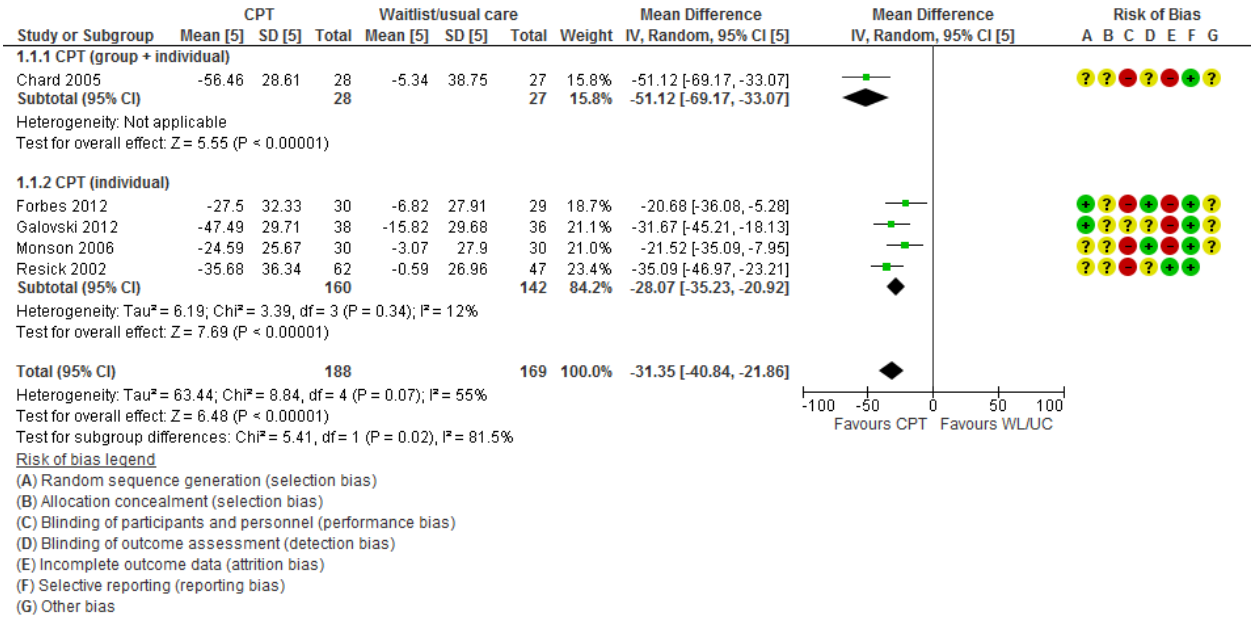
First Author, Publication Year, Country, Design	Strengths	Limitations
		• It was unclear if follow-up was the same for all participants *Internal validity — confounding (selection bias)* • It was unclear if patients in different intervention groups were recruited from the same population • It was unclear if patients in different intervention groups were not recruited over the same period of time • Patients were not randomized to intervention groups *Power* • A power calculation was not reported for the primary outcome • The study did not have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%
Jeffreys et al., 2014[26] USA Retrospective chart review (N = 263)	*Reporting* • The objective was clearly described • The main outcome measures were clearly described • The baseline characteristics of the patients included in the study were clearly described • Actual probability values were reported *External validity* • The participants might be representative of the entire population from which they were recruited *Internal validity — confounding (selection bias)* • Patients in different intervention groups were recruited from the same population • Patients in different intervention groups were recruited over the same period of time	*Reporting* • Important adverse events were not reported *Internal validity — bias* • It was unclear if there was an attempt to blind those measuring the main outcomes of the intervention • It was unclear if follow-up was the same for all participants *Internal validity — confounding (selection bias)* • Patients were not randomized to intervention groups *Power* • A power calculation was not reported for the primary outcome • The study did not have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%
Meyers et al., 2013[29] USA Cohort (N = 70)	*Reporting* • The objective was clearly described • Actual probability values were reported	*Reporting* • The main outcome measures were not clearly described • The baseline characteristics of the patients included in the study were not clearly described

First Author, Publication Year, Country, Design	Strengths	Limitations
		• Important adverse events were not reported *External validity* • The participants might not be representative of the entire population from which they were recruited *Internal validity — bias* • It was unclear if there was an attempt to blind those measuring the main outcomes of the intervention • It was unclear if follow-up was the same for all participants *Internal validity — confounding (selection bias)* • It was unclear if patients in different intervention groups were recruited from the same population • It was unclear if patients in different intervention groups were not recruited over the same period of time • Patients were not randomized to intervention groups *Power* • A power calculation was not reported for the primary outcome • The study did not have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%
Resick and Schnicke, 1992[27] USA Cohort (N = 39)	*Reporting* • The objective was clearly described • The main outcome measures were clearly described • Actual probability values were reported	*Reporting* • The baseline characteristics of the patients included in the study were not clearly described • Important adverse events were not reported *External validity* • The participants might not be representative of the entire population from which they were recruited *Internal validity — bias* • It was unclear if there was an attempt to blind those measuring the main outcomes of the intervention • It was unclear if follow-up was the same for all participants *Internal validity — confounding (selection bias)* • It was unclear if patients in different intervention groups were recruited from the same population

First Author, Publication Year, Country, Design	Strengths	Limitations
		• It was unclear if patients in different intervention groups were not recruited over the same period of time • Patients were not randomized to intervention groups *Power* • A power calculation was not reported for the primary outcome • The study did not have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%
Williams et al., 2014[28] USA Cohort (N = 21)	*Reporting* • The objective was clearly described • Actual probability values were reported	*Reporting* • The main outcome measures were not clearly described • The baseline characteristics of the patients included in the study were not clearly described • Important adverse events were not reported *External validity* • The participants might not be representative of the entire population from which they were recruited *Internal validity — bias* • It was unclear if there was an attempt to blind those measuring the main outcomes of the intervention • It was unclear if follow-up was the same for all participants *Internal validity — confounding (selection bias)* • It was unclear if patients in different intervention groups were recruited from the same population • It was unclear if patients in different intervention groups were not recruited over the same period of time • Patients were not randomized to intervention groups *Power* • A power calculation was not reported for the primary outcome • The study did not have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%

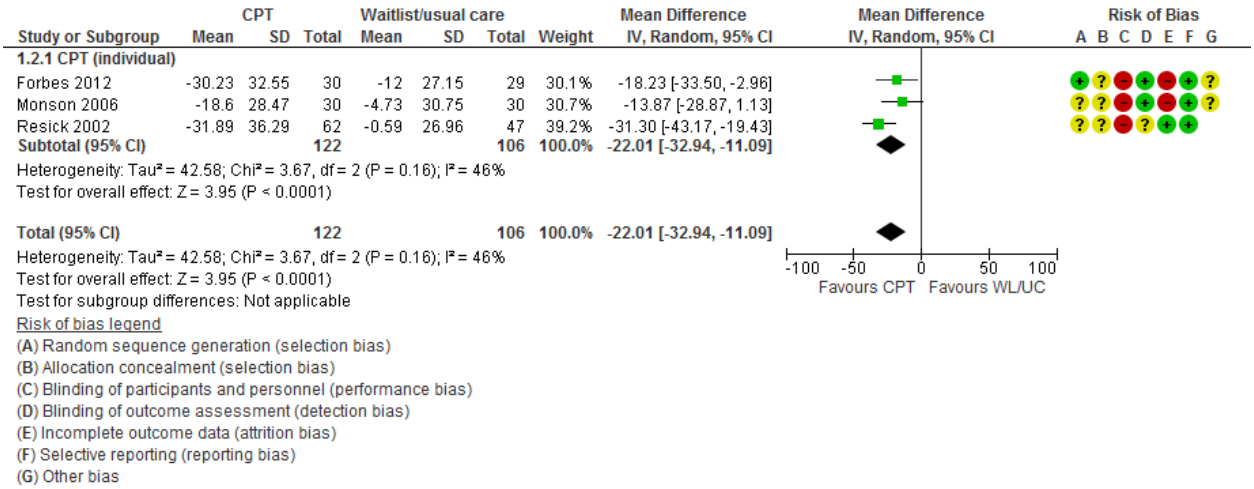
Appendix 7: Cognitive Processing Therapy Compared With Wait-List or Usual Care

Figure 1: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; at End of Treatment



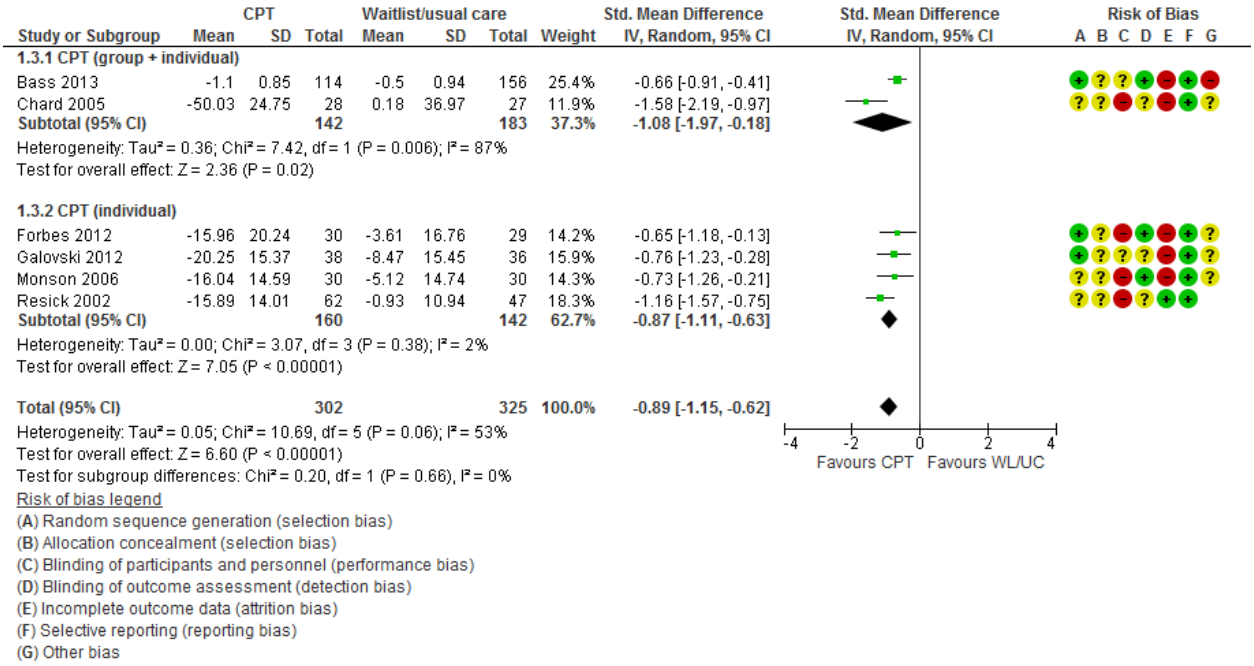
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 2: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; at Longest Follow-Up



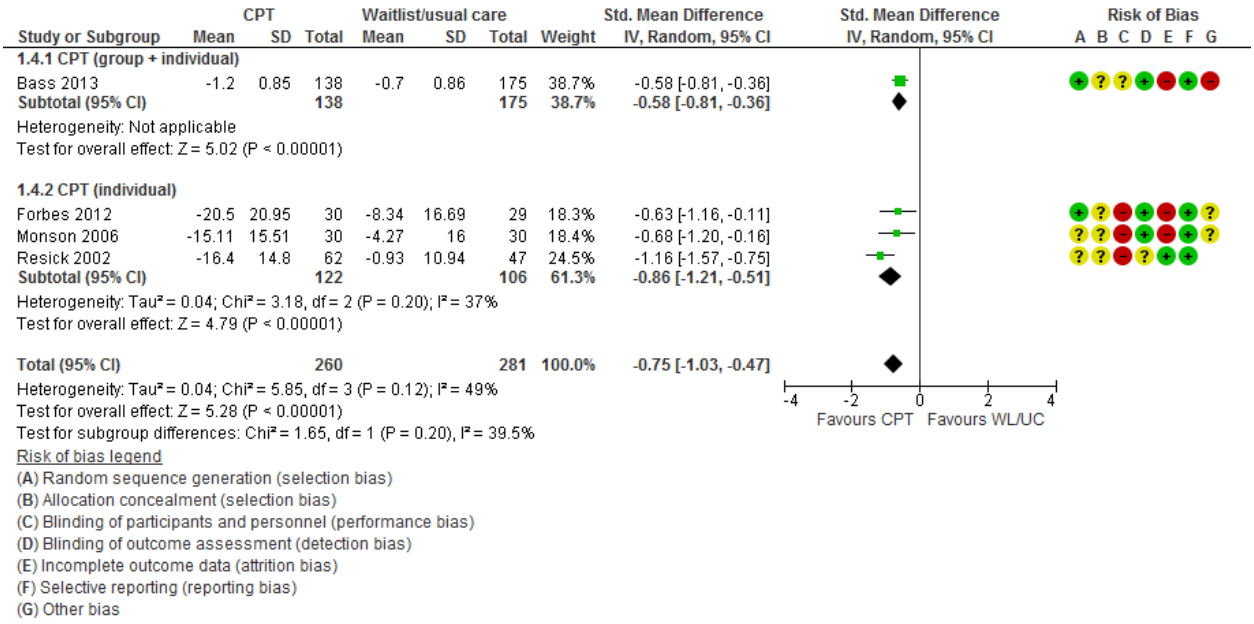
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 3: Change in Severity of Post-traumatic Stress Disorder – Self-Reported; Randomized Controlled Trials; at End of Treatment



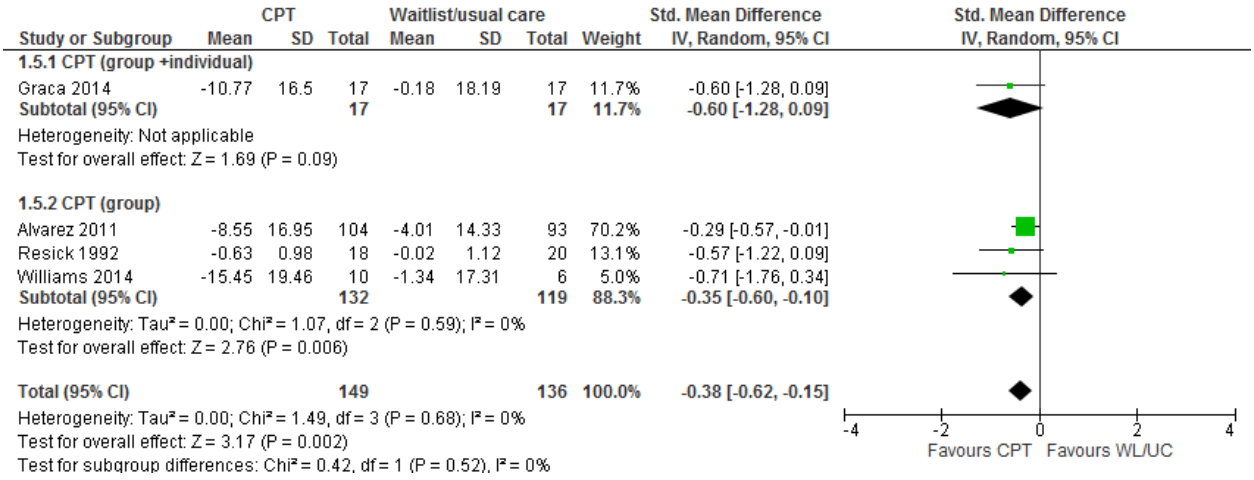
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 4: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



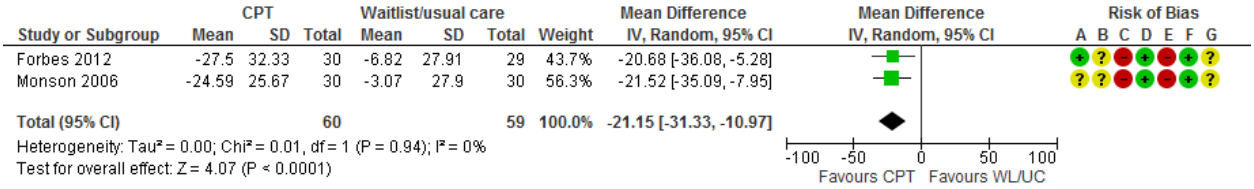
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 5: Change in Severity of Post-traumatic Stress Disorder – Self-Reported; Observational; at End of Treatment



CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

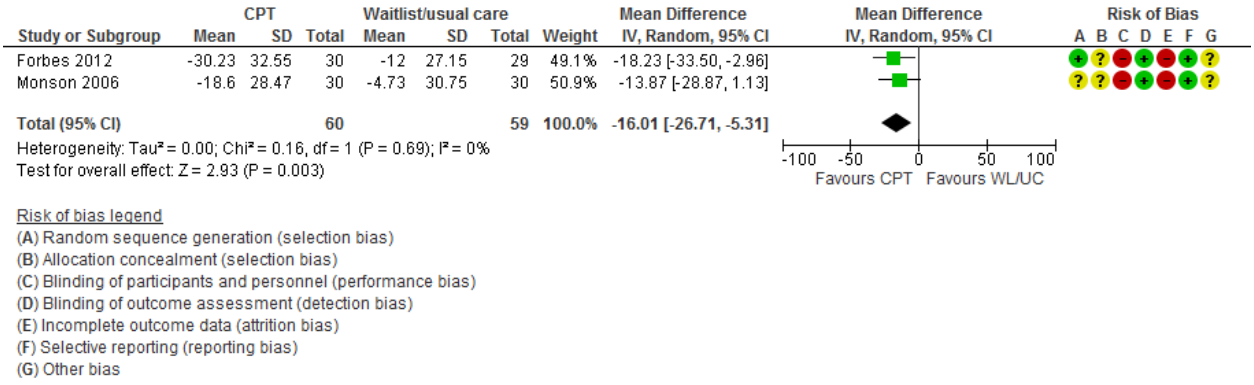
Figure 6: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; Military; at End of Treatment



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

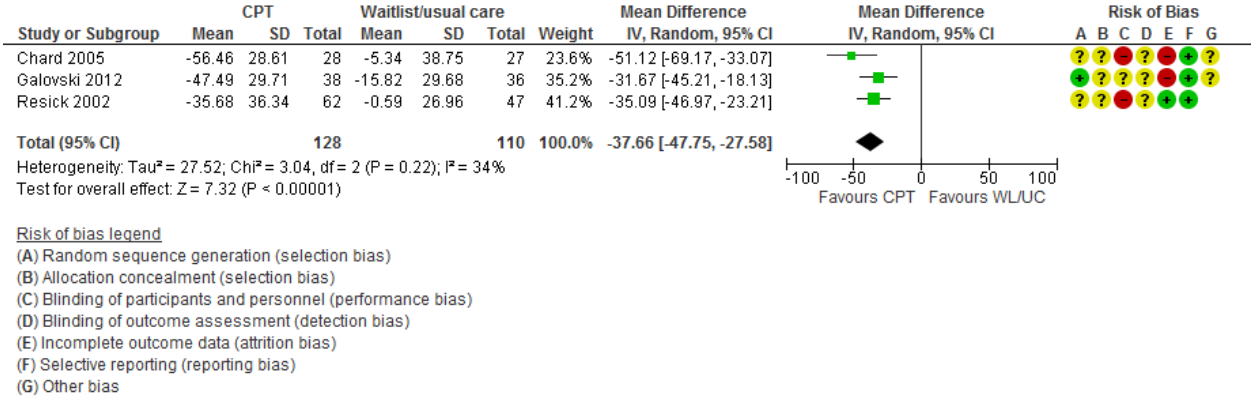
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 7: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; Military; at Longest Follow-Up



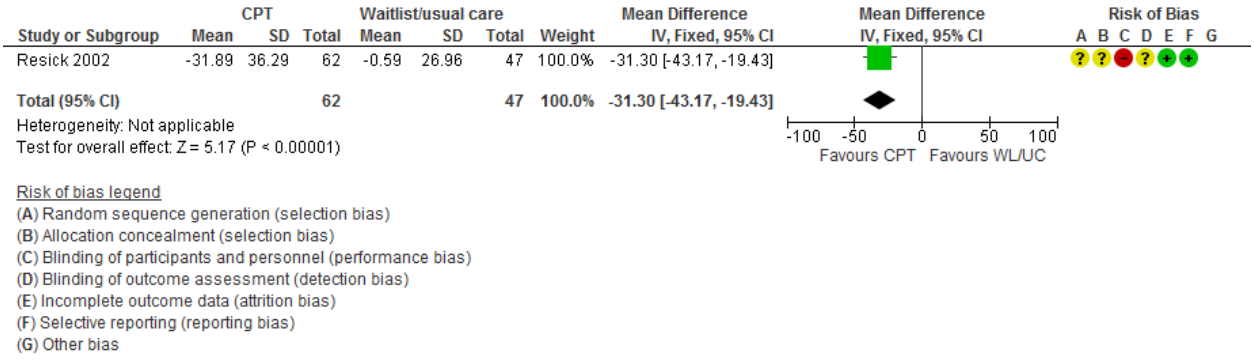
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 8: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; Civilian; at End of Treatment



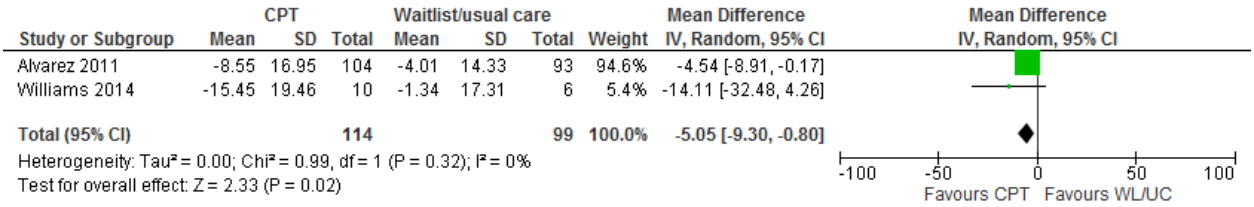
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 9: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; Civilian; at Longest Follow-Up



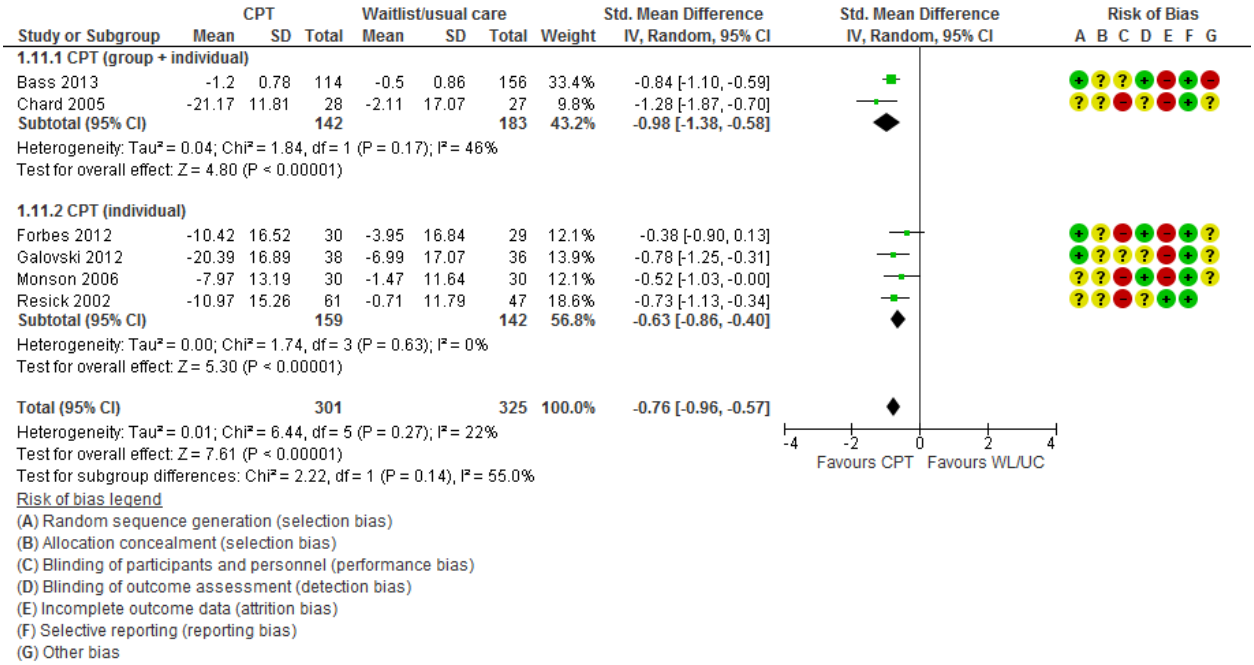
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 10: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Observational; Military; at End of Treatment



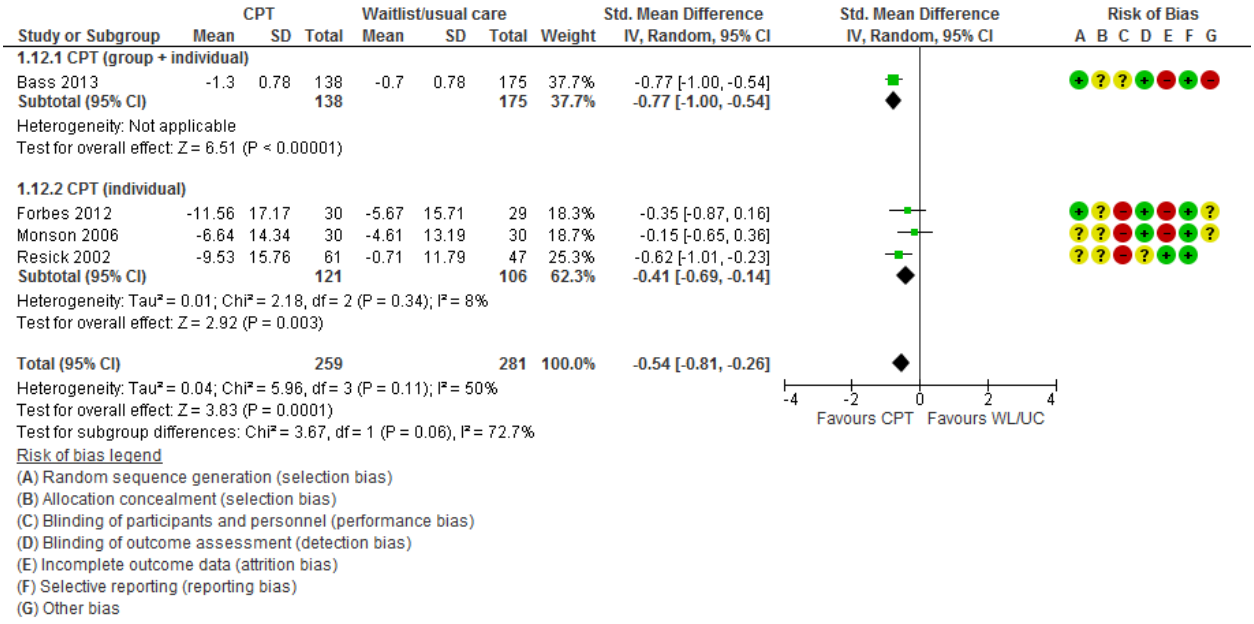
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 11: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at End of Treatment



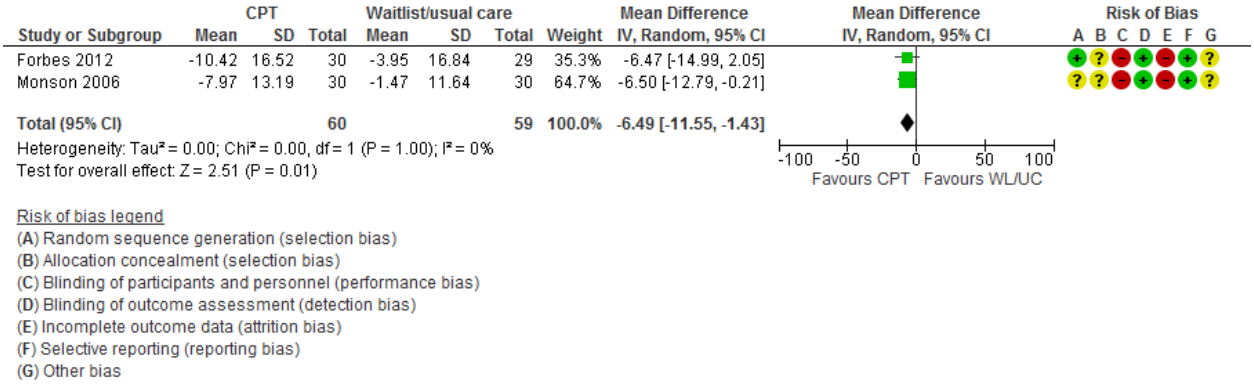
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 12: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



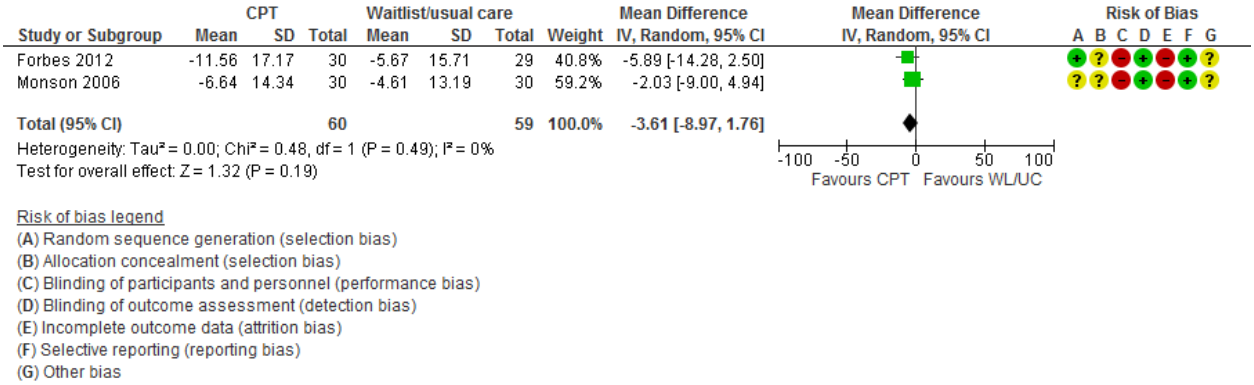
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 13: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; Military; at End of Treatment



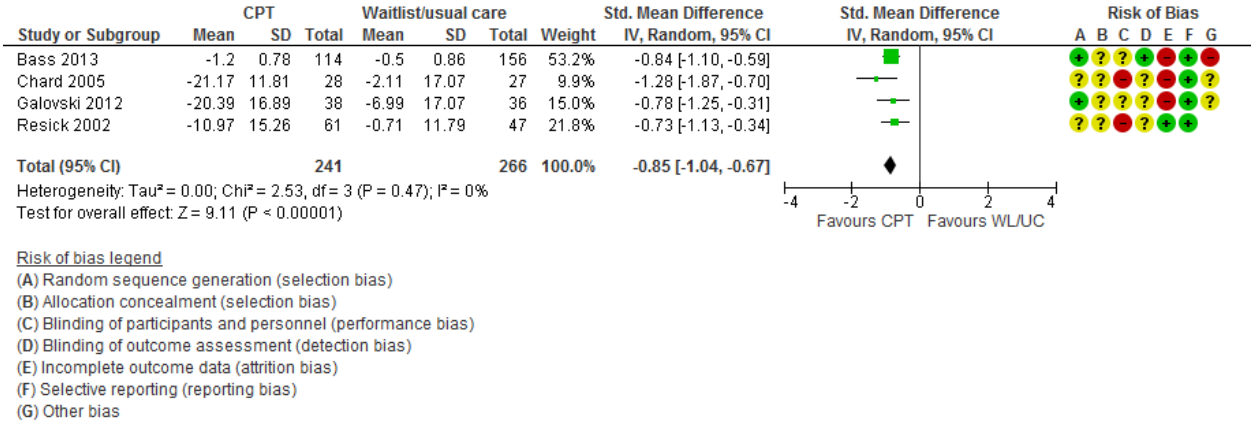
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 14: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; Military; at Longest Follow-Up



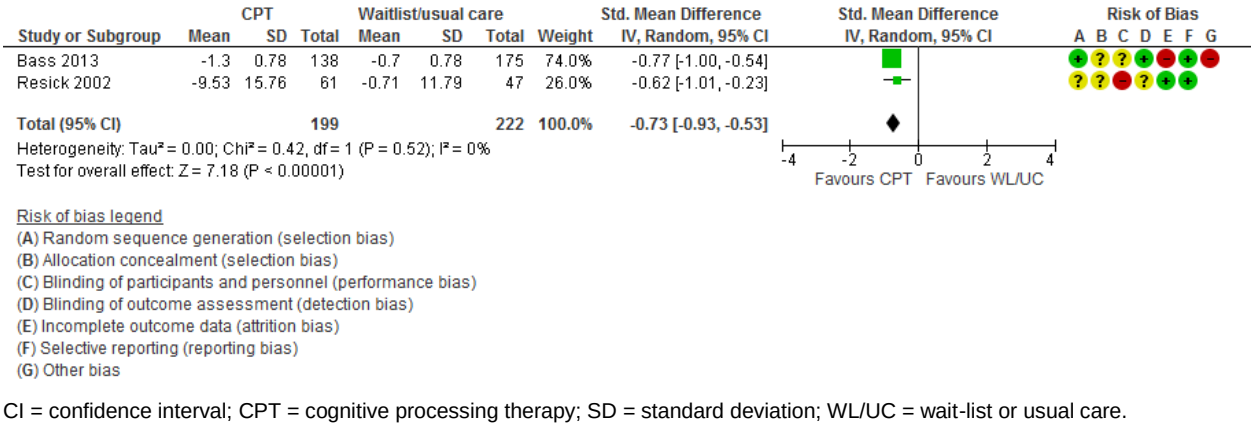
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 15: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; Civilian; at End of Treatment



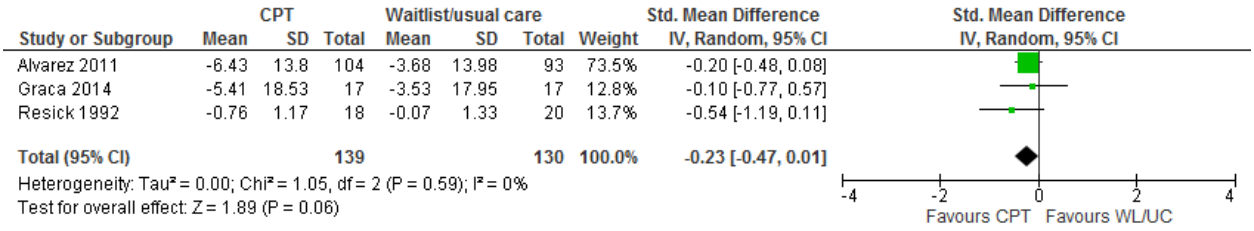
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 16: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; Civilian; at Longest Follow-Up



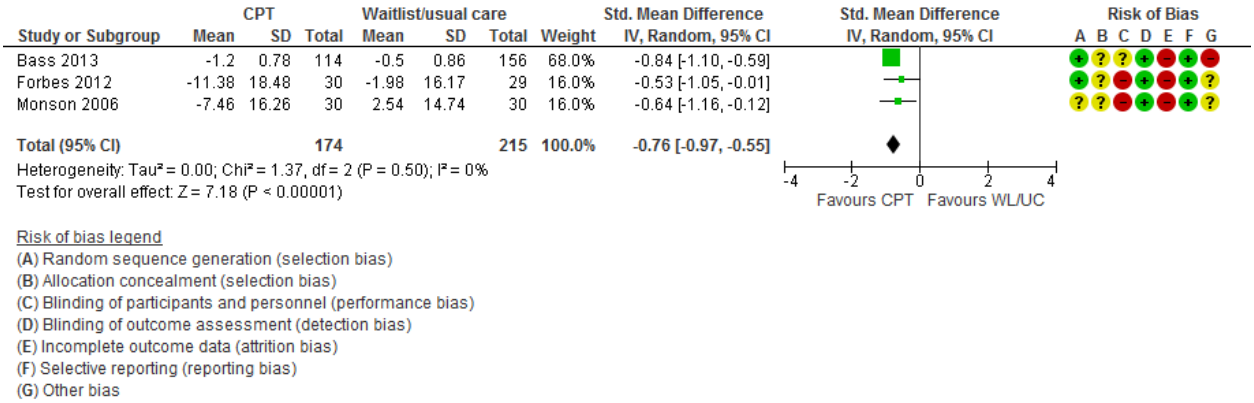
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 17: Change in Depression Symptoms — Self-Reported; Observational; at End of Treatment



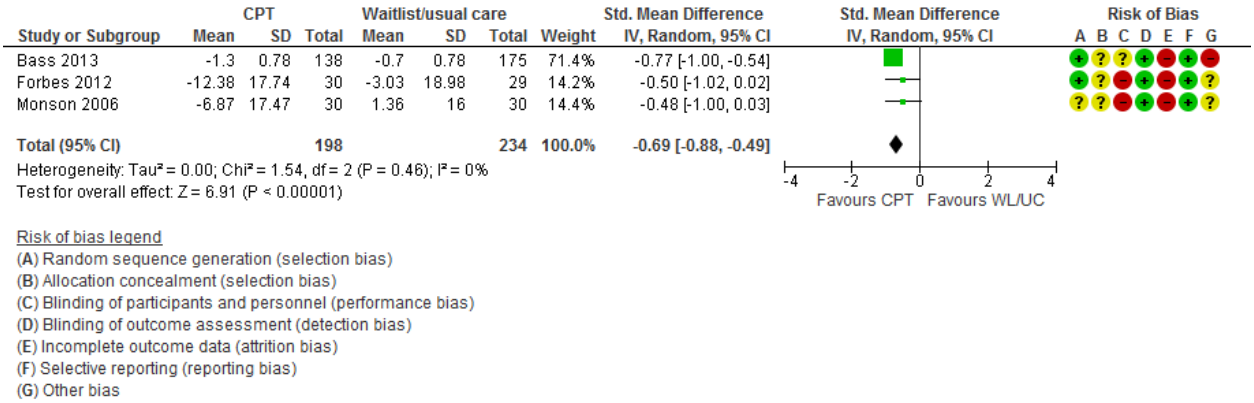
CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 18: Change in Anxiety Symptoms — Self-Reported; Randomized Controlled Trials; at End of Treatment



CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 19: Change in Anxiety Symptoms – Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

Figure 20: Patients Completed at End of Treatment

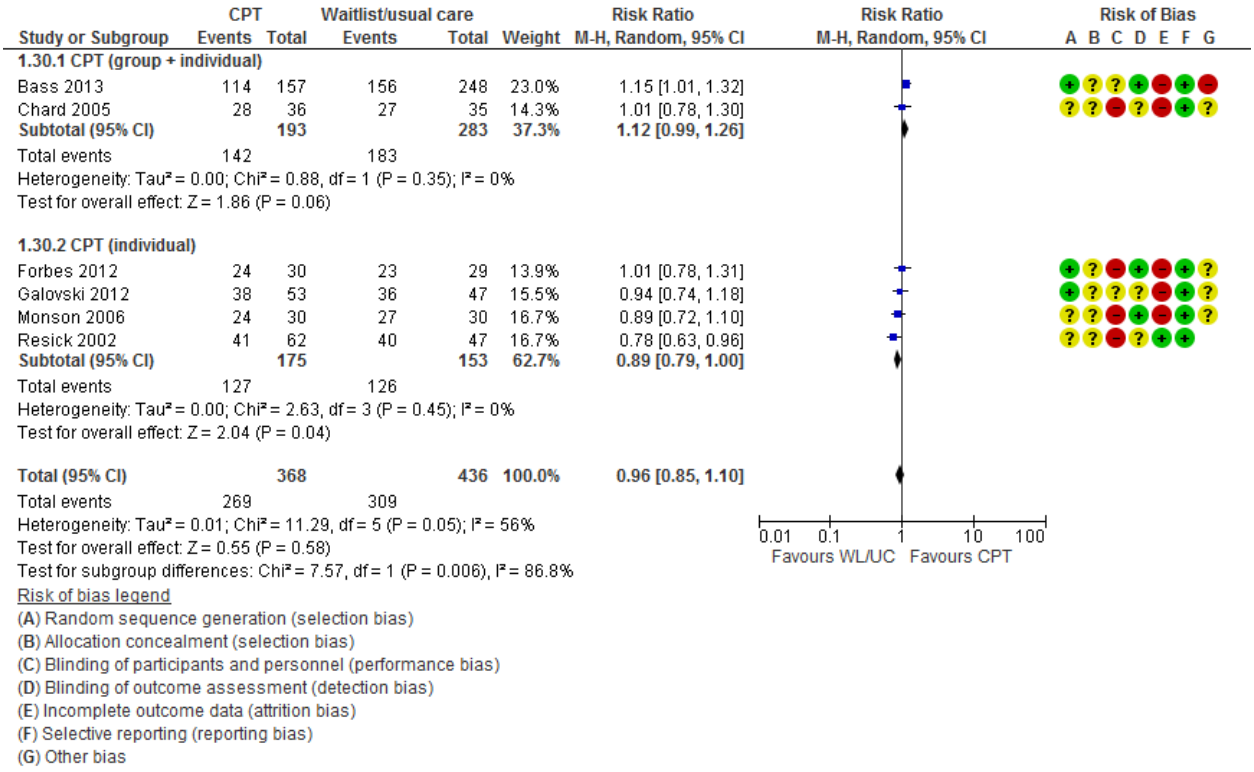
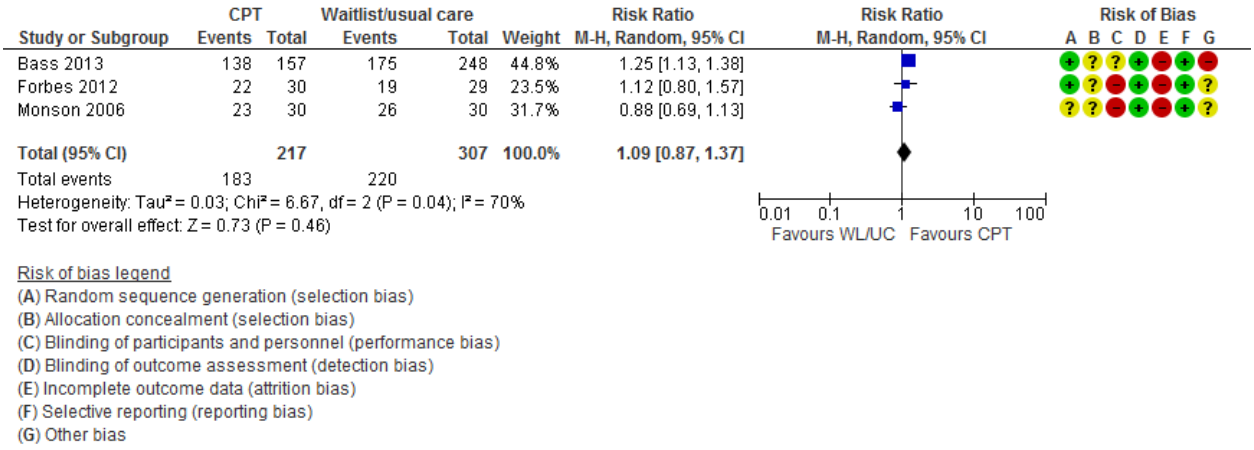


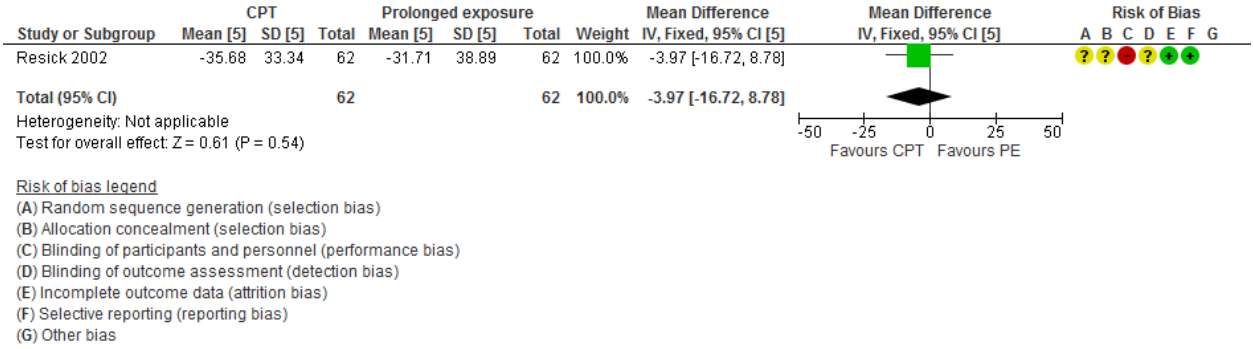
Figure 21: Patients Completed at Longest Follow-Up



CI = confidence interval; CPT = cognitive processing therapy; SD = standard deviation; WL/UC = wait-list or usual care.

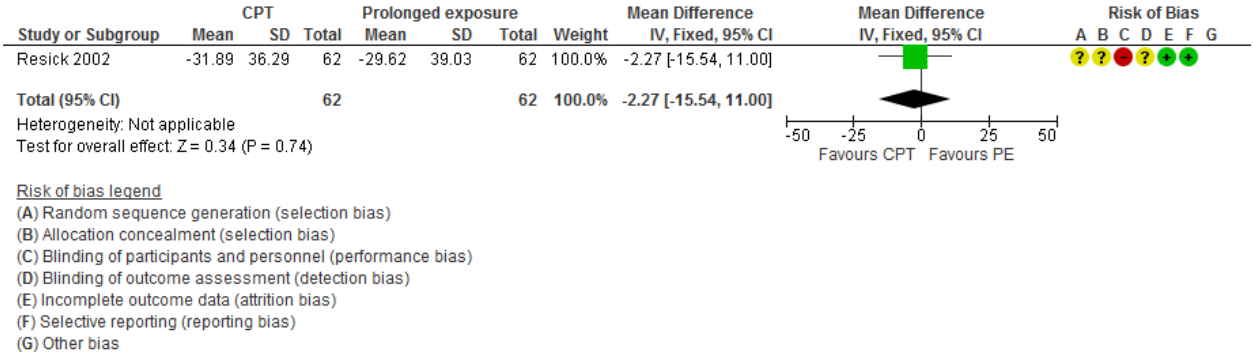
Appendix 8: Cognitive Processing Therapy Compared With Prolonged Exposure

Figure 22: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; at End of Treatment



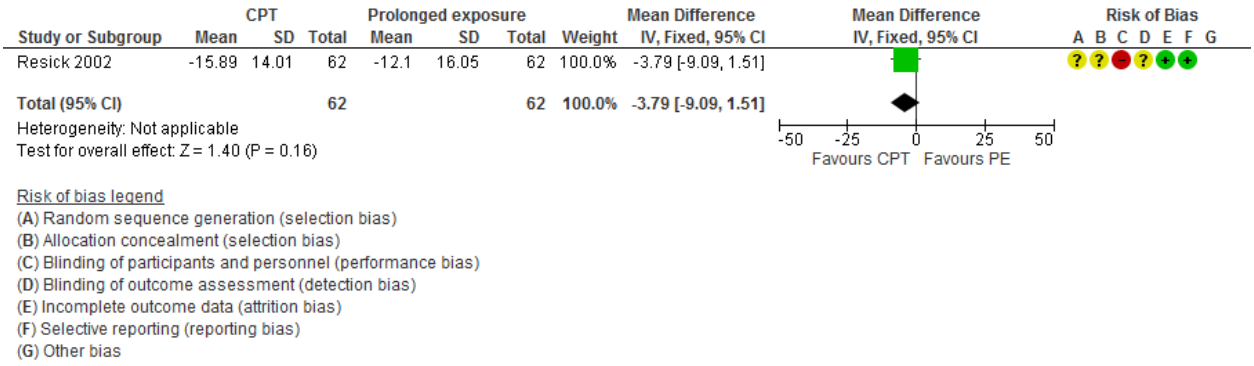
CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

Figure 23: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; at Longest Follow-Up



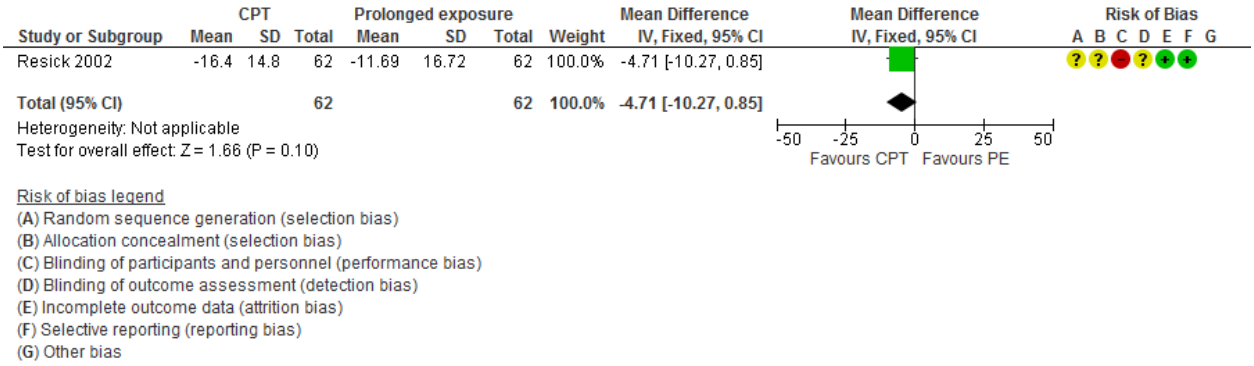
CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

Figure 24: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at End of Treatment



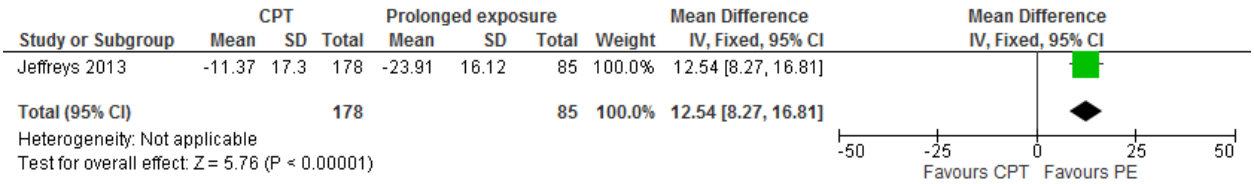
CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

Figure 25: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



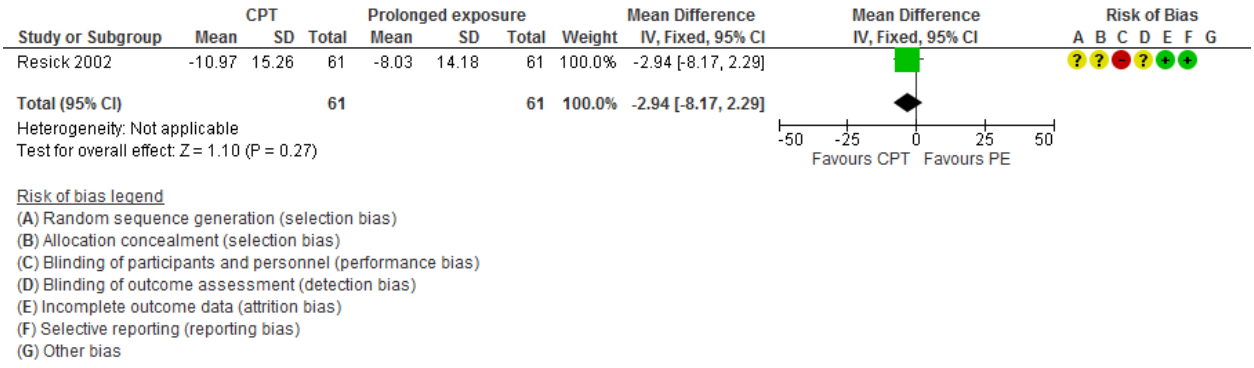
CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

Figure 26: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Observational; at End of Treatment



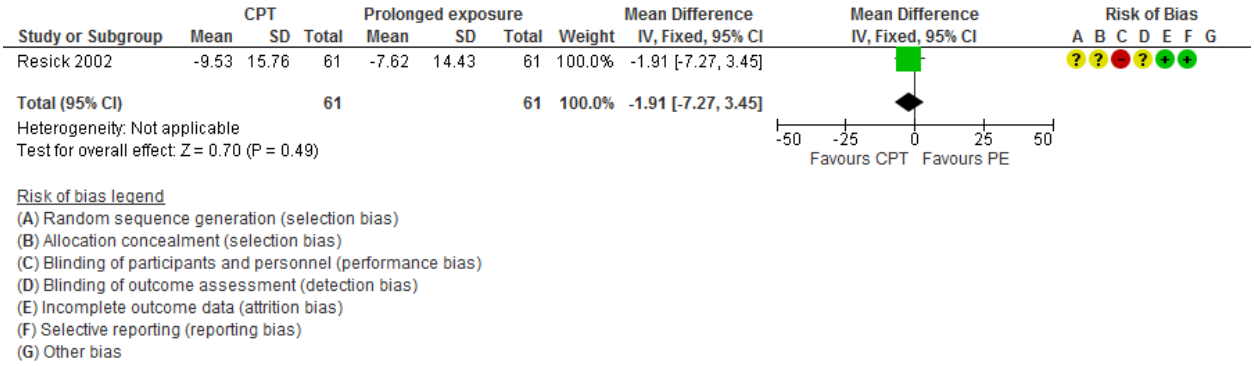
CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

Figure 27: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at End of Treatment



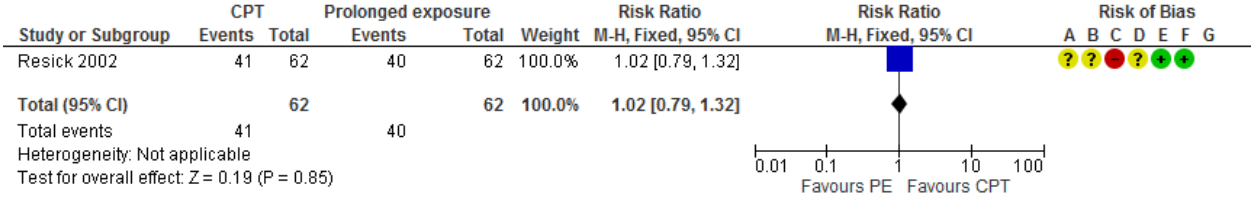
CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

Figure 28: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



CI = confidence interval; CPT = cognitive processing therapy; PE = prolonged exposure; SD = standard deviation.

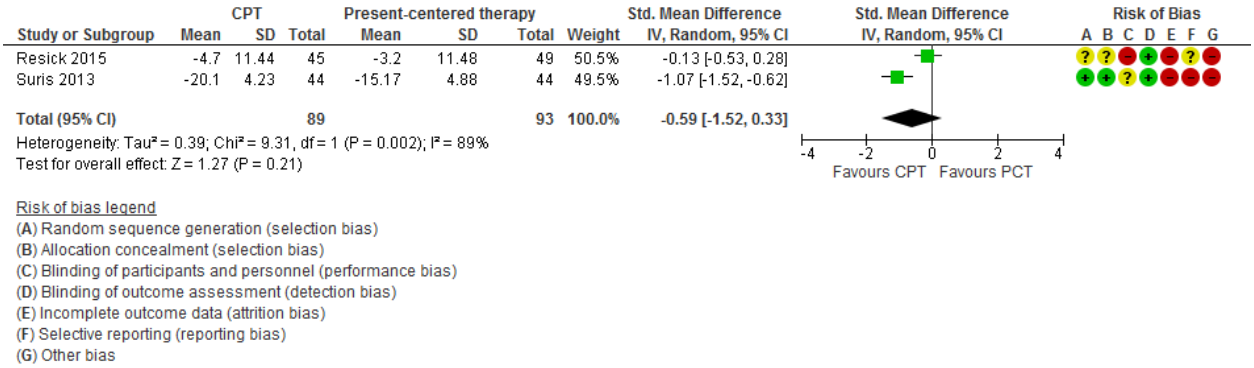
Figure 29: Patients Completed at End of Treatment



CI = confidence interval; CPT = cognitive processing therapy; M-H = Mantel Haenszel; PE = prolonged exposure; SD = standard deviation.

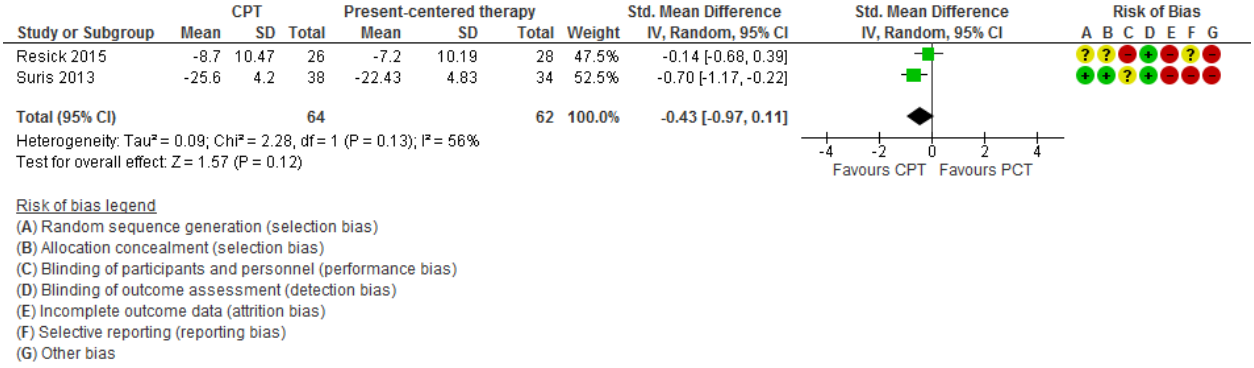
Appendix 9: Cognitive Processing Therapy Compared With Present-Centred Therapy

Figure 30: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; at End of Treatment



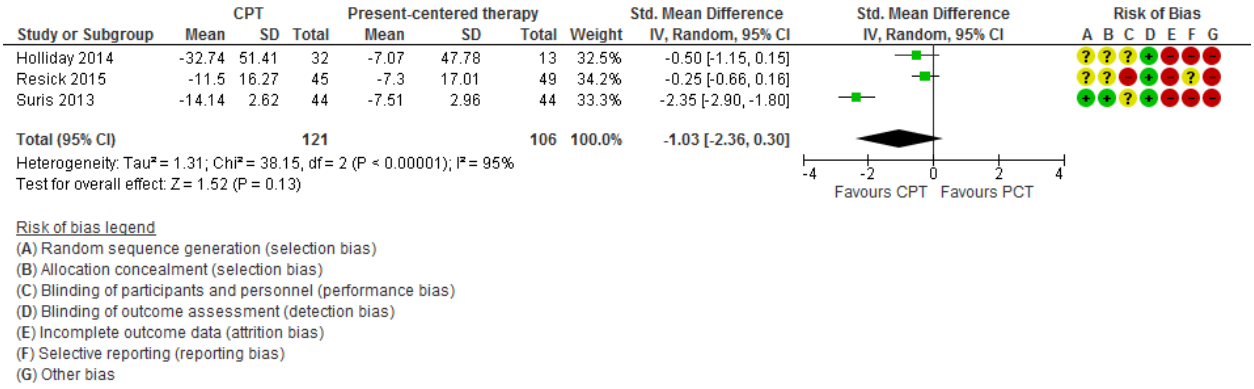
CI = confidence interval; CPT = cognitive processing therapy; PCT = present-centred therapy; SD = standard deviation.

Figure 31: Change in Severity of Post-traumatic Stress Disorder — Clinician-Administered; Randomized Controlled Trials; at Longest Follow-Up



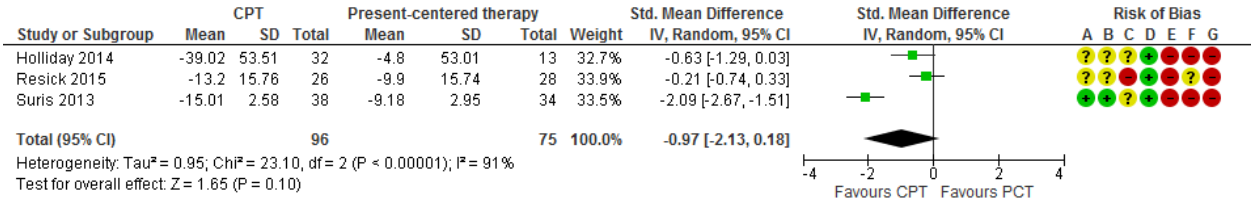
CI = confidence interval; CPT = cognitive processing therapy; PCT = present-centred therapy; SD = standard deviation.

Figure 32: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at End of Treatment



CI = confidence interval; CPT = cognitive processing therapy; PCT = present-centred therapy; SD = standard deviation.

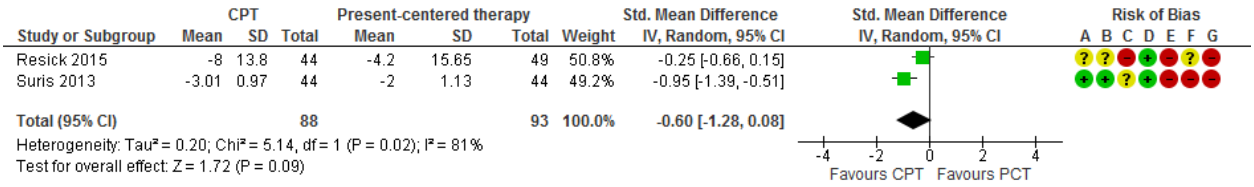
Figure 33: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

CI = confidence interval; CPT = cognitive processing therapy; PCT = present-centred therapy; SD = standard deviation.

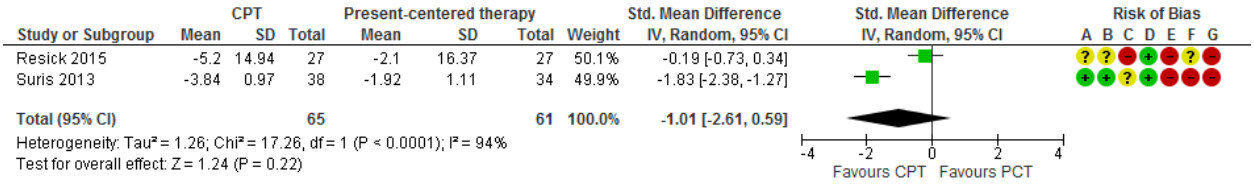
Figure 34: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at End of Treatment



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

CI = confidence interval; CPT = cognitive processing therapy; PCT = present-centred therapy; SD = standard deviation.

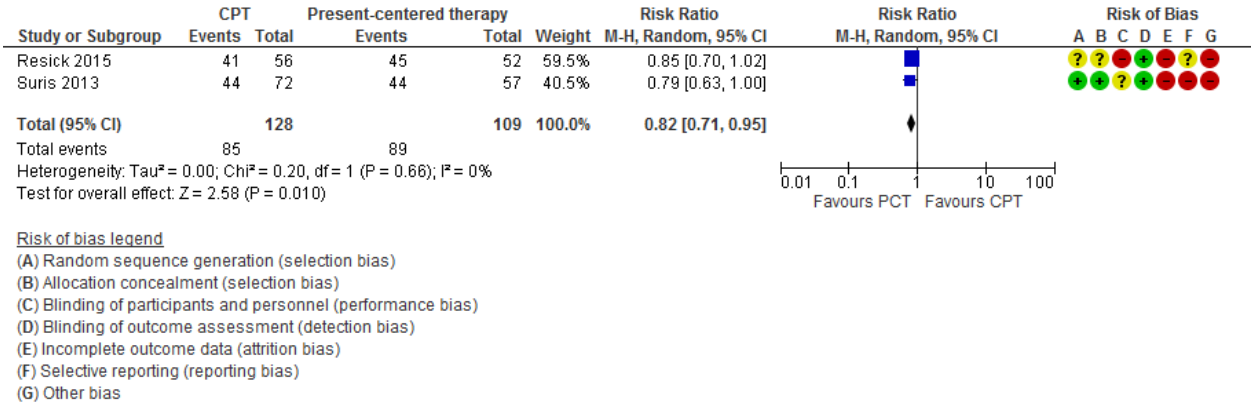
Figure 35: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

CI = confidence interval; CPT = cognitive processing therapy; PCT = present-centred therapy; SD = standard deviation.

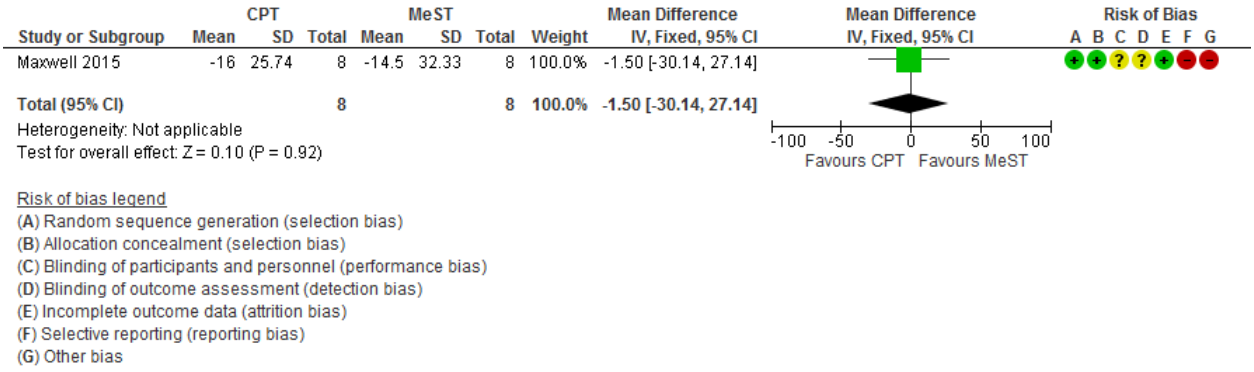
Figure 36: Patients Completed at End of Treatment



CI = confidence interval; CPT = cognitive processing therapy; M-H = Mantel Haenszel; PCT = present-centred therapy; SD = standard deviation.

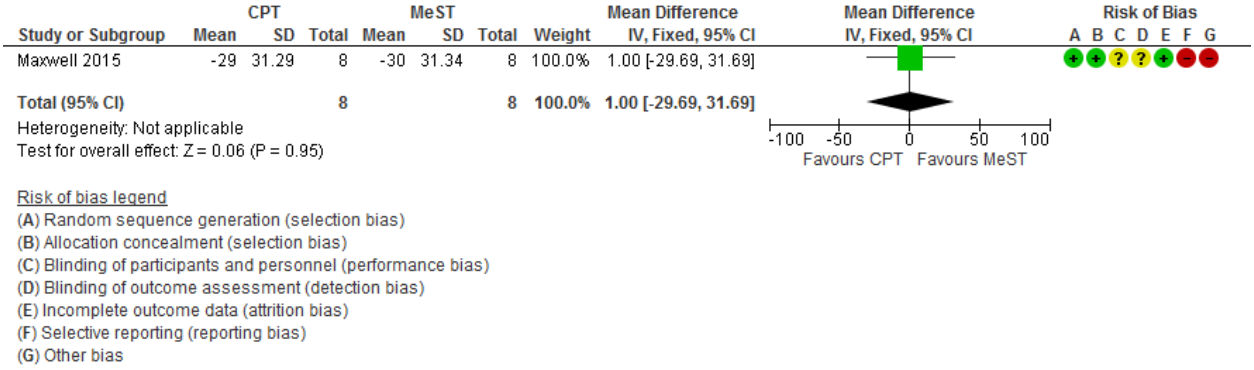
Appendix 10: Cognitive Processing Therapy Compared With Memory Specificity Training

Figure 37: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at End of Treatment



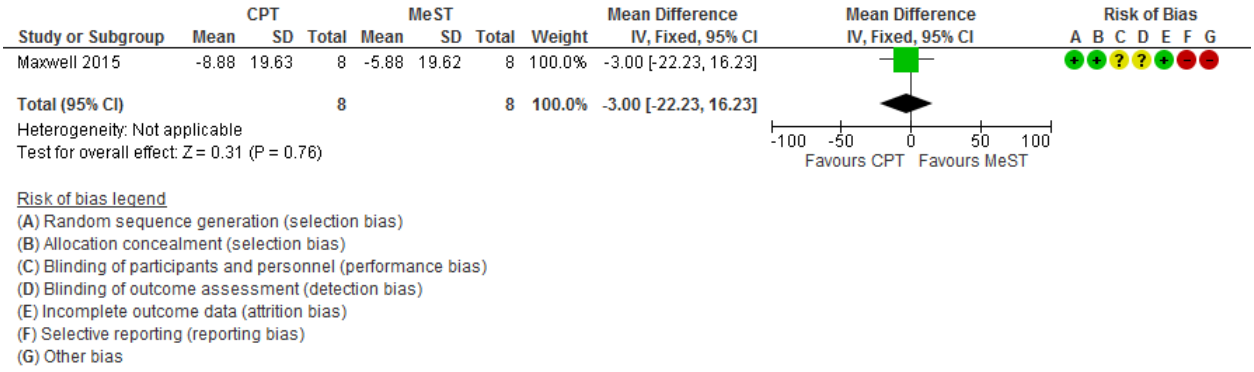
CI = confidence interval; CPT = cognitive processing therapy; MeST = memory specificity training; SD = standard deviation.

Figure 38: Change in Severity of Post-traumatic Stress Disorder — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



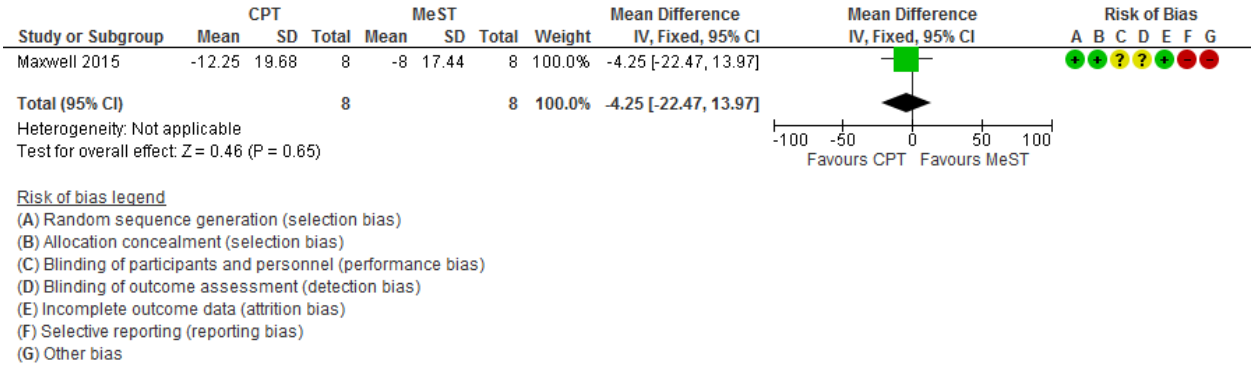
CI = confidence interval; CPT = cognitive processing therapy; MeST = memory specificity training; SD = standard deviation.

Figure 39: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at End of Treatment



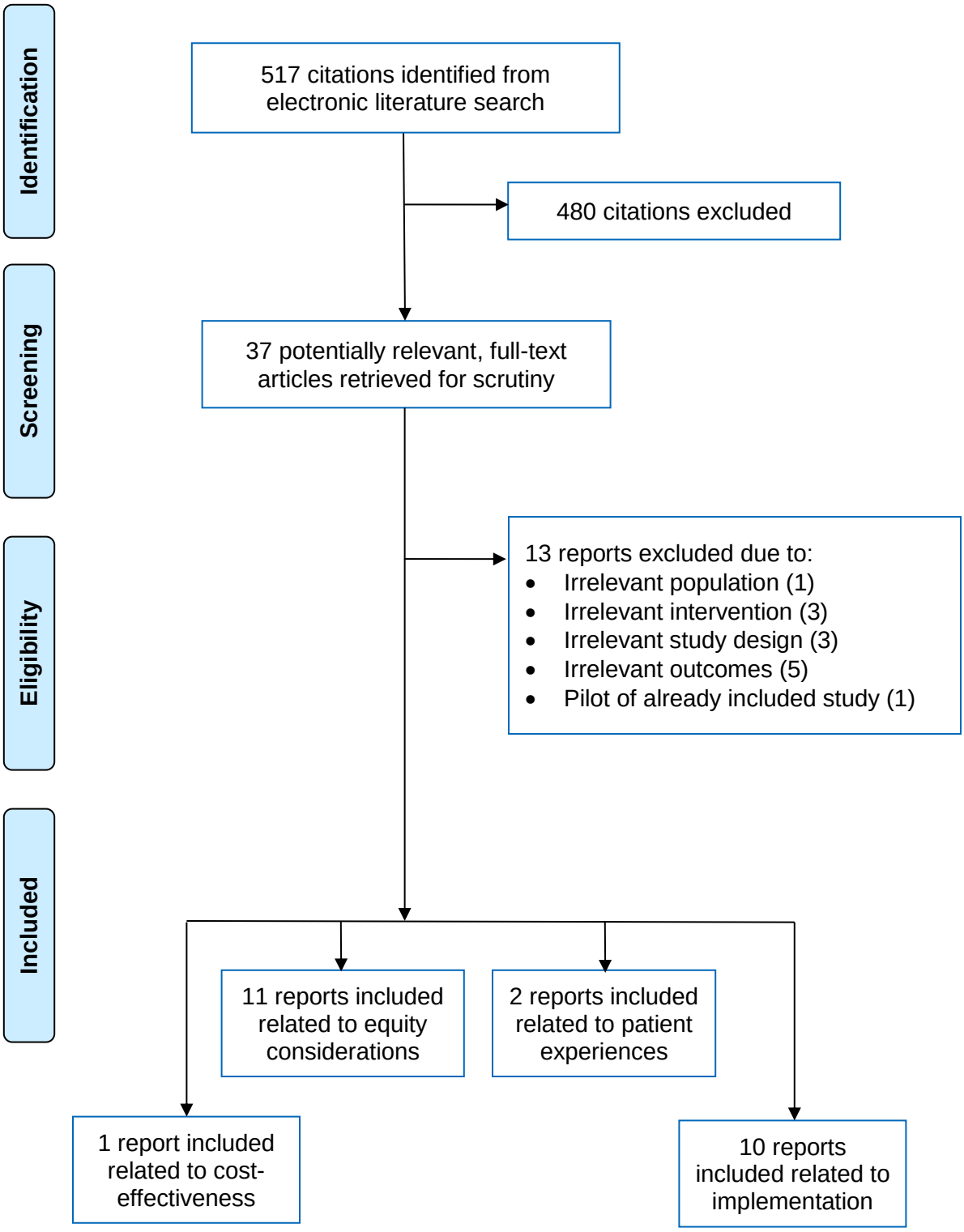
CI = confidence interval; CPT = cognitive processing therapy; MeST = memory specificity training; SD = standard deviation.

Figure 40: Change in Depression Symptoms — Self-Reported; Randomized Controlled Trials; at Longest Follow-Up



CI = confidence interval; CPT = cognitive processing therapy; MeST = memory specificity training; SD = standard deviation.

Appendix 11: Prisma Flow Diagram for Included Contextual Studies



Appendix 12: Study and Patient Characteristics for Contextual Studies

Table A4: Study and Patient Characteristics for Studies Related to Equity

First Author; Year; Study Setting; Study Design	Objectives	Intervention Details	Patient Population	Outcomes Reported
Sex and Gender				
Galovski, 2013;[52] US; post-hoc analysis of an RCT	To evaluate sex differences in the treatment response trajectory for male and female interpersonal assault survivors using a modified CPT protocol[a]	12 sessions of CPT, with an additional 6 sessions available if needed	22 men and 47 women seeking outpatient CPT following assault; all had a diagnosis of PTSD and were at least 3 months post-trauma	Clinician- and self-reported changes in PTSD; anxiety, depression, guilt, trauma symptoms
Race, Ethnicity, Language, and Culture				
Marques, 2016;[49] US; cross-sectional	To examine the differences and similarities among non-Latino, Latino Spanish-speaking, and Latino English-speaking clients in rigid beliefs (or "stuck points") associated with PTSD symptoms in community mental health clients	Manualized CPT	37 patients (approximately 69% female)[b] with a primary diagnosis of PTSD Analytic sample: 29 patients	Stuck points, content, and themes that emerged related to their PTSD and to living with PTSD
Schumm, 2013;[46] US; cohort study[c]	To test the hypothesis that multiple latent classes will explain individual differences in PTSD symptom change during the course of CPT	Manualized CPT	207 military veterans (89% male, 81% white, 62% with combat as their worst trauma)	Clinician- and self-reported changes in PTSD; depression
Schultz, 2006;[47] US; program evaluation	To determine whether CPT was effective for the treatment of PTSD in war refugees and to evaluate the impact of the use of interpreters in the delivery of CPT	CPT Written materials were translated into Serbo–Croatian, but not into Farsi. Sessions were 90 to 120 minutes long; the average number of sessions was 17	53 adults (46 women, 7 men) who were refugees from Afghanistan (n = 9) or Bosnia–Herzegovina (n = 44) and who emigrated to the US between 1993 and 2004	PTSD symptoms
Schultz, 2006;[48] US; program evaluation	To Illustrate how CPT can be used with Bosnian refugees with PTSD, and how culture	CPT Written materials were translated into Serbo–Croatian. (Same	Bosnian refugees being treated for PTSD (N = not reported). Patients	Treatment adaptations, description of client

First Author; Year; Study Setting; Study Design	Objectives	Intervention Details	Patient Population	Outcomes Reported
	and language affect the process	protocol and group of Bosnian patients as Schultz[47])	discussed were part of the War Trauma Recovery Project	and clinician relationship and interaction with the system
Military and Childhood Sexual Trauma				
Walter, 2014;[51] US; cohort study	To examine whether a history of childhood sexual abuse influenced treatment outcome among female veterans with an index trauma of military sexual trauma receiving residential treatment (that included CPT) for PTSD	2 group, 2 individual sessions per week for 7 weeks. Additional sessions available as needed	Female veterans (N = 110) who were admitted to a 7-week residential PTSD program. Met the diagnostic criteria for PTSD; their index trauma was military sexual trauma	Clinician-administered and self-reported PTSD symptoms, depression
Intimate Partner Violence				
Iverson, 2011;[50] US; RCT subgroup analysis of a randomized trial	To determine if having been exposed to intimate partner violence predicts whether women start or complete CPT therapy for PTSD therapy	12 sessions of CPT, CPT-C, or the WA portion of CPT[d]	150 women undergoing CPT for PTSD (within a study that examined the components of CPT). 32% (n = 42) had not experienced IPV, 52.7% (n = 79) had experienced past IPV, and 15.3% (n = 25) had experienced IPV with their current partner within the last year.	Self-reported PTSD symptoms, depression, conflict and aggression, trauma-related guilt
Resource-Poor, Low-Literacy Environment				
Bass, 2013;[14] Congo; mixed methods RCT	To examine adapted CPT vs. individual support for survivors of sexual violence in the Congo	CPT: 1 individual and 11 group sessions using the cognitive-only model[e] Support: Could access support services as desired. Available services included psychosocial support and economic, medical, and legal referrals	405 women from 16 villages in the Congo. (352 completed baseline and at least one follow-up assessment.)	Functional impairment,[f] PTSD symptoms, depression, anxiety

First Author; Year; Study Setting; Study Design	Objectives	Intervention Details	Patient Population	Outcomes Reported
Access				
Maieritsch, 2015,[53] US RCT	To evaluate equivalence between in-person and videoconference psychotherapy for PTSD in veterans of the Iraq and Afghanistan conflict	Telemental health via videoconference (n = 45) vs. in-person delivery (n = 45) of CPT	Veterans being treated for PTSD (N = 90). Primarily male (93.3%); most (76%) had served active duty in Afghanistan	Clinician- and self-reported PTSD, depression, working alliance
Morland, 2015,[55] US RCT (non-inferiority)	To examine the effectiveness of telemedicine in providing psychotherapy to women with PTSD who might be otherwise unable to access treatment	Twelve 90-minute CPT sessions via videoconference (n = 63) or in person (n = 63); group therapy	Veteran (n = 73) and civilian (n = 214) women with PTSD	Clinician-reported PTSD, treatment expectancy, working alliance
Morland, 2014,[54] US RCT (non-inferiority)	To compare clinical and process outcomes of CPT-C (cognitive-only CPT) delivered via teleconference vs. in person in a rural, ethnically diverse sample of male veterans with PTSD	Manualized CPT-C protocol with twelve 90-minute, twice-weekly group sessions, either in person (n = 64) or via teleconference (n = 61). The same therapists delivered both types of care	Male veterans (n = 125) with a current diagnosis of PTSD	Clinician-reported PTSD severity, patient satisfaction, treatment expectancy, working alliance

CPT = cognitive processing therapy; CPT-C = cognitive processing therapy, cognitive only; GGMM = general growth mixture modelling; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial; vs. = versus; WA = written accounts.
[a] Modified protocol allowed survivors to receive up to18 sessions of CPT; treatment end was determined by therapy progress.
[b] Demographic data not available for all participants.
[c] Used GGM: Quantitative method that tests the existence of categorically distinct trajectories of change in outcomes over time. Can be seen as a cross between latent class analysis and random-effects modelling.
[d] CPT-C was the cognitive portion only (full CPT sessions without the written account). WA involved using only the written account portion of CPT; therefore, it likely more closely resembled prolonged exposure therapy.
[e] Trauma narrative not included. Individual sessions were 1 hour; group sessions were 2 hours.
[f] Functional impairment was based on the degree of difficulty in performing important tasks of daily living.

Table A5: Study and Patient Characteristics for Studies Related to Patient Preference

First Author; Year; Study setting; Study Design	Objectives	Intervention Details	Patient Population	Outcomes Reported
Hundt, 2015;[56] US; qualitative description	To examine barriers to accessing EBT for PTSD and determine how patients came to the decision to engage in treatment	Prolonged exposure therapy (n = 11) CPT (n = 3 for individual therapy; n = 6 for group therapy) n = 3 patients had received both PE and CPT	Purposive sample; patients who had received at least 8 sessions of EBT (including CPT) for PTSD. N = 23 (6 female, 17 male)	Pathways to therapy, opinions of therapy
Schumm, 2015;[57] US; descriptive study	To explore veteran satisfaction with a VA PTSD specialty clinic pre-treatment orientation group, and to test differences in treatment preference in response to the group	60-minute orientation group led by a licensed psychologist. Outlined bullet-specific, PTSD-focused psychotherapies and medication options that were offered through the PTSD clinic, including CPT	183 veterans (n = 164 male) attending an outpatient pre-treatment orientation prior to PTSD therapy	Preference toward the type of treatment they would choose to participate in for the treatment of their PTSD

CPT = cognitive processing therapy; EBT = evidence-based therapy; PE = prolonged exposure; PTSD = post-traumatic stress disorder; VA = Veterans Affairs.

Table A6: Study Characteristics for Studies Related to Implementation

First Author; Year; Study Setting; Study Design	Objectives	Interventions Being Evaluated	Program or Participant Details	Outcomes Reported
In-patient				
Cook, 2015;[61] US; program evaluation	To examine the implementation of PE and CPT in the Department of Veterans Affairs (implementation evaluated using the Rogers–Greenhalgh framework)[a]	In-patient CPT (individual and group), in-patient PE (individual). VA PTSD clinicians were trained to provide the treatments and they were introduced in the in-patient clinics	201 care providers from 38 treatment centres participated in an online survey. Bivariate and multivariate associations between constructs and outcomes were examined.	Factors affecting the uptake of PE and CPT
Cook, 2015;[60] US; program evaluation (using Rogers-Greenhalgh model)	To evaluate an implementation model regarding factors influencing provider use of PE and CPT for PTSD (implementation evaluated using the Rogers–Greenhalgh framework)[a]	In-patient CPT (individual and group), in-patient PE (individual). VA PTSD clinicians were trained to provide the treatments and they were introduced in the in-patient clinics	243 treatment directors, providers, and staff from 38 VA residential PTSD treatment programs. 191 completed a quantitative survey and qualitative interview; 13 completed only the survey; 7 completed only the interview; 32 did not participate	The challenges, successes, strengths, and weaknesses of the treatments, program and implementation
Cook, 2014;[59] US; program evaluation (formative evaluation)	To understand implementation and adaptation of PE CPT at 2 time points over a 4-year period	In-patient CPT and in-patient PE. VA PTSD clinicians were trained to provide the treatments and they were introduced in the in-patient clinics	38 programs, followed up 2 years later. Web-based surveys and telephone interviews conducted. Data on 190 of 243 providers were available	Level of adoption of CPT, details on program operations, level of provider training for the therapies, adaptation of therapy
Cook, 2013;[58] US; program evaluation	To report findings on the initial adoption of PE and CPT in residential VA PTSD programs during the initial stages of the system-wide dissemination	In-patient CPT and in-patient PE. VA PTSD clinicians were trained to provide the treatments and they were introduced in the in-patient clinics	38 sites offering PTSD treatment in 22 Veterans' Integrated Service Networks Semi-structured interviews conducted regarding implementation of the EBTs	Descriptive information related to programs, adoption of PE and CPT, level of adoption, care providers' perception of the treatments

First Author; Year; Study Setting; Study Design	Objectives	Interventions Being Evaluated	Program or Participant Details	Outcomes Reported
Outpatient				
Finley, 2015;[62] US; program evaluation	To describe the utilization of PE and CPT and to identify factors associated with treatment uptake and adherence in outpatient VA PTSD programs	Outpatient CPT and PE delivered by VA PTSD clinicians in outpatient VA clinics	138 providers of PTSD treatment at outpatient VA clinics (53.9% clinical psychologists; 69.5% had worked at the clinic < 5 years)	Clinician demographics, training, organizational work factors, perceived effectiveness and utilization of PE and CPT in individual and group formats
Hamblen, 2015;[63] US; program evaluation	To understand local challenges by examining VA PTSD clinic director perspectives on implementation of PE and CPT in a nationally representative sample of PTSD outpatient programs	Outpatient CPT and PE delivered by VA PTSD clinicians in outpatient VA clinics	Directors of programs at VA sites offering outpatient PTSD treatment (38 of 42 directors participated)	Clinic operation (from intake to discharge), treatments offered, primary factors that influence patient flow, challenges faced
Raza, 2015;[64] US; survey	To determine the clinical features clinicians consider as they select PE or CPT to treat a given patient; which exclusionary criteria they are using; and how helpful clinicians find the extant literature on comorbid conditions and associated clinical features when making treatment decisions	Outpatient CPT and PE delivered by VA PTSD clinicians in outpatient VA clinics	247 clinicians who had participated in VA training sessions on PE or CPT	Factors that influence the selection of PE or CPT, clinician demographics
Watts, 2014;[65] US; program evaluation database; used the PARiHS framework	To evaluate the US VA efforts to promote the use of EBTs for PTSD	Outpatient CPT and PE delivered by VA PTSD clinicians in outpatient VA clinics	30 VA PTSD programs in New England	Rate of EBT use, implementation of EBT

First Author; Year; Study Setting; Study Design	Objectives	Interventions Being Evaluated	Program or Participant Details	Outcomes Reported
Borah, 2013;[67] US; survey	To identify and hypothesize perceived barriers related to the clinical environment that influence the uptake of EBT use for PTSD	Outpatient PE and CPT delivered to veterans	103 US Air Force behavioural health providers who had been trained (via workshops) in CPT (n = 61) or in PE (n = 42)	Barriers to use of EBT, provider interest in using EBT, provider preference for PTSD treatment, provider confidence in using CPT and PE
In-patient and Outpatient				
Garcia, 2015;[66] US; survey	To examine the relationship between burnout and the use of EBTs for the treatment of PTSD among VHA mental health clinicians	In-patient and outpatient CPT and PE	Licensed and unlicensed, trained, non-prescribing VHA providers, employed at least half time; 138 responded to the survey and 98 responses were analyzed.	Clinician demographic characteristics, hours providing PE and CPT, burnout

CPT = cognitive processing therapy; EBT = evidence-based treatment; PARiHS = promoting action on research implementation in health services; PE = prolonged exposure; PTSD = post-traumatic stress disorder; VA = Veterans Affairs; VHA = Veterans Health Administration.
[a] The Rogers–Greenlaugh framework postulates that the implementation process is influenced by 5 broad constructs: perceived characteristics of innovation, potential adopter characteristics, communication and influence, inner organizational context, and outer organizational context.

Table A7: Characteristics of Costing Study

First Author, Year, Study Setting	Data Sources	Objectives	Participants	Outcomes Measured
Meyers 2013[29]; costing study	Retrospective database evaluation: data on VA health service utilization and health care costs obtained from national VA databases	To evaluate the impact of a course of PE or CPT on mental health and medical service utilization and health care service costs provided by VA	70 veterans (75% male) who completed PE or CPT for the treatment of PTSD at a Midwestern VA medical centre	Primary care use, emergency department use, direct costs associated with mental health care

CPT = cognitive processing therapy; PE = prolonged exposure; PTSD = post-traumatic stress disorder; VA = Veterans Affairs.

Appendix 13: Critical Appraisal of Contextual Studies

Table A8: Strengths and Limitations of Non-Randomized Studies, Surveys, and Qualitative Studies

Study	Strengths	Limitations
Equity: Sex and Gender		
Galovski[52]	• Measured outcomes were validated scales • ITT analysis used • Groups were similar with respect to demographic characteristics	• Small sample size — particularly small number of men (N = 69; n = 22) • May not be generalizable to those who are not on concomitant medications • May not be generalizable to those with substance abuse
Walter[51]	• Measured outcomes were validated scales • Treatment completion rate was good	• May not have been adequately powered to detect all outcomes • May not be generalizable to outpatient clinics • Other psychoeducational treatment did occur; difficult to determine if just CPT was contributing to the treatment effect
Marques[49]	• 37 of 51 clients consented to participate • Coding data were audited by a team member • Consensus was reached regarding coding • Data saturation was achieved	• The Spanish CPT manual may not be culturally appropriate • The Spanish CPT manual was difficult to use; thus, CPT may not have been delivered the same in English and Spanish • Data may not be generalizable to another set of clients (this was a higher-income community) • Not randomized; no methods used to control for differences
Schulz[48]	• Verbatim transcriptions presented	• Group of case samples • Limited data presented in the citation
Schulz[47]	• Non-translated versions of outcome measures were validated	• No random assignment to treatment (however, assignment based on availability of therapist and no other characteristic) • Adherence to treatment protocol was suggested but not strictly enforced; number of sessions was flexible • The “no-interpreter” group all received therapy from the same clinician • The translated version of the PTSD Symptom Scale may not be valid • May not be generalizable to a different population
Schumm[46]	• Validated measures used • Missing data were addressed • Clinicians had various levels of training (reflecting the real world) • Sample was fairly heterogeneous	• Fidelity to treatment manual was not rated • Therapy sessions were not recorded for review

Study	Strengths	Limitations
Patient Preference		
Hundt[56]	• Themes were explored • Audio recording of the interviews occurred • Recruitment ended when saturation reached (which was defined a priori) • Verbatim statements reported	• May not be generalizable outside the VA PTSD clinic setting • Unclear if lack of awareness of evidence-based treatment is a barrier, because this did not come up in the study
Schumm[57]	• Both quantitative and qualitative methods were used to answer the appropriate questions	• No control group • Family members were usually involved in treatment decisions, but were not interviewed • May not reflect findings for women, as the sample was so predominantly male • Not clear if the quantitative data were validated
Implementation		
Cook[58]	• Part of a "suite" of studies that examines many aspects of the implementation of CPT in VA centres; therefore, many facets of the implementation were examined • Verbatim statements reported • Ratings were discussed until consensus reached	• Residential care only; likely not applicable to outpatient care • VA centres are standardized; thus, results may be applicable only to those centres
Cook[59]	• Part of a "suite" of studies that examine many aspects of the implementation of CPT in VA centres; therefore, many facets of the implementation were examined • Multiple procedures used at baseline and follow-up in order to increase internal validity (interview standardization, audio recording, professional transcription, data analysis software)	• Residential care only; likely not applicable to outpatient care • VA centres are standardized; thus, results may only be applicable to those centres • Relied on self-report • Programs were not evaluated at the same intervals
Cook[60]	• Part of a "suite" of studies that examine many aspects of the implementation of CPT in VA centres; therefore, many facets of the implementation were examined • Methods taken to increase internal validity (standardized coding scheme, audio recording, searching for deviant cases,	• Residential care only; likely not applicable to outpatient care • VA centres are standardized; thus, results may only be applicable to those centres • Relied on self-report (providers may have been reluctant to report negative aspects of their programs)

Study	Strengths	Limitations
	transcription techniques of conversion analysis)	
Cook[61]	• Part of a "suite" of studies that examine many aspects of the implementation of CPT in VA centres; therefore, many facets of the implementation were examined • Not reported in current study, but authors engaged in further triangulation by examining data from databases	• Residential care only; likely not applicable to outpatient care • VA centres are standardized; thus, results may be applicable only to those centres • Not clear if the outcome measures were validated
Finley[62]	• Anonymity was ensured by not recording IP addresses as part of survey • Authors made clear that this was an exploratory study and therefore had limitations	• Small sample size • Perceptions do not necessarily reflect reality • One-time measure — does not reflect change over time • Unclear if the outcome measures were validated • *P* values not corrected for multiple analyses
Hamblen[63]	• Interviews independently coded and reviewed to reach consensus • Half of the interviews were re-analyzed and examined holistically (as well as coded)	• VA context (even outpatient) may not be generalizable to other PTSD clinics • Despite semi-structured interview guide, not all respondents answered all questions and not all responses were sufficiently detailed
Raza[64]	• Relatively large sample size • Diverse sample of clinicians	• Unclear if the sample of clinicians who participated differed from those who did not • Did not ask clinicians how frequently they used the treatment options • Did not include questions regarding PTSD that presents with a comorbid disorder • Unclear if the VA setting is generalizable to other PTSD clinic settings
Watts[65]	• Coding was automated using algorithm-based software • Coding was validated by hand;10% were double-coded • Interview guide was used • Interviews were recorded and transcribed	• Examined 6 clinics in a small region; results could be reflective of that region only • Cross-sectional design means that trends across time could not be examined; directionality of associations is unknown • VA clinics are highly structured; results may not be generalizable to other types of clinics
Borah[67]	• Anonymity was ensured by not recording race, ethnicity, and gender (it was thought	• Response rate was 34.2% • No reliability and validity data are available for the survey instrument

Study	Strengths	Limitations
	that those variables would reveal provider identity) • Those who participated in the pre-survey training were representative of the care providers for the Air Force	
Garcia[66]	• Outcome measures were validated • Steps were taken to ensure confidentiality; therefore, respondents were more likely to respond honestly	• Cross-sectional design means that trends across time could not be examined; directionality of associations is unknown • Providers who answered the survey self-selected • Exact response rate unknown (study authors relied on clinic directors to pass along invitation to participate)
Costing		
Meyers[29]	• Mental health, primary care, and emergency department costs all considered • Clinical sample was considered a "real world" sample (medical records examined)	• VA clinics are highly structured; results may not be generalizable to other types of clinic • Small sample • Non-medical costs were not considered

CPT = cognitive processing therapy; IP = Internet Protocol; ITT = intention-to-treat; PTSD = post-traumatic stress disorder; VA = Veterans Affairs.

Table A9: Cochrane Risk of Bias for Randomized Controlled Trials Tool[10]

Item	Response
Bass[14]	
Was the allocation sequence adequately generated?	Yes. Block randomization based on proximity. Village was randomized.
Was allocation adequately concealed?	Unclear (likely; no mention that it could not be or was not concealed).
Was knowledge of the allocated intervention adequately prevented during the study (participants and personnel)?	No. Could not be blinded.
Was knowledge of the allocated intervention adequately prevented during the study (outcome assessors)?	Yes. Those who were evaluating outcomes were not aware of the intervention assignment.
Were incomplete outcome data adequately addressed?	Yes.
Are reports of the study free of suggestion of selective outcome reporting?	Yes.
Was the study apparently free of other problems that could put it at a high risk of bias?	No. The small number of village clusters (6) made randomization less likely to result in comparability. There may also have been biases in recruitment that resulted in higher average symptom scores in villages that provided individual

Item	Response
	support, because psychosocial assistants recruiting patients knew ahead of time whether they would be providing therapy or individual support. Measure may not have been valid for PTSD with anxiety and depression; additionally, it wasn't clear if the measure of functional impairment was validated. May not generalize to men.
Iverson[50]	
Was the allocation sequence adequately generated?	Unclear. Sufficient detail not provided.
Was allocation adequately concealed?	Not clear. Sufficient detail not provided.
Was knowledge of the allocated intervention adequately prevented during the study (participants and personnel)?	No. Blinding not possible.
Was knowledge of the allocated intervention adequately prevented during the study (outcome assessors)?	Yes. Outcome assessors blinded.
Were incomplete outcome data adequately addressed?	Yes. ITT analysis conducted.
Are reports of the study free of suggestion of selective outcome reporting?	Yes.
Was the study apparently free of other problems that could put it at a high risk of bias?	Unclear. Relied on self-report. May not generalize to other patient groups (sample was primarily low-income). Sample size of those with recent intimate partner violence was small.
Maieritsch[53]	
Was the allocation sequence adequately generated?	Yes. Block randomization.
Was allocation adequately concealed?	Unclear. Not indicated one way or another.
Was knowledge of the allocated intervention adequately prevented during the study (participants and personnel)?	No. Could not be blinded.
Was knowledge of the allocated intervention adequately prevented during the study (outcome assessors)?	Unclear. Not mentioned.
Were incomplete outcome data adequately addressed?	Yes. Addressed as a limitation.
Are reports of the study free of suggestion of selective outcome reporting?	Yes.
Was the study apparently free of other problems that could put it at a high risk of bias?	No. Discontinuation rates too high to reach statistical power. However, rates were similar in each group. Started recruitment with sessions twice weekly, but that was a barrier to participation, so they switched it to one time per week. That

Item	Response
	may have been a barrier to retention, because it may not have been enough.
Morland 2014[54]	
Was the allocation sequence adequately generated?	Yes. Block randomization.
Was allocation adequately concealed?	Unclear.
Was knowledge of the allocated intervention adequately prevented during the study (participants and personnel)?	No. Could not be blinded.
Was knowledge of the allocated intervention adequately prevented during the study (outcome assessors)?	Yes. Outcome assessors were blinded.
Were incomplete outcome data adequately addressed?	Yes. Both ITT and completer analyses were performed.
Are reports of the study free of suggestion of selective outcome reporting?	Yes.
Was the study apparently free of other problems that could put it at a high risk of bias?	No. Not all rural areas may have the necessary videoconferencing equipment. Patients with acute safety concerns (suicidal, homicidal) were excluded. There was an observer in the room during the videoconference.
Morland 2015[55]	
Was the allocation sequence adequately generated?	Unclear. Not reported.
Was allocation adequately concealed?	Unclear. Not mentioned.
Was knowledge of the allocated intervention adequately prevented during the study (participants and personnel)?	No. Could not be blinded.
Was knowledge of the allocated intervention adequately prevented during the study (outcome assessors)?	Unclear.
Were incomplete outcome data adequately addressed?	Unclear.
Are reports of the study free of suggestion of selective outcome reporting?	Yes.
Was the study apparently free of other problems that could put it at a high risk of bias?	No. Poorly reported. The main outcome measure questionnaire (CAPS) was administered 2 weeks post-treatment, which may not accurately reflect the entire therapy progress, as the CAPS assesses symptoms over the previous 30 days.

CAPS = Clinician-Administered PTSD Scale; ITT = intention-to-treat; PTSD = post-traumatic stress disorder.

Appendix 14: Trials Comparing Telehealth With In-Person Care

Table A10: Randomized Trials Comparing Telehealth With In-Person Care

Author, Year	Patients	Results
Maieritsch, 2015[53]	93% male; 45 patients randomized to each group; 25 completed TMH, 26 completed IP	Large number of dropouts — number to determine equivalence not reached; however, results trended toward equivalence with respect to reduction of PTSD symptoms and the strength of the therapeutic alliance.
Morland, 2015[55]	63 patients in the TMH group, 63 patients in the IP group; 48 patients in the TMH group and 50 in the IP group attended at least 10 of the 12 sessions (n = 214 were civilian; n = 73 were veterans).	After 6 months, no difference between the number who completed in-person _n = 41) and TMH treatment (n = 43); no differences between ratings of the therapeutic alliance (average rating was 6 of 7 points in both groups); patients undergoing both treatment modalities had reductions in PTSD symptoms (mean improvement on CAPS: 15.0 for IP and 21.1 for TMH; between group *P* = NS). Civilians tended to have better improvement than veterans.
Morland, 2014[54]	In-person treatment: 64 patients; TMH treatment: 61 patients; no group differences in dropouts	The therapeutic alliance was rated as high; treatment compliance was high; and patient satisfaction was high. These results were similar to the pilot in which patients did not have reduced confidence in TMH therapy.[40] No effect size differences between the two treatment groups. Immediately following treatment, 29.0% of participants no longer met the criteria for PTSD, followed by 29.8% at the 3-month follow-up and 26.4% at the 6-month follow-up. A clinically significant change was seen in 57.1% of patients immediately following treatment, followed by 58.7% at 3 months and 52.9% at 6 months.

CAPS = Clinician-Administered PTSD Scale; IP = in-person; NS = not significant; PTSD = post-traumatic stress disorder; TMH = telemental health.