Effective Health Care Program

Comparative Effectiveness Review
Number 109

Interventions for the Prevention of Posttraumatic Stress Disorder (PTSD) in Adults After Exposure to Psychological Trauma

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The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input.

We welcome comments on this systematic review. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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The investigators deeply appreciate the considerable support, commitment, and contributions of the EPC staff at RTI International and the University of North Carolina at Chapel Hill. We express our gratitude to the following individuals for their contributions to this project: Megan Van Noord, M.S.L.S., and Christiane Voisin, our EPC librarians; Sharon Barrell, M.A., editor; Loraine Monroe, our EPC publications specialist; Elizabeth Harden, M.P.H. and Andrea Yuen, B.S., who reviewed articles for eligibility and completed data abstractions; and Claire Baker, who aided us in retrieving full-text literature.

Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicted opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

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Prior to publication of the final evidence report, the EPC sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential non-financial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

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Interventions for the Prevention of Posttraumatic Stress Disorder (PTSD) in Adults After Exposure to Psychological Trauma

Structured Abstract

Objectives. To assess efficacy, comparative effectiveness, and harms of psychological, pharmacological, and emerging interventions to prevent posttraumatic stress disorder (PTSD) in adults.

Data Sources. PubMed®, the Cochrane Library, CINAHL, Embase, PILOTS, International Pharmaceutical Abstracts, PsycINFO®, Web of Science, reference lists of published literature (from January 1, 1980, to July 30, 2012). In addition, we searched various sources for grey literature.

Review methods. Two investigators independently selected, extracted data from, and rated risk of bias of relevant studies. If data were sufficient, we conducted quantitative analyses using random-effects models to estimate pooled effects. We graded strength of evidence (SOE) based on established guidance.

Results. We included 19 trials with a range of populations exposed to a variety of psychological traumas. Participants suffered from symptoms of PTSD but did not meet diagnostic criteria for PTSD. For most interventions studied, we did not find reliable evidence to support efficacy for the prevention of PTSD or for the reduction of PTSD-related symptom severity. Evidence was sufficient to justify conclusions about three treatments. First, debriefing does not reduce either the incidence or the severity of PTSD or related psychological symptoms in civilian victims of crime, assault, or accident trauma (low SOE). Second, our meta-analyses of three trials showed that, in subjects with acute stress disorder, brief trauma-focused cognitive behavioral therapy (CBT) was more effective than supportive counseling (SC) in reducing the severity of PTSD (moderate SOE). Pooled results did not reach statistical significance for incidence of PTSD, depression symptom severity (both low SOE), and anxiety symptom severity (moderate SOE), but numerically favored CBT over SC. Finally, collaborative care for a traumatic injury requiring hospitalization produces a greater decrease in PTSD symptom severity at 6, 9, and 12 months after injury than does usual care (low SOE).

The efficacy of psychological interventions to prevent PTSD did not differ between men and women (low SOE). Evidence was insufficient to determine whether previous depression or a history of child abuse or baseline PTSD symptoms influence the effectiveness of interventions. Evidence was insufficient to determine the effect of timing, intensity, or dosing on the effectiveness or risk of harms of interventions or to justify conclusions about the comparative risk of harms. For emerging interventions such as yoga, dietary supplements, and complementary or alternative interventions, no studies met our eligibility criteria. Evidence was insufficient to determine whether any treatment approaches were more effective for victims of particular trauma types.

Conclusions. Evidence supporting the effectiveness of most interventions used to prevent PTSD is lacking. If available in a given setting, brief trauma-focused CBT might be the preferable choice for reducing PTSD symptom severity in persons with acute stress disorder and collaborative care might be preferred for trauma patients requiring surgical hospitalization; by contrast, debriefing appears to be an ineffective intervention to reduce symptoms and prevent PTSD.

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Executive Summary

Background—The Condition and Preventive Strategies

Posttraumatic stress disorder (PTSD) may develop following exposure to a traumatic event. According to the fourth edition of the "Diagnostic and Statistical Manual of Mental Disorders, Text Revision" (DSM-IV-TR),[1] the essential feature of PTSD is the development of characteristic symptoms following exposure to an extreme traumatic stressor. The stressor may include having direct personal experience of an event that involves actual or threatened death or serious injury or other threat to one's physical integrity; witnessing an event that involves death, injury, or a threat to the physical integrity of another person; or learning about unexpected or violent death, serious harm, or threat of death or injury experienced by a family member or other close associate. The DSM-IV-TR also requires that the person's subjective response to the event involve intense fear, helplessness, or horror.

Some traumatic events that are directly experienced or to which individuals can be exposed include military combat, violent personal assault, being taken hostage, a terrorist attack, torture, natural or manmade disasters, and being diagnosed with a life-threatening illness.[1] Psychological trauma is common and leads to PTSD in a substantial number of adults exposed to trauma. The 1990–1992 National Comorbidity Survey indicated that 60 percent of men and 51 percent of women reported experiencing at least one traumatic event in their lifetimes.[2] Shortly after exposure, many people experience some symptoms of PTSD; in most people, those symptoms resolve within several weeks of the trauma. However, in approximately 10 to 20 percent, PTSD symptoms persist and are associated with impairment in functioning.[3] Although approximately 50 percent of those diagnosed with PTSD improve without treatment in 1 year, 10 to 20 percent develop a chronic unremitting course.[4]

The 2000 National Comorbidity Survey–Replication (NCS-R) estimated lifetime prevalence of PTSD among trauma-exposed adults in the United States to be 6.8 percent (9.7% in women and 3.6% in men) and current (12-month) prevalence to be 3.6 percent (5.2% in women and 1.8% in men), or more than 7.7 million American adults per year.[5-7] Some demographic or occupational groups, such as military personnel, are at higher risk of PTSD because of higher rates of exposure to trauma.

Prevention of PTSD can potentially reduce a significant burden of individual and societal suffering. Two different prevention strategies have been used. The first strategy, universal prevention, is to deliver interventions to all people exposed to a trauma, regardless of symptoms or risk of developing PTSD. The second strategy, targeted prevention, is based on the fact that although many people experience some symptoms of PTSD after trauma, only a relatively small percentage develop the psychiatric disorder of PTSD and its associated disability. The goal of targeted prevention is to identify, from among all people exposed to a trauma, those who are at high risk of developing the disorder of PTSD and then intervene only with those at high risk.

Interventions to prevent PTSD involve various psychological and pharmacological approaches; they also include emerging interventions such as approaches from complementary and alternative medicine. These interventions have been used both separately and in combination. Despite evidence that some early interventions, such as debriefing, are not effective for preventing PTSD or might even cause harm, they are still widely used. Such use indicates that uncertainty and controversy still exist within the field about providing an intervention that intuitively seems as if it should help, and that not enough consideration is given to scientific evidence when weighing intervention benefits and harms.

Scope and Key Questions

This review compares the efficacy, effectiveness, and harms of psychological, pharmacological, and emerging interventions to prevent PTSD in adults. We include studies of both universal and targeted prevention. We also address the clinical importance of effect modifiers or subgroup status that may affect the impact of traumatic exposure on specific outcomes; these include sex, comorbidities, refugee status, and military or civilian status.

Our report is limited to adults who had been exposed to a traumatic event and who received an early intervention designed to prevent progression to PTSD within the first 3 months after the trauma.

We approach each Key Question (KQ) by considering the relevant populations, interventions, comparators, outcomes, timing, and settings (PICOTS). In this review, we address the following KQs:

KQ 1: For adults exposed to psychological trauma, what is the efficacy or comparative effectiveness (or both) of early interventions to prevent PTSD or to improve health outcomes?

KQ 2: For adults exposed to psychological trauma, does timing, intensity, or dosage of intervention have an impact on the effectiveness or harms of approaches to prevent PTSD or to improve health outcomes?

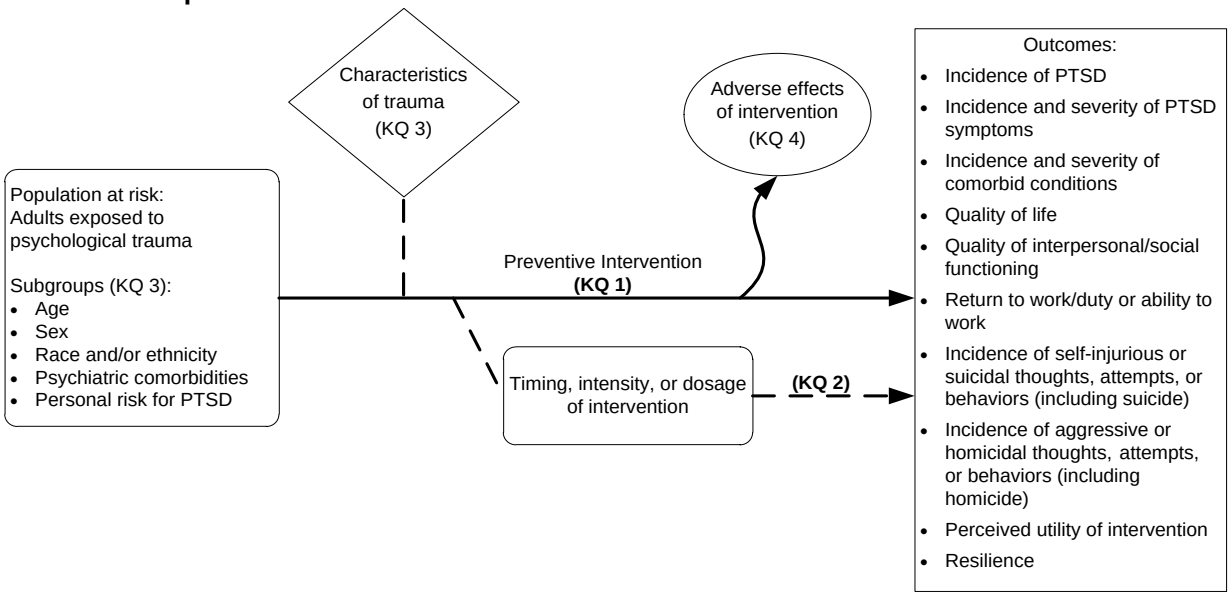
KQ 3: For adults exposed to psychological trauma, how does efficacy, effectiveness, or harms of early interventions to prevent PTSD differ for characteristics of traumatic exposure or subpopulations with respect to:

- demographic groups (defined by age, ethnic and racial groups, and sex),
- psychiatric comorbidities, or
- personal risk factors for developing PTSD (e.g., having a diagnosis of acute stress disorder (ASD) vs. not having the diagnosis)?

KQ 4: For adults exposed to psychological trauma, what are the absolute and comparative risks of harms from early interventions to prevent PTSD?

Figure A depicts the analytic framework for the comparative effectiveness of psychological, pharmacological, and emerging interventions for preventing PTSD in adults after exposure to trauma.

Figure A. Analytic framework for comparative effectiveness of interventions to prevent PTSD in adults after exposure to trauma



KQ = Key Question; PTSD = posttraumatic stress disorder

Methods

Literature Search Strategy

To identify articles relevant to each KQ, we searched PubMed®, CINAHL (Cumulative Index to Nursing and Allied Health Literature), the Cochrane Library, Embase, PILOTS (Published International Literature on Traumatic Stress), International Pharmaceutical Abstracts, PsycINFO®, and Web of Science. We used either Medical Subject Headings (MeSH) or major headings as search terms when available or key words when appropriate, focusing on terms to describe the relevant populations and interventions of interest. We limited the electronic searches to English-language and human-only studies. We searched sources from January 1, 1980, to July 30, 2012. In addition, we manually searched reference lists of pertinent reviews, included trials, and background articles for relevant citations that our searches might have missed. We searched for unpublished studies using ClinicalTrials.gov, the Web site of the U.S. Food and Drug Administration, the World Health Organization's International Clinical Trials Registry Platform, GreyMatters, and OpenGrey. In addition, the Scientific Resource Center requested scientific information packets from the relevant pharmaceutical companies, asking for any unpublished studies or data relevant for this review.

We developed eligibility criteria with respect to PICOTS and study designs for each KQ. Our population of interest was adults (ages 18 or older) exposed to psychological trauma. We included psychological (e.g., cognitive behavioral therapy, cognitive processing therapy, debriefing), pharmacological (e.g., beta blockers, second-generation antidepressants), and emerging (e.g., yoga, acupuncture) interventions used to prevent PTSD. Both inactive and active comparators of interest were eligible as control interventions. Our outcomes of interest focused on the incidence of PTSD and PTSD-related symptoms; PTSD symptom severity; and quality of life, functional capacity, and other patient-relevant health outcomes. Our subgroups of interest included demographic groups (defined by age, sex, and ethnic or racial groups), populations with

psychiatric comorbidities, and populations with different personal risk factors for developing PTSD.

For efficacy and comparative effectiveness, we focused on randomized controlled trials (RCTs) and prospective cohort studies. For assessment of the risk of harms, we also included retrospective controlled cohort studies. For studies to be eligible, the intervention had to be administered within 3 months of the traumatic event.

Two trained members of the research team independently reviewed all titles and abstracts for eligibility against our inclusion/exclusion criteria. We retrieved the full text of all articles included during the title and abstract review phase. If both reviewers agreed that a study did not meet the eligibility criteria, we excluded it. If the reviewers disagreed, conflicts were resolved with a third, senior team member.

Risk-of-Bias Assessment of Individual Studies

To assess the risk of bias (a threat to internal validity) of studies for major outcomes of interest, we used guidance from the AHRQ "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[8] We assessed selection bias, confounding, performance bias, detection bias, and attrition bias. We included questions about adequacy of randomization, allocation concealment, similarity of groups at baseline, blinding, attrition, whether intention-to-treat (ITT) analysis was used, method of handling dropouts, and treatment fidelity. We rated the studies as low, medium, or high risk of bias. Because our primary outcome of interest was the incidence of PTSD, we adopted a threshold of 20 percent for overall attrition. For outcomes with low event rates, attrition can substantially bias findings.[9]

Two independent reviewers assessed the risk of bias for each study; one of the two reviewers was always an experienced or senior investigator. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting with a third member of the team. If medium or low risk-of-bias studies were available, we omitted from our main analyses studies deemed high risk of bias by two reviewers. Such studies would not have increased the strength of the evidence and the certainty of our conclusions. If we were able to conduct quantitative syntheses, we used high-risk-of-bias studies for sensitivity analyses. In cases in which relevant information was unclear or not reported, we attempted to contact authors to get additional or unpublished information. When successful, we used this information in the findings.

For studies that met inclusion criteria and were of low or medium risk of bias, we extracted important information into evidence tables, which included characteristics of study populations, settings, interventions, comparators, study designs, methods, and results. We did not extract complete data from studies that we rated as high risk of bias.

Data Synthesis

In general, we used a "best evidence" approach to synthesize the available evidence. That is, we prioritized the evidence to emphasize studies that provided the most solid base for conclusions. If we did not find any studies with a low or medium risk of bias rating, we present results of high risk of bias studies. Conversely, if studies with low or medium risk of bias were available, we omitted high risk of bias studies from our syntheses because of the lack of reliability of their findings.

We conducted quantitative syntheses using meta-analyses of outcomes reported by multiple studies that were sufficiently homogeneous to justify combining their results. When quantitative synthesis was not appropriate (e.g., because of clinical heterogeneity, insufficient numbers of

similar studies, or insufficiency or variation in outcome reporting), we synthesized the data qualitatively.

We used random-effects models to estimate pooled effects. For continuous outcomes (e.g., scales for symptom reduction), we used weighted mean differences (WMD). If we had to combine multiple scales in one meta-analysis, we used the standardized mean difference (Cohen's d). For binary outcomes (e.g., incidence of PTSD), we calculated the relative risk (RR) between groups. For each meta-analysis, we conducted sensitivity analyses by adding studies that we rated as high risk of bias. We calculated the chi-squared statistic and the I^2 statistic to assess statistical heterogeneity in effects between studies. Heterogeneity was also explored through sensitivity analyses. Quantitative pairwise meta-analyses were conducted using Stata® version 11.1.

Strength of the Body of Evidence

We graded the strength of evidence (SOE) based on the guidance established for the Evidence-based Practice Center program.[10] Developed to grade the overall strength of a body of evidence, this approach incorporates four key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, strength of association (magnitude of effect), and publication bias.

We specified several outcomes a priori (with input from members of a technical expert panel) as important for grading strength of the body of evidence: incidence of PTSD; incidence and severity of PTSD symptoms; measures of depression and anxiety symptoms; quality of life; return to work or duty; incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide); incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide); rates of adverse events (overall or for specific events such as organ failure); mortality; and dropout rate because of adverse effects.

Two reviewers assessed each domain for each key outcome and determined an overall SOE grade based on domain ratings. For each assessment one of the two reviewers was always an experienced investigator. In the event of disagreements on the domain or overall grade, they resolved differences by consensus discussion or by consulting with a third, senior investigator. Appendix G in the main report provides the detailed rationale for SOE grades.

Applicability

We assessed applicability of the evidence following guidance from the "Methods Guide for Comparative Effectiveness Reviews."[11] We used the PICOTS framework to explore factors that affect applicability. Some factors identified a priori that may limit the applicability of evidence include the following: age of enrolled populations, sex of enrolled populations, race or ethnicity of enrolled populations, few studies enrolling subjects with exposure to certain types of trauma, or few studies distinguishing or reporting the type of traumatic exposure for a heterogeneous population.

Throughout the report, we use the terms "efficacy" and "comparative effectiveness." By efficacy, we mean the efficacy or effectiveness of an intervention tested against some type of inactive control (e.g., placebo or waitlist). By comparative effectiveness we mean the efficacy or effectiveness of an intervention compared with another intervention of interest. In this report, we did not distinguish between explanatory (or efficacy) and pragmatic (or effectiveness) studies.

Results

First, we describe results of the literature searches and ratings of the risk of bias. Second, we present available evidence for each KQ, focusing on efficacy or risk of harms and then comparative effectiveness or risk of harms. Within each section, we discuss evidence on psychological interventions first, followed by studies on pharmacological interventions, and lastly by studies on emerging interventions. We give SOE grades for major outcomes on which we had any evidence at all; several specified a priori were not present in our evidence base. The main report gives detailed descriptions of included studies in text and in the evidence tables in its Appendix E.

Results of the Literature Searches

We identified 2,563 citations from searches, reviews of reference lists, and grey literature. Overall, we included 19 trials in our main analyses. Another 37 studies otherwise meeting inclusion criteria were omitted from our main analyses because of a high risk of bias. If not stated otherwise, trials described below are of medium risk of bias.

KQ 1: Efficacy and Comparative Effectiveness of Interventions To Prevent PTSD

Efficacy

Thirteen studies addressed efficacy.[12-24] Of these, each involved psychological interventions; one study included a pharmacological intervention, and one evaluated an emerging intervention (collaborative care). These studies were conducted in[15,18,23,24] and outside the United States.[12-14,16,17,19-21] They included a variety of trauma-exposed populations such as victims of crime, motor vehicle accidents (MVAs), other types of accidents, intimate partner violence, sexual assault, and terrorist attacks; critically ill patients; and mothers experiencing traumatic childbirth or caring for a critically ill child. We did not find any evidence on most pharmacological interventions. In addition, we had little or no evidence about terrorist attacks, sexual assault, natural disaster, or combat.

We identified trials that reported on one or more of eight different psychological interventions: debriefing, cognitive behavioral therapy (CBT), CBT combined with hypnosis, cognitive therapy (CT), prolonged exposure therapy (PE), psychoeducation, self-help materials, and supportive counseling (SC). The two key outcomes are incidence of PTSD (i.e., preventing PTSD) and reducing the severity of PTSD symptoms. From these studies, we concluded that debriefing is not effective in preventing PTSD or reducing the severity of PTSD symptoms in civilian victims of crime, assault, or accident trauma at 6-month followup (low SOE). We had insufficient data (single study) to determine the efficacy of debriefing at 2- or 6-week or 11-month followup.

From a single study, we concluded that collaborative care (CC), a stepped combination of care management, psychopharmacology, and CBT, produces a greater decrease in PTSD symptom severity at 6, 9, and 12 months after injury than usual care (low SOE).[24] However, data addressing whether groups differed in PTSD diagnosis 12 months after injury were not conclusive (insufficient SOE).

For most other interventions—namely, CBT, CBT combined with hypnosis, CT, PE, psychoeducation, self-help material, SC, and the two pharmaceuticals escitalopram (a selective

serotonin reuptake inhibitor [SSRI]) and hydrocortisone—we had single studies with small treatment arms (generally fewer than 80 subjects). This paucity of information led us to conclude that the evidence was insufficient to support their efficacy for preventing PTSD or reducing PTSD symptom severity.

For studies that had assessed the efficacy of interventions in terms of reducing symptoms of anxiety and depression, we found insufficient evidence. Table A summarizes the main findings and the SOE for the efficacy of psychological, pharmacological, and emerging interventions for this section of KQ 1.

Comparative Effectiveness

Eight studies addressed the effectiveness of a psychological intervention compared with another psychological intervention.[13,17,20,21,25-28] The interventions included Battlemind training, CBT, CBT combined with hypnosis, CT, PE, various forms of debriefing, and SC. One study compared psychological interventions with an SSRI.[20] All these studies were conducted outside the United States and included samples exposed to a variety of traumas, such as combat, crime, physical assault, motor vehicle and other types of accidents, and terrorist attacks. We did not include studies comparing two or more medications; the one study we had identified was rated high risk of bias. We did not identify any studies that evaluated the comparative effectiveness of any emerging interventions.

Our meta-analyses of trials that compared CBT with SC in a sample of participants with ASD found that at both the end of treatment and at 6-month followup, CBT was more effective than SC in reducing the severity of PTSD symptoms as measured by the Impact of Event Scale (IES) (moderate SOE). However, at both the end of treatment and at 6-month followup, CBT was no more effective than SC for preventing PTSD (low SOE), reducing symptoms of anxiety (moderate SOE), or reducing symptoms of depression (low SOE).

Because the knowledge base comprises largely single studies with small sample sizes, we concluded that the evidence was insufficient to determine the comparative effectiveness of most of the psychological interventions in preventing PTSD or reducing PTSD symptom severity.

Only one study compared psychological interventions (CT and PE) with a medication (escitalopram, an SSRI). Because of methods limitations, we could not draw any conclusions about the comparative effectiveness of an SSRI and a psychological intervention.

Table B summarizes the main findings and the SOE for the comparative effectiveness of psychological and pharmacological interventions for this section of KQ 1.

Table A. Summary of findings and strength of evidence for the efficacy of psychological, pharmacological, and emerging interventions to prevent PTSD and reduce PTSD symptom severity

Intervention, Population	Outcome	Results	SOE
CBT, Civilian, mixed trauma types[16]	Incidence of PTSD	Inconclusive, single trial (N=46)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=46)	Insufficient
CT, Civilian, mixed trauma types[13,20]	Incidence of PTSD	Inconclusive, single trial (n=133)	Insufficient
	PTSD symptom severity	Inconclusive, 2 trials (n=193), inconsistent findings at different assessment intervals	Insufficient
CC, Civilian, mixed trauma types requiring hospitalization[24]	Incidence of PTSD	Inconclusive, single trial (N=207)	Insufficient
	PTSD symptom severity	CC produces a greater decrease in PTSD symptom severity at 6, 9, and 12 months after injury than usual care (N=207)	Low
Debriefing, Civilian mixed trauma types[17,21]	Incidence of PTSD	Debriefing not significantly different than control at multiple followup assessment intervals across 2 trials (n=341)	Low
	PTSD symptom severity	Debriefing not significantly different than control at multiple followup assessment intervals across 2 trials (n=341)	Low
Exposure-based therapies, Civilian, mixed trauma types[13,18,20]	Incidence of PTSD	Inconclusive, 3 trials (n=355), inconsistent findings at different assessment intervals	Insufficient
	PTSD symptom severity	Inconclusive, 3 trials (n=355) with different assessment intervals that prevent direct comparisons	Insufficient
Hydrocortisone stress dose, Civilians undergoing high-risk cardiac surgery[22]	Incidence of PTSD	Inconclusive, single trial (n=28)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=28)	Insufficient
Psychoeducation, Civilian crime[17] and injury[23] victims	Incidence of PTSD	Inconclusive, 2 trials (N=182) with different assessment intervals that prevent direct comparisons	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=103)	Insufficient
Self-help materials, Women newly diagnosed with breast cancer[12]	PTSD symptom severity[a]	Inconclusive, single trial (N=49)	Insufficient
SSRI (escitalopram), Civilian, mixed trauma types[20]	Incidence of PTSD	Inconclusive, single trial (n=139)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=139)	Insufficient
SC, Women, mixed trauma types[14,15,19]	Incidence of PTSD	Inconclusive, single trial (N=103)	Insufficient
	PTSD symptom severity	Inconclusive, 2 trials (n=336), inconsistent findings at different assessment intervals using different outcome measures	Insufficient

CBT = cognitive behavioral therapy; CC = collaborative care; CT = cognitive therapy; N = entire sample; n = subset of sample; PTSD = posttraumatic stress disorder; SC = supportive counseling; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitor

[a]Incidence of PTSD not reported.

Table B. Summary of findings and strength of evidence for the comparative effectiveness of psychological, pharmacological, and emerging interventions to prevent PTSD and reduce PTSD symptom severity

Intervention, Population	Outcome	Results	SOE
Battlemind training vs. standard brief, UK military service members[28]	PTSD symptom severity	Inconclusive, single trial (n=2,443)	Insufficient
CBT vs. CBT+Hypnosis, Civilian, mixed trauma types[27]	Incidence of PTSD	Inconclusive, single trial (n=63)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=63)	Insufficient
CBT vs. SC, Civilian, mixed trauma types with ASD[25-27]	Incidence of PTSD	CBT not significantly different than SC at end of treatment (RR, 0.27; 95% CI [0.05 to 1.29]; I^2=71.8%) or at 6 months (RR, 0.46; 95% CI [0.21 to 1.01]; I^2=44.9%); 3 trials (n=105)	Low
	PTSD symptom severity	Greater reduction for CBT than for SC on IES-I at the end of treatment (WMD, -7.85; 95% CI [-11.18 to -4.53]; I^2=1.3%) and at 6 months (WMD, -8.19; 95% CI [-11.79 to -4.58]; I^2=6.8%); 3 trials (n=105) Greater reduction for CBT than for SC on IES-A at end of treatment (WMD, -14.04; 95% CI [-19.37 to -8.71]; I^2=53.8%) and 6 months (WMD, -9.94; 95% CI [-15.06 to -4.83]; I^2=44.0%); 3 trials (n=105)	Moderate
CBT+Hypnosis vs. SC, Civilian, mixed trauma types[27]	Incidence of PTSD	Inconclusive, single trial (n=54)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=54)	Insufficient
CT vs. PE Civilian, mixed trauma types[13,20]	Incidence of PTSD	Inconclusive, 2 trials (n=163), inconsistent findings at different assessment intervals; 1 trial used a "completer analysis"	Insufficient
	PTSD symptom severity	Inconclusive, 2 trials (n=163), inconsistent findings at different assessment intervals; 1 trial used a "completer analysis"	Insufficient
CT vs. SSRI (escitalopram). Civilian, mixed trauma types[20]	Incidence of PTSD	Inconclusive, single trial (n=54)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=54)	Insufficient
Emotional debriefing vs. Educational debriefing Civilian, mixed trauma types[21]	Incidence of PTSD	Inconclusive, single trial (n=155)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=155)	Insufficient
PE vs. SSRI (escitalopram) Civilian, mixed trauma types[20]	Incidence of PTSD	Inconclusive, single trial (n=71)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=71)	Insufficient
Psychoeducation vs. Debriefing combined with psychoeducation Civilian, crime victims[17]	Incidence of PTSD	Inconclusive, single trial (n=106)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=106)	Insufficient

ASD = acute stress disorder; CBT = cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; CI = confidence interval; CT = cognitive therapy; IES-A = Impact of Event Scale-Avoidance subscale; IES-I = Impact of Event Scale-Intrusions subscale; n = subset of sample; PE = prolonged exposure therapy; PTSD = posttraumatic stress disorder; RR = relative risk; SC = supportive counseling; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitor; UK = United Kingdom; WMD = weighted mean difference

KQ 2: Impact of Timing, Intensity, and Dosing

The evidence is scarce on the impact of timing, intensity, and dosing on the effectiveness or risk of harms of interventions used to prevent PTSD. Overall, studies addressed timing and dosing questions;[29-32] two were rated as high risk of bias.[30,31] We found no studies on the impact of intensity of intervention for any psychological or emerging interventions. Table C summarizes the main findings and the SOE for KQ 2 for incidence of PTSD and PTSD symptom severity.

Table C. Summary of evidence of the impact of timing, intensity, and dosing on the effectiveness of interventions and strength of evidence

Intervention, Population	Outcome	Results	SOE
Debriefing (CISD) timing (early vs. late), Robbery victims[29]	PTSD symptom severity	Inconclusive, single trial (N=77)	Insufficient
Pharmacological sedation depth (light vs. deep) Critically ill patients[32]	Incidence of PTSD	Inconclusive, single trial (N=137)	Insufficient

CISD = critical incident stress debriefing; N = entire sample; PTSD = posttraumatic stress disorder; SOE = strength of evidence

One RCT addressed the impact of timing of a psychological intervention.[29] Immediate debriefing (within 10 hours) compared with late debriefing (after 48 hours) led to significantly fewer posttraumatic symptoms that victims experienced (insufficient SOE). No evidence was available on the impact of timing for any other psychological, pharmacological, or emerging interventions or any other outcomes.

In one RCT, dosing of sedation (light vs. deep) in critically ill patients did not affect posttraumatic symptoms, depression, or anxiety (insufficient evidence).[32] We did not find any eligible evidence on the effect of dosing for any other pharmacological or emerging interventions to prevent PTSD.

KQ 3: Subgroups

Evidence is also sparse on whether the effect of early interventions differs among groups defined by sociodemographic characteristics, psychiatric diagnoses and comorbidities, personal risk factors for developing PTSD, or types of trauma. Eight studies met our inclusion criteria for subgroup analyses,[12,17,18,21,28,29,33,34] but we rated two as high risk of bias.[33,34] Table D summarizes the main findings and the SOE for KQ 3 for two main categories of outcomes—the numbers of PTSD symptoms and depression symptoms. We report the outcomes in terms of whether the subgroup characteristic, such as sex, modified the effect of any intervention(s)—that is, whether individuals in the intervention and control subgroups did or did not differ at various followup measurements.

Two trials reported consistent results that effects of early psychological interventions on PTSD symptoms were similar for men and women.[17,29] However, because neither trial reported the magnitude of the estimated effect or its precision, we graded the SOE as low.

One trial tested the effect of a debriefing intervention—critical incident stress debriefing (CISD)—in subgroups with a history of either depression or child abuse, but it did not report magnitude or precision of effects (SOE insufficient in all cases).[17]

One trial reported that the severity of trauma exposure did not modify the effect of Battlemind training among United Kingdom returning military service members (insufficient SOE).[28]

One trial reported that PE reduced symptoms of PTSD among survivors of sexual assault but not physical assault or motor vehicle accidents (SOE insufficient).[18]

Table D. Summary of evidence and strength of evidence for the effect of early interventions in various subgroups

Subgroup; Intervention; Population	Outcome	Results	SOE
Demographic groups: sex; CBT, CISD; Crime victims[17,29]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	The effect of CBT or CISD did not differ between men and women; 2 trials (N=234), consistent findings	Low
Type of trauma; PE, Mixed civilian trauma[18]	Incidence of PTSD	Inconclusive, single trial (N=137)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=137)	Insufficient
Psychiatric diagnosis: previous depression; Debriefing; Crime victims[17]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=157)	Insufficient
History of child abuse[a]; psychoeducation vs. debriefing combined with psychoeducation; Crime victims[17]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=157)	Insufficient
Severity of baseline distress[a]; Debriefing, self-help workbook; Crime victims, women with breast cancer[12,21]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconsistent findings, 2 trials (N=285); 1 trial reported that debriefing increased PTSD symptoms among those with high baseline PTSD arousal symptoms; and 1 trial reported that a self-help workbook decreased PTSD symptoms to a greater extent in those with high baseline PTSD symptom severity	Insufficient
Severity of combat exposure[a]; UK military service members[28]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=2,443)	Insufficient

CBT = cognitive behavioral therapy; CISD = critical incident stress debriefing; N = entire sample; n = subset of sample; PE = prolonged exposure therapy; PTSD = posttraumatic stress disorder; SOE = strength of evidence; UK = United Kingdom
[a]Personal risk factor for PTSD.

Two trials provided inconsistent findings on whether baseline severity of PTSD symptoms modified the effect of two different psychological interventions (SOE insufficient).[12,21]

KQ 4: Risk of Harms

Little evidence exists addressing either the general or the comparative risks of harms from early interventions to prevent PTSD. Four studies assessed harms;[21,32,35,36] two were rated as high risk of bias.[21,32] For most interventions, no evidence was available. Table E summarizes the main findings and the SOE for KQ 4.

Table E. Summary of findings and strength of evidence about harms

Intervention, Population	Outcome	Results	SOE
Emotional debriefing vs. no debriefing, Civilian, medical trauma[21]	PTSD symptom severity	For subgroup with hyperarousal, inconclusive, single trial (N=236), inconsistent findings at different assessment intervals	Insufficient
Pharmacological sedation (light vs. deep), Critically ill patients[32]	Mortality	Inconclusive, single trial (N=137)	Insufficient
	Incidence of adverse events	Inconclusive, single trial (N=137)	Insufficient

N = entire sample; PTSD = posttraumatic stress disorder; SOE = strength of evidence

A three-armed RCT (low risk of bias) considered absolute risk of greater severity of PTSD symptoms in patients presenting to an outpatient psychiatric clinic after psychological trauma.[21] In a subgroup of patients with early hyperarousal, those receiving emotional debriefing experienced higher PTSD severity at 6 weeks than those not receiving such debriefing. The investigators did not find this difference in this subgroup at either 2 weeks or 6 months or in any other subgroups (insufficient evidence). We found no other trials of psychological or pharmacological interventions that provided information on risks of early interventions.

One randomized open-label trial considered comparative risk of harms from light versus deep sedation for patients requiring mechanical ventilation.[32] The two groups did not differ with regard to rates of mortality (either during their stays in the intensive care unit or in their overall hospitalization) or in the incidence of adverse events (organ dysfunction, hypertension, and tachycardia) (insufficient evidence).

High-Risk-of-Bias Studies

Table 7 in the main report presents a summary of the study designs, prevention type (i.e., universal or targeted), study comparisons, results, and methodological shortcomings of the 37 studies we rated as high risk of bias. In most cases, we had data from studies of either low or medium risk of bias, and we did not include these high-risk-of-bias studies in our analyses. For some interventions, however, we found only high-risk-of-bias studies. We summarize their findings in the main report.

Discussion

Key Findings and Strength of Evidence

In this comprehensive comparative effectiveness review (CER), we conducted a systematic review of the efficacy, comparative effectiveness, and harms of psychological, pharmacological, and emerging interventions for the prevention of PTSD in adults exposed to psychological trauma. Overall, for most interventions and outcomes of interest, evidence was either entirely lacking or insufficient to draw conclusions. In addition, in the available body of evidence, the majority of eligible studies were fraught with methodological shortcomings and were rated as high risk of bias. Consequently, we are able to draw only a few conclusions with some degree of certainty:

- CC is effective at reducing the severity of PTSD symptoms for civilian victims of injuries requiring inpatient surgical admission at 6-month, 9-month, and 12-month followup (low SOE, one RCT).
- Debriefing is not effective in reducing either the incidence of PTSD or severity of PTSD or depressive symptoms in civilian victims of crime, assault, or accident trauma at 6-month followup (low SOE, two RCTs).
- In individuals with ASD, a meta-analysis found that adults who received CBT had greater reductions in severity of PTSD symptoms than those who received SC (moderate SOE, three RCTs). Differences between CBT and SC with respect to preventing PTSD (low SOE, three RCTs), reducing the severity of depression symptoms (low SOE, three RCTs), or reducing the severity of anxiety symptoms (moderate SOE, three RCTs) also favored CBT; results, however, did not reach statistical significance.

- The effectiveness of psychological interventions to prevent PTSD does not differ between men and women (low SOE).

For many interventions we did not have sufficient evidence to draw conclusions about either efficacy or comparative effectiveness. How available results from some head-to-head studies might be extrapolated to comparisons with other interventions remains unclear. Consistent with other reviews,[37-39] we also concluded that psychological debriefing is not useful for preventing PTSD. One of these reviews also concluded that debriefing could actually be harmful to participants and should cease;[38] we cannot confirm this conclusion from our evidence base.

Our primary outcome measures were prevention of PTSD as a DSM-IV-TR disorder (defined as incidence of PTSD) and reduction of PTSD symptom severity. Most of the studies we reviewed, however, determined PTSD symptom scores without establishing the incidence of PTSD. Whether such findings can be extrapolated reliably to differences in the incidence of PTSD remains unclear on the basis of our results.

Overall, two major limitations characterize this body of evidence. First, for many interventions, the evidence was insufficient on the efficacy, comparative effectiveness, or risk of harms of interventions. Despite our eligibility criteria, including observational studies for effectiveness and harms, we could not draw conclusions for or against benefits and harms for the majority of our interventions of interest. Even when studies assessing the effectiveness of an intervention were available, they often did not assess harms. Although lack of evidence cannot be equated with lack of effectiveness or harms, incautious use of interventions without proven net benefit has the potential to cause more harms than benefits.[38]

Second, available evidence frequently showed shortcomings in study methods. Of 56 studies meeting our eligibility criteria, we rated 37 as high risk of bias using standard criteria and only 3 as low risk of bias. Studies assessed as high risk of bias have significant flaws of various types (stemming from serious errors in design, conduct, or analysis) that may invalidate their results. Consequently, the evidence base for most of the major outcomes we sought to review was insufficient to draw conclusions. The SOE grades for only a few outcomes for only a few interventions could be rated as low or moderate, indicating reasonable confidence in effect estimates of those studies.

Which early psychological or pharmacological interventions would be most effective and least harmful in preventing PTSD among all adults exposed to trauma cannot be specified from our results. Among adults exposed to trauma who meet criteria for ASD, however, our findings support the use of brief CBT interventions over SC for reducing PTSD symptom severity, although the SOE supporting this conclusion is low. Our results did not identify any class of drugs that has been shown to be effective in preventing PTSD.

We found that being male or female did not modify the effect of early intervention among crime victims (low SOE), suggesting that clinicians may not need to take the sex of a patient into consideration when choosing a preventive intervention for crime victims. Whether that observation would generalize to other types of trauma is unclear. We found no evidence about which early interventions are more or less effective for other subgroups of interest.

Evidence addressing the absolute risks or comparative risks of harms from early interventions intended to prevent PTSD was similarly insufficient.

Applicability

The included studies covered diverse populations exposed to a wide range of traumas and not diagnosed with PTSD, but the findings may not generalize to survivors of terrorist attack, natural

disaster, sexual assault, or combat who were underrepresented or unrepresented. In addition, there were too few data to assess whether outcomes differed according to type of trauma or specific demographic factors such as age, since only adults over age 18 years were studied. Many of the included studies were conducted outside the United States with civilian populations (not U.S. military abroad), but there were too few data to analyze whether cross-cultural differences in setting or intervention delivery systems had any impact on outcome. Generally, the findings reflect interventions that were representative of those used in the treatment of PTSD, outcomes that were derived using clinically meaningful and valid measures, and settings that provided real-world context; but, because there is no accepted "usual clinical care" model for preventing PTSD in trauma victims, we cannot draw conclusions about the applicability of the findings to primary care or any other specific setting in which trauma victims present for care. Finally, with respect to the comparative effectiveness of two or more treatments, our meta-analyses indicated some benefit of CBT over SC in reducing PTSD severity in trauma victims who met criteria for ASD.[25-27] However, because individuals with ASD constitute the minority of those who later develop PTSD,[40-43] these findings may not generalize to the broader population of individuals at risk for developing PTSD.

Research Gaps

The most striking finding from this review is the paucity of high-quality evidence to address each of the four Key Questions. As a result of the small number of studies of low or moderate risk of bias that assessed different interventions, no findings from the included studies could be graded as high SOE. With respect to differences between interventions in PTSD-specific benefits, we had only one finding with moderate SOE (that CBT is more effective than SC in reducing symptoms of PTSD for individuals with ASD) and one with low SOE (that collaborative care produces a greater decrease in PTSD symptom severity after injury compared with usual care). All other findings for incidence of PTSD or PTSD symptom severity were graded as having insufficient strength of evidence.

Specific and important methodological flaws that we identified included the following:

- Inadequate randomization procedures
- High rates of attrition
- Inadequate statistical approaches for data analysis (e.g., lack of ITT analysis, or lack of statistical adjustment for significant between-group differences at baseline)

An important task of systematic reviews is to assess whether design and conduct of included studies provide adequate protection against bias. The methodological shortcomings of many studies conducted to test interventions to prevent PTSD substantially limit our confidence that results accurately reflect the truth. Therefore, the focus of this report is on evidence from studies rated as having low or medium risk of bias.

Future studies on early interventions to prevent PTSD should institute procedures to avoid or minimize these methodological problems if possible. Adequate and concealed methods of randomization should be relatively easy to implement. Statistical consultation can help investigators use more appropriate methods than "completers analysis" or "last observation carried forward" for handling missing data.

Minimizing attrition, however, may be more difficult to achieve, for multiple reasons. Adults exposed to trauma may have difficulty building the commitment required for long-term followup because their first contact with the research team occurs at a time when they are likely to be highly distressed. Survivors who are exposed to traumas that disrupt community infrastructure,

such as natural disasters, are likely to be highly mobile and difficult to locate for followup interviews. Specific protocols for minimizing attrition in studies of traumatized populations may help maintain high rates of followup.[44]

Among the 19 studies that we included and rated as low or medium risk of bias, there was frequently insufficient or no evidence to address KQ 2 (timing and dose of intervention), KQ 3 (effectiveness in subgroups), or KQ 4 (harms). Future research can fill the gaps in multiple ways. For KQ 2, future studies could evaluate the comparative effectiveness of the same intervention given at different time intervals after exposure to trauma, while incorporating inactive control interventions. For studies in which the timing of the intervention is not explicitly randomized, investigators could measure the time between trauma exposure and intervention and carry out preplanned subgroup analyses by time to intervention. Investigators could also attempt to recruit sample sizes that provide sufficient power to detect prespecified group-by-intervention interaction effects. All the following subgroups could be considered: (1) demographic groups: sex, race, or ethnicity; (2) types of trauma; and (3) severity of trauma and severity of baseline distress. In examining harms or unintended side effects of both psychological and pharmacological treatments, researchers should identify potential adverse effects before starting their study and use or adapt validated instruments to measure adverse effects.

Psychological first aid has gained rapid acceptance as a universal intervention for people in the acute aftermath of trauma, but no studies of this intervention met inclusion criteria for our review. Although psychological first aid was not designed as an intervention to reduce the incidence of PTSD, it may have beneficial or adverse effects on mental health among trauma survivors.[45,46] Rigorous studies of psychological first aid should be conducted.

One key research gap for studies of targeted prevention is the limited ability to identify people who are at high risk of developing PTSD shortly after they have been exposed to trauma. The development of a clinical prediction rule to identify, shortly after exposure to trauma, the relatively small percentage of such individuals who will develop PTSD would be an enormous help to the field.

We recommend that additional work be devoted to developing a clinical prediction rule based on inclusion of key variables that, together, are highly predictive of PTSD. Those variables could include pretrauma factors, event characteristics, and peri-event responses. An ideal prediction rule would have strong ability to discriminate between people who do or do not develop PTSD, be composed of a relatively small number of variables that can be measured easily and quickly, and produce results that are easily interpretable by health care providers who interact with survivors shortly after they are exposed to trauma. After a clinical prediction rule has been derived and validated in populations exposed to a variety of trauma types, it should be evaluated, in a randomized trial, to determine whether use of the rule, in concert with an intervention to reduce the incidence of PTSD, results in reduced incidence of PTSD. We believe that this is a promising approach to realizing the potential of targeted strategies for preventing PTSD.

Conclusions

Evidence supporting the efficacy of most interventions used to prevent PTSD is lacking. If available in a given setting, brief trauma-focused CBT might be the preferable choice for reducing PTSD symptom severity in adults with ASD; CC may be helpful for reducing PTSD symptom severity post-injury; and debriefing is not an effective prevention intervention.

Our findings highlight the inherent difficulties of conducting research on prevention interventions—difficulties that are often more challenging for mental-health-related research than for research on medical or other health-related issues. Our body of evidence was highly limited because of the paucity of methodologically sound studies. Although disappointing, our findings underscore the need for ongoing research efforts in the field of PTSD prevention. Our findings lead us to conclude that developing a clinical prediction algorithm to identify those who are at high risk of developing PTSD after trauma exposure is perhaps a more crucial next step in the field of PTSD prevention than continuing to study which interventions are more effective than others. The ability to identify people most at risk for developing PTSD and then to evaluate the effectiveness of prevention interventions in those individuals should be the focus of future clinical and research efforts.

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Introduction

Background

The Condition

Posttraumatic stress disorder (PTSD) may develop following exposure to a traumatic event. According to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders, Text Revision (DSM-IV-TR),[1] the essential feature of PTSD is the development of characteristic symptoms following exposure to an extreme traumatic stressor. The stressor may include having direct personal experience of an event that involves actual or threatened death or serious injury or other threat to one's physical integrity; witnessing an event that involves death, injury, or a threat to the physical integrity of another person; or learning about unexpected or violent death, serious harm, or threat of death or injury experienced by a family member or other close associate. The DSM-IV-TR also requires that the person's response to the event involve intense fear, helplessness, or horror. Table 1 lists the full DSM-IV-TR criteria.

Table 1. Diagnostic criteria (DSM-IV-TR) for posttraumatic stress disorder

Criterion	Symptom or Description
Criterion A: Trauma (both)	• Traumatic event that involved actual or threatened death, serious injury, or threat to physical integrity • Intense response of fear, helplessness, or horror
Criterion B: Reexperiencing symptoms (one or more)	• Intrusive recollections of events • Recurrent distressing dreams of the event • Acting or feeling as if the traumatic event were recurring • Distress at internal or external reminders of the trauma • Physiological reaction to internal or external reminders
Criterion C: Persistent avoidance and numbing (three or more)	• Avoidance of thoughts, feelings, or conversations associated with trauma • Avoidance of activities, places, or people that arouse recollections of trauma • Failure to recall an important aspect of trauma • Loss of interest or participation in significant activities • Detachment from others • Restricted range of affect • Lost sense of the future
Criterion D: Hyperarousal (two or more)	• Difficulty falling or staying asleep • Irritability or outburst of anger • Difficulty concentrating • Hypervigilance • Exaggerated startle response
Criterion E: Duration of disturbance	• Duration of disturbance symptoms is more than 1 month
Criterion F: Clinically significant distress or impairment	• Disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of function

DSM-IV-TR = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision

Some traumatic events that are directly experienced or to which one can be exposed include military combat, violent personal assault, being taken hostage, a terrorist attack, torture, natural or man-made disasters, and being diagnosed with a life-threatening illness.[1] PTSD is also highly comorbid with other psychiatric disorders; data from epidemiologic studies have found that a majority of adults with PTSD have another psychiatric disorder, mostly notably substance use disorders and major depressive disorder.[2] Subgroups of people with PTSD who could have

different responses to various treatments include military personnel or veterans, people with comorbid conditions, groups defined by sex, first responders, refugees, disaster victims, racial and ethnic minorities, and those with different PTSD symptoms.

Prevalence of Traumatic Events

Studies suggest that adults experience a broad range of traumatic events throughout their lives. The frequency of these events may vary by the group studied, for example, civilian versus noncivilian samples. Studies conducted in the 1990s attempted to identify and describe the prevalence of traumatic events in nonclinical samples. Resnick et al. found that lifetime exposure to any type of traumatic event was 69 percent in a sample of 4,008 adult U.S. women.[3] The National Comorbidity Survey indicated that 60 percent of men and 51 percent of women reported experiencing at least one traumatic event in their lifetimes.[4]

Most of the research has focused on assessing the burden of trauma in different populations. Not surprisingly, studies among groups at risk of occupational exposure to trauma, such as police officers, firefighters, and military service members, have shown high rates of trauma exposure.[5] Several studies of the prevalence of traumatic events among college students all showed that exposure to traumatic events was relatively common, with lifetime prevalence ranging from 39 to 84 percent.[6-8]

Development of PTSD and Rationale for Early Intervention To Prevent PTSD

Many theories focus on the role of disturbances in memory (e.g., problems with memory formation, retrieval, bias, and saliency); they argue that alterations in the normal processes of memory are key to understanding the development and maintenance of PTSD. One of these theories suggests that when trauma-related experiences are not properly integrated into memory, individuals may re-experience symptoms of PTSD.[9]

Intense affect during a traumatic event and its accompanying physiological arousal have been associated with the development of PTSD.[10,11] Dissociation or detachment during the event has also been found to be a significant predictor of PTSD.[10] In extreme threat situations, strong affect can result in dissociation which prevents trauma-related information from being fully consolidated within memory. Incomplete memory consolidation may cause an individual to retain a limited amount of information about the event, make the memory less accessible, or both. The ability to access full or complete trauma-related memories is a core feature of several psychological theories of PTSD prevention and/or treatment.

Stress hormones released during exposure to a traumatic event have also been implicated in the development of PTSD. Heightened peri-traumatic noradrenergic activity may enhance consolidation of memory for the event.[12] Central noradrenergic activity also has other effects on information processing, for example narrowing attentional focus.[13] Thus, peri-traumatic hyperarousal might lead to explicit memory for a traumatic event which is strongly consolidated but relatively poor in quality, thus contributing to some of the symptoms of PTSD.

Cognitive theories of PTSD are based on the concept that information associated with a traumatic event is inconsistent with the information contained in an individual's core schema about themselves, others, and the world. An individual exposed to a traumatic event tries to make sense of the experience but has difficulty fully integrating it into his or her existing schema. Over time, this disintegration manifests itself in the symptoms and behaviors classified as PTSD.

Maladaptive beliefs related to the traumatic event have also been identified as a risk factor for the development of PTSD.[14]

The implications of these various theories provide a rationale for myriad early intervention strategies, which for this review we consider to be those provided within 3 months of the trauma. We chose to define early interventions as those offered within the first 3 months post-trauma for two reasons. One, because the onset of symptoms of PTSD usually occurs within 3 months after the traumatic event[15] and two, because in order to meet the diagnostic criteria for PTSD, symptoms must be present for at least 1 month. By focusing on interventions that occur within 3 months post-trauma, we are allowing sufficient time for posttraumatic symptoms to develop and identifying interventions offered during the period of time when people could have symptoms of PTSD, but not yet meet the diagnostic criteria for PTSD. Variability of types of trauma, contexts in which trauma occur, and individual differences of those exposed to traumatic events are likely to prohibit a "one size fits all" model for early intervention.

Burden and Cost of PTSD

Shortly after exposure to trauma, many people experience some of the symptoms of PTSD. In most people, those symptoms resolve spontaneously in the first several weeks after the trauma. However, in approximately 10 percent to 20 percent of those exposed to trauma, PTSD symptoms persist and are associated with impairment in social or occupational functioning.[5] Although approximately 50 percent of those diagnosed with PTSD improve without treatment in 1 year, 10 percent to 20 percent develop a chronic unremitting course.[16]

The 2000 National Comorbidity Survey-Replication (NCS-R) estimated lifetime prevalence of PTSD among trauma-exposed adults in the United States to be 6.8 percent (9.7% in women and 3.4% in men) and current (12-month) prevalence to be 3.6 percent (5.2% in women and 1.8% in men), or more than 7.7 million American adults per year.[17-19] Some demographic or occupational groups, such as military personnel, are at higher risk of PTSD because of higher rates of exposure to trauma.

Estimates from the National Vietnam Veterans Readjustment Survey (NVVRS) found a lifetime PTSD prevalence estimate of 18.7 percent and a current PTSD prevalence estimate of 9.1 percent[20] among Vietnam veterans. Surveys of military personnel returning from operations in Afghanistan and Iraq have yielded estimates ranging from 6.2 percent for U.S. service members who fought in Afghanistan to 12.6 percent for those who fought in Iraq.[21] In addition to lives lost from increased risk of suicide, PTSD is associated with high medical costs and high social costs because PTSD is a strong risk factor for crime, poor work performance and associated job losses, and familial discord. The economic cost of the PTSD and depression cases among Operation Enduring Freedom/Operation Iraqi Freedom veterans alone (including medical care, foregone productivity, and lives lost through suicide) is estimated at $4 billion to $6 billion over 2 years.[22]

Many people with PTSD do not seek treatment. Among those who do, many receive inadequate treatment or care that is not empirically based.[17,23] Several PTSD outcome studies demonstrate the cost-effectiveness of early diagnosis and appropriate treatment, especially when compared with the cost of inadequate or ineffective treatment occurring prior to a correct diagnosis.[24] In addition to consequences related to PTSD, people affected by these disorders have higher rates of psychiatric comorbidity, suffer decreased role functioning such as work impairment (on average, 3.6 days of work impairment per month), and experience many different

adverse life-course consequences (e.g., reduced educational attainment, work earnings, marriage attainment, and child rearing).[25]

Prevention Strategies

The first generation of research on PTSD prevention focused primarily on universal prevention (i.e., the delivery of interventions to all people exposed to trauma, regardless of symptoms or risk of developing PTSD). However, based on evidence that 1) debriefing interventions for all people exposed to particular traumas did not reduce PTSD and 2) most people exposed to trauma experience symptoms of PTSD but do not develop PTSD and its attendant functional impairment, a new model of PTSD prevention, targeted prevention, has generated a second generation of PTSD prevention research. The goal of targeted prevention is to identify, from among all people exposed to trauma, those individuals who are at high risk of developing the disorder of PTSD and then intervene only with those at high risk.[26]

Interventions to prevent PTSD and reduce symptoms of PTSD involve various psychological and pharmacological approaches; they also include emerging interventions such as approaches from complementary and alternative medicine (CAM). These interventions have been used both separately and in combination with one another.

Psychological Interventions

Specific psychological interventions that have been studied for the prevention of adult PTSD are described below and include the following: Battlemind training; trauma-focused cognitive behavioral therapy (CBT); cognitive processing therapy (CPT); cognitive therapy, or cognitive restructuring; coping skills therapy, including stress inoculation therapy; debriefing interventions, including critical incident stress debriefing (CISD) and critical incident stress management (CISM); exposure-based therapies; eye movement desensitization and reprocessing (EMDR); interpersonal therapy (IPT); psychoeducation; and psychological first aid (PFA). These therapies are designed to prevent the onset of PTSD and development of trauma-related stress symptoms soon after exposure to a traumatic event.

Battlemind Training

Postdeployment Battlemind training is an early intervention program designed by the U.S. Army to assist soldiers with reintegration and transition to home life following combat.[27] Battlemind training is based on research from the Walter Reed Army Institute of Research and takes a cognitive- and skills-based approach to educating military personnel about postdeployment transition. Additionally, Battlemind training encourages military personnel to seek support from military peers and leaders.

Cognitive Behavioral Therapy

CBT uses principles of learning and conditioning to treat psychological disorders and includes components from both behavioral and cognitive therapy. In trauma-focused CBT, components such as exposure, cognitive restructuring, and various coping skills have been used either alone or in combination with one another. Most forms of trauma-focused CBT are brief and involve weekly sessions lasting 60 to 90 minutes, although the number of sessions varies across studies. CBT can be administered as either group or individual therapy.[23,28,29]

Cognitive Processing Therapy

CPT, a type of cognitive restructuring, includes psychoeducation, written exposures about the traumatic event, and cognitive restructuring addressing the beliefs about the event's meaning and the implications of the trauma for one's life.[30] The treatment is based on the idea that affective states, such as a depressed mood, can interfere with emotional and cognitive processing of the trauma memory, which can lead to traumatic symptomatology. Cognitive processing therapy is generally delivered over 12 sessions lasting 60 to 90 minutes.

Cognitive Therapy

Cognitive therapy, or cognitive restructuring, is based on the theory that the interpretation of the event, rather than the event itself, determines an individual's mood. It aims to facilitate relearning thoughts and beliefs generated from a traumatic event, increase awareness of dysfunctional trauma-related thoughts, and correct or replace those thoughts with more adaptive or more rational cognitions (or both). Cognitive restructuring generally takes place over 8 to 12 sessions lasting 60 to 90 minutes.[23,28]

Coping Skills Therapy

Coping skills therapy may include components such as stress inoculation therapy, assertiveness training, biofeedback (including brainwave neurofeedback), or relaxation training. All may use techniques such as education, muscle relaxation training, breathing retraining, role playing, etc., to manage anxiety or correct misunderstandings conditioned at the time of trauma. The therapy is designed to increase coping skills for current situations. Most types of coping skills therapies require at least eight 60- to 90-minute sessions; more comprehensive interventions such as stress inoculation therapy require 10 to 14 sessions.[23,28]

Debriefing Interventions, Critical Incident Stress Debriefing, and Critical Incident Stress Management

Debriefing interventions aim to educate victims about normal reactions to trauma and to encourage them to share their experiences and emotional responses to the event. Debriefing is a universal prevention strategy, typically offered in a single session within hours or days following the event. Although several variations of these single-session interventions have been tested, the most common form of psychological debriefing is CISD.[31]

CISD is a preventive intervention originally developed for use with individuals indirectly exposed to traumatic events because of their occupation, such as firefighters or emergency medical personnel. CISD is administered in a single 3- to 4-hour session by a team composed of individuals familiar with the organization (e.g., officers within a police department) and mental health professionals.[32,33] In addition to helping normalize individuals' responses to stress and encouraging them to talk about their experiences and reactions, the team teaches coping skills and offers additional resources for those who may need them.[34] By design, the CISD approach is flexible and loosely structured.

CISD was not designed to prevent PTSD; nonetheless, it has been applied directly to victims of trauma despite evidence that it may be ineffective for that purpose and actually may have harmful effects.[35-37] A 2002 update of a previous 1997 Cochrane Review assessed the effectiveness of brief, single-session psychological debriefing for managing psychological distress after trauma and preventing PTSD and concluded that there is no current evidence that

psychological debriefing is a useful treatment for the prevention of PTSD and that compulsory debriefing of victims of trauma should cease.[38]

CISD has expanded to become CISM, a multicomponent, comprehensive crisis intervention program; it aims to reduce the severity of and related impairment associated with traumatic stress.[35] CISM incorporates additional methods such as preincident training for people with high-risk occupations, one-on-one individual crisis support, demobilizing (i.e., giving information about coping and stress to large groups of emergency workers as they rotate off duty), and defusing (i.e., small-group interventions during which participants are asked to explore and discuss the incident and their emotional reactions to it).[32] CISM also has a family support component whereby family members of the emergency personnel are debriefed. Lastly, additional procedures involve referring people for psychological services.[35]

Exposure-Based Therapy

Exposure-based therapy involves confrontation with frightening stimuli, which is continued until anxiety is reduced. The exposure is based on mental imagery from memory or introduced in scenes presented by the therapist (imaginal exposure). In some cases, exposure is from the actual scene or similar events in life (in vivo exposure). The aim is to extinguish the conditioned emotional response to traumatic stimuli (i.e., for the subject to learn that nothing "bad" will happen when encountering trauma-related cues). This eventually reduces or eliminates avoidance of feared situations and the affect associated with them. Exposure therapy is typically conducted for 8 to 12 weekly or biweekly sessions lasting 60 to 90 minutes.[23,24,28]

Eye Movement Desensitization and Reprocessing

EMDR combines imaginal exposure with the concurrent induction of saccadic eye movements (quick, simultaneous movements of both eyes in the same direction) that are believed to help reprogram brain function so that the emotional impact of trauma can be resolved. In the EMDR process, the individual is instructed to imagine a traumatic memory, engage in negative cognition, and then articulate an incompatible positive cognition (e.g., personal worth). The clinician asks the individual to contemplate the memory while focusing on rapid movement of clinicians' fingers. After 10 to 12 eye movements (back and forth), the clinician asks the individual to rate the strength of the memory and his or her belief in the positive cognition. Although earlier versions of EMDR consisted of 1 to 3 sessions, current standards consist of 8 to 12 90-minute weekly sessions.[23,39]

Interpersonal Therapy

Interpersonal therapy is a time-limited, dynamically informed psychotherapy that aims to alleviate patients' suffering and improve their interpersonal functioning. This type of therapy focuses specifically on interpersonal relationships and aims to help patients either improve their interpersonal relationships or change their expectations about them. In addition, it aims to help patients improve their social support so they can better manage their current interpersonal distress. Interpersonal therapy generally requires 10 to 20 weekly sessions in the acute phase followed by a time unlimited maintenance phase.[40]

Psychoeducation

Psychoeducation uses structured or semistructured forms of patient information designed to teach individuals about a range of health-related issues. Post-trauma prevention psychoeducation

can focus on variety of issues; these include the typical responses one might experience after exposure to a traumatic event, characteristic symptoms and early warning signs of illness, self-care, coping skills, relapse prevention, community resources, and guidelines for when to seek treatment. Psychoeducation can be offered in different forms including individual or group information sessions, brochures, books, videos, and other forms of media.

Psychological First Aid

PFA is a systematic set of helping actions aimed at reducing initial post-trauma distress and supporting short- and long-term adaptive functioning. PFA is designed as an initial component of a comprehensive disaster or trauma response. It is constructed around eight core actions: (1) contact and engagement, (2) safety and comfort, (3) stabilization, (4) information gathering, (5) practical assistance, (6) connection with social supports, (7) information on coping support, and (8) linkage with collaborative services.[41]

PFA is concept driven; its application requires assessment and clinical judgment by the provider given the complexity of presentations, variability of context, need, and logistical constraints. PFA is intended for use by disaster mental health responders, counselors, and others who may provide immediate support for trauma survivors. Two of PFA's major advantages are that it is highly portable and designed for delivery anywhere recent trauma survivors can be found—such as shelters, schools, hospitals, homes, staging areas, feeding locations, family assistance centers, and other community settings. The principles of PFA can also be applied immediately following a traumatic event in nondisaster field settings, including hospital trauma centers, rape crisis centers, and war zones.[42]

Supportive Counseling

Supportive therapy is a type of psychological intervention that aims to help an individual function better by providing personal support. In general, change is not the goal of supportive counseling. Supportive counseling allows an individual to reflect on his or her life situation in an environment where he or she feels accepted and therefore better able to cope.

Pharmacological Interventions

Various neurobiological pathways have been implicated in the development of PTSD. Accordingly, pharmacotherapy has been tried as a preventive intervention for PTSD. Several drugs have been studied for the treatment and prevention of PTSD including selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), other second-generation antidepressants, tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), beta-blockers, alpha-blockers, benzodiazepines, anticonvulsants, nonbenzodiazepine sedatives/hypnotics, atypical antipsychotics, narcotic medication, steroids, and opioid antagonists.[13,29,43]

Alpha Blockers

Some symptoms of PTSD are related to central nervous system adrenergic hyperarousal.[44] Medications targeting central noradrenergic dysregulation may be effective in preventing or treating symptoms of PTSD. Studies have demonstrated effectiveness of alpha-1 and alpha-2 adrenoreceptor agonists in treating sleep disturbances, especially nightmares, and general symptoms of hyperarousal associated with PTSD.[43]

Anticonvulsants

Several anticonvulsant medications have been used to treat symptoms of PTSD.[45] Gabapentin has several pharmacological and pharmacokinetic properties that make it a potentially useful medication for treating and preventing PTSD.[46,47] Similar to benzodiazepines, gabapentin may exert its effects through its structural relationship to GABA (gamma-aminobutyric acid), playing an important role in decreasing excitatory input (glutamate) at the *N*-methyl-d-aspartate (NMDA) and alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptors, thought to play a role in sensory transmission important in the psychobiology of PTSD.[48]

Benzodiazepines

Benzodiazepines enhance the effect of the neurotransmitter GABA and can produce sedative, hypnotic, anxiolytic, anticonvulsant, muscle relaxant, and amnesic effects. These properties make benzodiazepines useful in mediating symptoms of anxiety. Benzodiazepine use in PTSD is directed largely toward symptomatic management of hyperarousal-related symptoms such as sleep disturbances; these agents have not been shown to treat PTSD effectively.[45,49]

Beta-Blockers

A large body of research suggests that PTSD is associated with hyper-reactivity of the sympathetic nervous system, specifically the noradrenergic system. Heart rate is elevated in the peritraumatic event period among people exposed to trauma who develop PTSD; stress-induced norepinephrine levels are higher among people with PTSD; and corticotrophin-releasing factor, which stimulates release of norepinephrine, is elevated in people with PTSD.[50] Propranolol, a beta-adrenergic antagonist that crosses the blood-brain barrier, has been evaluated in several studies for its ability to prevent PTSD.[47,51,52] So far results have failed to show any clear benefit of propranolol compared with placebo in reducing physiological reactivity during traumatic imagery, severity of PTSD symptoms, or the rate of the PTSD diagnostic outcome. In addition, significant controversy exists about the use of propranolol for PTSD prevention because of its ability to attenuate the emotional response and memory of a traumatic event. Studies have shown that propranolol not only decreases emotional memory but also episodic memory for the traumatic event.[53] This effect leads to various ethical concerns, considering that the long-term implications of emotional and episodic memories are not yet well understood.

Monoamine Oxidase Inhibitors

MAOIs increase the concentration of amines in the cytoplasm and the synaptic terminals of neural cells. This accumulation of amines is believed to be responsible for their therapeutic action. In this context, the therapeutic effects of MAOIs might be mediated by the same mechanisms that are responsible for the efficacy of the tricyclic agents. Consequently, elevated levels of catecholamines and serotonin are thought to be able to correct abnormalities in the central nervous system that trauma has altered.[54]

Narcotics

The opiate analgesic, morphine, has shown promise in preventing PTSD in people experiencing physical injury from a traumatic event.[55,56] Researchers who have studied the protective effects of morphine administration in preventing PTSD have proposed two primary hypotheses. One is that pain relief as part of trauma care has a protective effect against the development of PTSD.[56-58] The other is that opiates may interfere with or prevent memory

consolidation through a beta-adrenergic mechanism.[59,60] These studies highlight and support the importance of pain control in physically injured people, but the potential role of opiates in preventing PTSD following severe psychological trauma in the absence of painful physical injury remains unclear.

Nonbenzodiazepine Sedatives or Hypnotics

Similar to benzodiazepines, nonbenzodiazepines enhance the effect of the neurotransmitter GABA; they can produce sedative, hypnotic, anxiolytic, anticonvulsant, muscle-relaxant, and amnesic effects. Trials of nonbenzodiaepines (buspirone and eszopiclone) have reported that these medications have been effective in reducing symptoms of PTSD.[61,62]

Opioid Antagonists

Abnormalities in the endogenous opioid system may underlie PTSD symptomatology; high comorbidity between PTSD and substance abuse might also suggest involvement of common pathways in the pathophysiology of these disorders.[63] These considerations raise the possibility that opioid antagonists might have a role in the treatment of PTSD. Some studies have provided evidence to support this conclusion.[64,65]

Other Second-Generation Antidepressants

Bupropion, nefazodone, and trazodone are believed to work through their effects on serotonin, norepinephrine, and dopamine, which are neurotransmitters related to fear, anxiety, and mood. Their primary mechanism of action is unknown. Bupropion is a relatively weak inhibitor of the neuronal uptake of norepinephrine, serotonin, and dopamine; nefazodone is believed to inhibit neuronal uptake of serotonin and norepinephrine. Trazodone appears to produce its primary effect by selectively inhibiting serotonin reuptake, but it also causes adrenoreceptor subsensitivity and induces significant changes in 5-hydroxytryptamine (5-HT) presynaptic receptor adrenoreceptors.

Second-Generation (Atypical) Antipsychotics

Atypical antipsychotics improve psychotic symptoms by blocking D2 receptors and decreasing dopamine activity in the central nervous system.[54] Neurobiological studies have examined the role of dopamine in the amygdala and other limbic structures implicated in PTSD symptomatology; they suggest that dopaminergic transmission might have a modulatory role in the function of these structures.[66]

Selective Serotonin Reuptake Inhibitors

SSRIs are currently the most widely used drugs to treat PTSD. SSRIs have been shown to be modestly effective for civilian trauma-related PTSD but no more effective than placebo for PTSD in military veterans.[67,68] As with beta blockers, such as propranolol, SSRIs may diminish the more severe clinical sequelae following a stress exposure, possibly through nonspecific effects on other monoamines, through neuroprotective effects in the brain, or through increases in neurotrophic factors that can block the down-regulation of brain-derived neurotrophic factors.[69]

Serotonin and Norepinephrine Reuptake Inhibitors

Like the SSRIs, SNRIs act on neurotransmitters related to fear, anxiety, and mood by inhibiting the reuptake of the neurotransmitters serotonin and norepinephrine. This increases the extracellular concentrations of serotonin and norepinephrine and, therefore, an increase in neurotransmission. The SNRI venlafaxine has been shown to be effective for treating PTSD.[70,71]

Steroids

A substantial body of research has suggested that alterations in the hypothalamic-pituitary-adrenal (HPA) axis are associated with PTSD. Much of the research suggests increased sensitivity of the HPA negative feedback loop between the release of corticotropin-releasing factor (CRF) from the hypothalamus and release of cortisol from the adrenal cortex, resulting in high levels of CRF and low levels of cortisol among people with PTSD.[50] This finding has led to the hypothesis that exogenous administration of cortisol shortly after trauma may prevent PTSD by preventing development of HPA axis dysregulation.

Tricyclic Antidepressants

TCAs block the reuptake of norepinephrine and serotonin to varying degrees. Central catecholamines and serotonin are involved in modulating arousal level and stress response and in regulating mood and anxiety. Aspects of PTSD (e.g., fear and arousal) suggest dysregulation in one or more of these functions in the etiology of PTSD; this provides a neurobiological rationale for the efficacy of pharmacological interventions that affect these systems.[54] Because the majority of TCAs are active in several neurotransmitter systems, their efficacy in PTSD could be mediated by their effect in increasing serotoninergic transmission, modulating alpha-2 adrenergic function, affecting monoamine transporters, or influencing secondary messenger systems or some combination of these effects.

Table 2 provides a summary of the medications used to prevent PTSD. Currently, the U.S. Food and Drug Administration has not approved any pharmacological interventions for the prevention of PTSD.

Table 2. Medications studied for the prevention or treatment of PTSD

Class	Drug
Alpha blockers	Prazosin
Anticonvulsants	Topiramate, tiagabine, lamotrigine, carbamazepine, divalproex, and gabapentin
Benzodiazepines	Alprazolam, diazepam, lorazepam, clonazepam, and temazepam
Beta blockers	Propranolol
Monoamine oxidase inhibitors	Phenelzine, isocarboxazid, selegiline, and tranylcypromine
Narcotic medication	Morphine
Nonbenzodiazepine sedatives or hypnotics	Zolpidem, eszopiclone, rozerem, and zaleplon
Opioid antagonists	Naltrexone
Other second-generation antidepressants	Bupropion, mirtazapine, nefazodone, and trazodone
Second-generation (atypical) antipsychotics	Olanzapine and risperidone
Selective serotonin reuptake inhibitors	Escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline
Serotonin and norepinephrine reuptake inhibitors	Duloxetine, desvenlafaxine, and venlafaxine
Steroids	Hydrocortisone
Tricyclic antidepressants	Imipramine, amitriptyline, and desipramine

PTSD = posttraumatic stress disorder

Emerging Interventions

In addition to traditional psychological and pharmacological interventions, a growing number of interventions and approaches derived from CAM, such as dietary supplements, yoga, and guided imagery,[72] or from different practice models of partnerships between mental health and other medical specialties, such as collaborative care,[73] are emerging. Use of such practices to prevent PTSD is relatively novel. Thus, their efficacy remains unclear.

Prevention Intervention Outcomes

Two primary outcomes in the prevention of PTSD are (1) incidence of PTSD diagnosis and (2) severity of PTSD symptoms that are assessed by both clinician-rated and self-reported measures. Appendix A, at the end of this report, describes each of the PTSD measures in detail. Some commonly used instruments are listed in the Methods section of this report.

In addition to preventing PTSD and reducing the severity of PTSD symptoms, other outcomes used in practice for evaluating the management of patients at risk of or with the diagnosis of PTSD include incidence and severity of comorbid psychiatric symptoms and conditions; quality of life; return to work or active duty; incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide); incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide); and perceived utility (subjective sense of helpfulness of the intervention).

Scope and Key Questions

Scope of the Review

Psychological trauma is common and leads to PTSD in a substantial number of adults exposed to trauma. Prevention of PTSD or reduction of PTSD symptom severity can potentially reduce a significant burden of individual and societal suffering. Despite evidence that some interventions are not effective for the prevention of PTSD, or might even cause harm, they are still widely used. Such use indicates that uncertainty and controversy still exist within the field about providing an intervention that intuitively seems as if it should help and that not enough consideration is given to scientific evidence when weighing intervention benefits and harms.

This review compares the efficacy, effectiveness, and harms of psychological, pharmacological, and emerging interventions for the prevention of PTSD and the reduction of PTSD symptom severity in adults. Highlighting the timeliness and relevance of this topic, the Institute of Medicine (IOM) and various Federal agencies (e.g., the U.S. Department of Veterans Affairs [VA] Health Administration) have identified PTSD as a priority area for quality improvement and comparative effectiveness research.[17,23,74] Increased attention on prevention of PTSD is based, in part, on evidence of higher rates of PTSD among service members returning from operations in Afghanistan and Iraq than previously reported and their increased need for mental health services.[22]

Although most of the newer research on PTSD prevention has focused on targeted prevention, our report focuses on both universal and targeted prevention interventions. There have been several meta-analyses reporting that debriefing, the most widely studied universal prevention intervention, does not reduce PTSD. However, debriefing is not the only universal prevention intervention. Findings from studies of other psychological interventions using the universal prevention model, such as Battlemind training, an intervention developed for returning

military service members, have been reported but never evaluated by a systematic review. Studies of medications, based on the universal prevention approach, have also been reported but never evaluated by a systematic review. Therefore, in this report, we included studies of both universal prevention as well as studies using the targeted prevention approach.

Our report focuses on interventions that have been used in clinical practice for the prevention of PTSD; they may or may not include interventions currently used to treat PTSD. We also address the clinical importance of effect modifiers or subgroup status that may affect the impact of traumatic exposure; these include sex, comorbidities, refugee status, and military or civilian status.

Our report is limited to adults who were exposed to psychological trauma and who received an intervention designed to prevent the development of PTSD within the first 3 months after the trauma (i.e., early in the clinical situation). This report does not address treatment of individuals who have been diagnosed with PTSD.

Key Questions

We approach each Key Question (KQ) by considering the relevant Populations, Interventions, Comparators, Outcomes, Timing, and Settings (PICOTS). In this review, we address the following four KQs:

KQ 1: For adults exposed to psychological trauma, what is the efficacy or comparative effectiveness (or both) of early interventions to prevent PTSD or to improve health outcomes?

KQ 2: For adults exposed to psychological trauma, does timing, intensity, or dosage of intervention have an impact on the effectiveness or harms of approaches to prevent PTSD or to improve health outcomes?

KQ 3: For adults exposed to psychological trauma, how does efficacy, effectiveness, or harms of early interventions to prevent PTSD differ for characteristics of traumatic exposure or subpopulations with respect to:

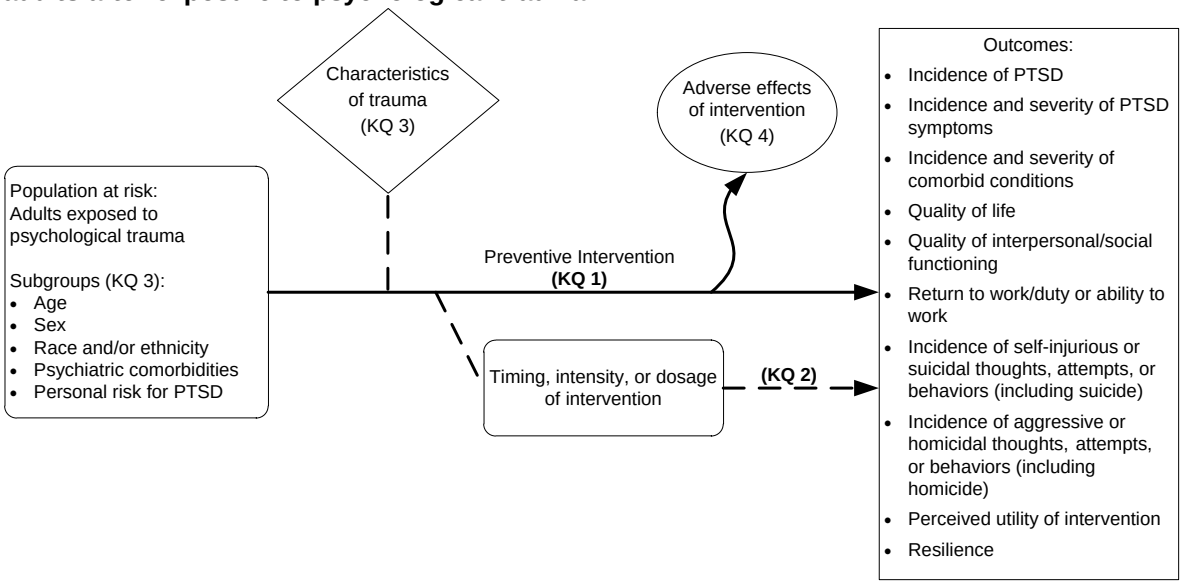
- Demographic groups (defined by age, ethnic and racial groups, and sex),
- Psychiatric comorbidities, or
- Personal risk factors for developing PTSD (e.g., having a diagnosis of acute stress disorder vs. not having the diagnosis)?

KQ 4: For adults exposed to psychological trauma, what are the absolute and comparative risks of harms from early interventions to prevent PTSD?

Figure 1 depicts the analytic framework for the comparative effectiveness of psychological and pharmacological interventions for the prevention of PTSD in adults following exposure to a traumatic event. KQs are displayed within the context of the PICOTS described in the previous section. Beginning with a population of adults exposed to psychological trauma, the figure illustrates the general and comparative effects of early preventive interventions on incidence of PTSD and health outcomes, including incidence and severity of trauma-related symptoms; incidence and severity of coexisting conditions; quality of life; quality of interpersonal and social

functioning; ability to return to work or active duty; incidence of self-injurious or suicidal thoughts, attempts, or behaviors including suicide; incidence of aggressive or homicidal thoughts, attempts, or behaviors including homicide; perceived utility; and resilience (KQ 1). Timing, intensity, and dosage of intervention as potential moderators of these interventions are explored in KQ 2. Characteristics of traumatic exposure and subgroups within the overall population identified based on age, sex, race and ethnicity, psychiatric comorbidities, and personal risk factors (e.g., a history of child abuse) of PTSD as effect modifiers of these interventions are explored in KQ 3. Finally, KQ 4 addresses the absolute and comparative risks of harms and adverse events from these interventions.

Figure 1. Analytic framework for comparative effectiveness of interventions to prevent PTSD in adults after exposure to psychological trauma



KQ = Key Question; PTSD = posttraumatic stress disorder

Organization of This Report

The remainder of this report describes our methods, presents the results of our synthesis of the literature, discusses our conclusions, and provides other information relevant to the interpretation of this work. The Methods section describes our scientific approach for this comparative effectiveness review in detail. The Results section presents our findings for all four of the KQs and includes summary tables. In the Discussion section, we summarize the findings, present the strength of the evidence for critical comparisons or outcomes, and discuss the implications for clinical practice and further research. A complete list of references, acronyms, and abbreviations follows the Discussion section.

This report contains the following appendixes: Appendix A contains detailed descriptions of each of the PTSD measures used in all studies included at the full text level. Appendix B contains the exact search strings we used in our literature searches. Appendix C documents the full-text review and data abstraction forms, including our criteria for rating risk of bias of individual studies. Studies excluded at the stage of reviewing full-text articles with reasons for exclusion are presented in Appendix D. Evidence tables appear in Appendix E. Appendix F lists studies rated high risk of bias and reasons for excluding them from relevant KQ analyses.

Strength of evidence tables appear in Appendix G. Quantitative sensitivity analyses are presented in Appendix H. Appendix I lists acronyms used in the report.

Methods

The methods for this comparative effectiveness review (CER) follow the methods suggested in the Agency for Healthcare Research and Quality (AHRQ) "Methods Guide for Effectiveness and Comparative Effectiveness Reviews" (www.effectivehealthcare.ahrq.gov/methodsguide.cfm). The main sections in this chapter reflect the elements of the protocol established for the CER; certain methods map to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).[75] All methods and analyses were determined a priori.

Topic Refinement and Review Protocol

This topic was nominated by a member of the American Psychological Association, which aims to use high-quality evidence syntheses to inform guideline development. During the topic development and refinement processes, we engaged in a public process to develop a draft and final protocol for the CER process. We generated an analytic framework, preliminary Key Questions (KQs), and preliminary inclusion/exclusion criteria in the form of PICOTS (populations, interventions, comparators, outcomes, timing, settings). The processes were guided by the information provided by the topic nominator, a scan of the literature, methods and content experts, and Key Informants. We worked with four Key Informants during the topic refinement, all of whom subsequently served as members of our Technical Expert Panel (TEP) for this report. The TEP consisted of five individuals in total. Key Informants and TEP members participated in conference calls and discussions through email to review the analytic framework, KQs, and PICOTS; discussed the preliminary assessment of the literature; provided input on the information and categories included in evidence tables; and provided input on the data analysis plan.

Our KQs were posted for public comment on AHRQ's Effective Health Care Web site from January 4, 2012, through February 1, 2012; we put them into final form after review of the comments and discussion with the TEP. We made minimal revisions to the KQs based on comments from the public, primarily for clarity and readability. We then drafted a protocol for this CER and refined the protocol in consultation with AHRQ and the TEP before it was posted on the Effective Health Care Web site on June 6, 2012. Additionally, we made amendments to the protocol and posted those on July 27, 2012, September 27, 2012, and November 8, 2012.

Literature Search Strategy

Search Strategy

To identify articles relevant to each KQ, we searched PubMed®, the Cochrane Library, EMBASE, PILOTS (Published International Literature on Traumatic Stress), International Pharmaceutical Abstracts, PsycINFO®, and Web of Science. The full search strategy is presented in Appendix B. We used either Medical Subject Headings (MeSH) or major headings as search terms when available or key words when appropriate, focusing on terms to describe the relevant populations and interventions of interest. We reviewed our search strategy with the TEP and incorporated their input. Searches were run by an experienced information scientist serving as the Evidence-based Practice Center (EPC) librarian.

We limited the electronic searches to English-language and human-only studies. Sources were searched from January 1, 1980, to January 5, 2012. We selected the start date based on the

introduction and definition of PTSD as a clinical entity, the earliest publication date of relevant studies found in previous systematic reviews, and expert opinion about when the earliest literature on this topic was published.

We manually searched reference lists of pertinent reviews, included trials, and background articles on this topic to look for any relevant citations that our searches might have missed. We imported all citations into an EndNote® X4 electronic database.

We also searched for unpublished studies relevant to this review using ClinicalTrials.gov, the Web site for the U.S. Food and Drug Administration, the World Health Organization's International Clinical Trials Registry, Grey Matters, and OpenGrey. In addition, the Scientific Resource Center requested scientific information packets (SIPs) from the relevant pharmaceutical companies, asking for any unpublished studies or data relevant for this CER. SIPs allow an opportunity for pharmaceutical companies to provide the EPC with both published and unpublished data that they believe should be considered for the review. Studies from the SIPs would be included in the post-peer/public review report.

In cases in which relevant information was unclear or not reported, we contacted authors to get additional or unpublished information. When successful, this information was included in the findings.

We conducted an updated literature search (of the same databases searched initially) concurrent with the peer review process. Any literature suggested by peer reviewers or the public was investigated and, if appropriate, incorporated into the final review. We determined appropriateness for inclusion in the review by the same methods described in this chapter.

Inclusion and Exclusion Criteria

We developed eligibility (inclusion and exclusion) criteria with respect to patient PICOTS and study designs and durations for each KQ (Table 3). For studies to be eligible, the intervention had to be administered within 3 months of the traumatic event.

Table 3. Eligibility criteria for studies of PTSD prevention

Category	Inclusion	Exclusion
Population	Adults (ages 18 or older) exposed to psychological trauma. Types of trauma include interpersonal or domestic violence or abuse; sexual abuse or assault; rape; combat- or military-related trauma; crime-related events; terrorism; slavery; natural disasters; injury; life-threatening illness; captivity; life-threatening medical procedures; witnessing a traumatic event; refugee trauma; prisoner of war-related trauma; and asylum seeking-related trauma Subgroups of interest include: • Demographic groups (defined by age, ethnic and/or racial groups, and sex) • Populations with psychiatric comorbidities • Populations with different personal risks of developing PTSD	Children, people with PTSD

Table 3. Eligibility criteria for studies of PTSD prevention (continued)

Category	Inclusion	Exclusion
Interventions	Psychological interventions including: • Cognitive behavioral therapy • Cognitive processing therapy • Cognitive therapy (including cognitive restructuring therapy) • Coping skills therapy (including stress inoculation therapy) • Debriefing interventions (including critical incident stress debriefing and critical incident stress management) • Exposure-based therapies (including imaginal and in vivo exposure) • Eye movement desensitization and reprocessing • Interpersonal therapy • Psychoeducation • Psychological first aid • Other clearly defined psychological interventions Pharmacological interventions including: • Alpha blockers (prazosin) • Anticonvulsants (topiramate, tiagabine, lamotrigine, carbamazepine, divalproex, and gabapentin) • Benzodiazepines (alprazolam, diazepam, lorazepam, clonazepam, and temazepam) • Beta blockers (propanolol) • Monoamine oxidase inhibitors (phenelzine, isocarboxazid, selegiline, and tranylcypromine) • Narcotics (morphine) • Nonbenzodiazepine sedative and hypnotics (zolpidem, eszopiclone, rozerem, and zaleplon) • Opioid antagonists (naltrexone) • Other second-generation antidepressants (bupropion, mirtazapine, nefazodone, and trazodone) • Second-generation (atypical) antipsychotics (olanzapine and risperidone) • Selective serotonin reuptake inhibitors (escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline) • Serotonin and norepinephrine reuptake inhibitors (duloxetine, desvenlafaxine and venlafaxine) • Steroids (hydrocortisone) • Tricyclic antidepressants (imipramine, amitriptyline and desipramine) • Other clearly defined pharmacological interventions Emerging interventions including: • Complementary and alternative medicine approaches (including dietary supplements, yoga, and guided imagery) • New models of health care delivery (including collaborative care) • Other clearly defined emerging interventions	Psychological or pharmacological interventions not listed as included Any intervention that has not been administered within 3 months of the traumatic event
Comparators	• Psychological treatments (listed above) • Pharmacological treatments (listed above) • Combination of psychological and pharmacological treatments • Emerging treatments (listed above) • Usual care or supportive control • No active intervention (e.g., wait list, placebo)	Psychological or pharmacological interventions not listed as included

Table 3. Eligibility criteria for studies of PTSD prevention (continued)

Category	Inclusion	Exclusion
Outcomes	• Incidence of PTSD • Incidence and severity of PTSD symptoms: assessor-rated or self-rated symptoms (e.g., sleep disturbance, anxiety) • Incidence and severity of coexisting conditions (e.g., depression, anxiety disorders, substance use, abuse, or dependence) • Quality of interpersonal or social functioning • Quality of life • Return to work or duty or ability to work • Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide) • Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) • Resilience • Perceived utility (subjective sense of helpfulness of the intervention) • Adverse events: overall adverse events, withdrawals attributed to adverse events, and specific adverse events (including, but not limited to, worsening of anxiety or agitation, increased distress, headaches, gastrointestinal effects, effects on blood pressure, heart rate, sexual side effects, sedation or insomnia, treatment-associated hypomania or mania, medication dependence or misuse, disturbed sleep, weight gain, metabolic side effects, and mortality) • Dropout rate (overall dropout rate, dropout because of adverse effects, dropout because of lack of efficacy)	
Publication language	English	All other languages
Time period	1980–present; searches to be updated after draft report goes out for peer review	
Settings	• Outpatient and inpatient primary care • Specialty mental health care settings • Community settings (e.g., churches, community health centers, rape crisis centers) • Military settings	
Geography	No limits	
Timing	Intervention must be administered any time ranging from immediately to 3 months after exposure to a traumatic event No limit for duration of followup	
Admissible evidence for KQ 1 through KQ 4	Original research For KQs 1 through 4, eligible study designs include: Randomized controlled trials Prospective controlled cohort studies For KQs 2 through 4 when outcomes of interest are focused on harms, additional eligible study designs are: Retrospective controlled cohort studies Case control studies	• Case series • Case reports • Systematic reviews and meta-analyses • Nonsystematic reviews • Editorials • Letters to the editor • Studies with historical, rather than concurrent, control groups • Pre-post studies without a separate control group

KQ = Key Question; PTSD = posttraumatic stress disorder

Study Selection

We developed and pilot-tested literature review forms for abstract and full-text reviews. Two trained members of the research team independently reviewed all titles and abstracts (identified through searches) for eligibility against our inclusion/exclusion criteria. Studies marked for possible inclusion by either reviewer underwent a full-text review. For studies that lacked adequate information to determine inclusion or exclusion, we retrieved the full text and then made the determination. If the necessary information in full-text articles was unclear or missing, we contacted authors of the publications. All results were tracked in an EndNote® database.

We retrieved the full text of all articles included during the title and abstract review phase. Two trained members of the research team independently reviewed each full-text article for inclusion or exclusion based on the eligibility criteria described above. If both reviewers agreed that a study did not meet the eligibility criteria, we excluded it. If the reviewers disagreed, they resolved conflicts by discussion and consensus or by consulting a third, senior member of the review team. All results were tracked in an EndNote database. We recorded the principal reason that each excluded full-text publication did not satisfy the eligibility criteria (Appendix D).

Data Extraction

For studies that met our inclusion criteria and were of low or medium risk of bias, we extracted important information into evidence tables. We designed, pilot tested, and used structured data extraction forms to gather pertinent information from each article; this included characteristics of study populations, settings, interventions, comparators, study designs, methods, and results. Trained reviewers extracted the relevant data from each included article into the data extraction forms. All data abstractions were reviewed for completeness and accuracy by a second more senior member of the team. We recorded intention-to-treat (ITT) results if available. All data abstraction was performed using Microsoft Excel® software. Evidence tables containing all extracted data of included studies are presented in Appendix E.

We did not extract complete data from studies that we rated as high risk of bias.[76]

Risk-of-Bias Assessment of Individual Studies

To assess the risk of bias (internal validity) of studies for major outcomes of interest, we used predefined criteria based on guidance from the AHRQ "Methods Guide for Effectiveness and Comparative Effectiveness Reviews."[76] We assessed selection bias, confounding, performance bias, detection bias, and attrition bias; we included questions about adequacy of randomization, allocation concealment, similarity of groups at baseline, blinding, attrition, whether ITT analysis was used, method of handling dropouts, and treatment fidelity. We rated the studies as low, medium, or high risk of bias.[77] If RCTs were rated as high risk of bias because of flawed randomization, we viewed them as prospective cohort studies and determined their risk of bias based on criteria for observational studies.

In general terms, a study categorized as low risk of bias implies confidence that results represent the true treatment effects. A study with medium risk of bias is susceptible to some risk of bias but probably not enough to invalidate its results. Studies with a medium risk of bias did not meet all criteria required for low risk of bias. These studies had some flaws in design or execution (e.g., imbalanced recruitment, high attrition) but they provided enough information to allow readers to determine that these flaws did not likely cause major bias. Missing information often led to ratings of medium as opposed to low risk of bias. A study assessed as high risk of

bias has significant flaws of various types (e.g., stemming from serious errors in design, conduct, or analysis) that may invalidate its results. Examples include poor randomization for randomized controlled trials or failure to control for confounding for observational studies, as well as overall attrition ≥ 20% or differential attrition ≥ 15% without appropriate handling of missing data such as the use of intention-to-treat analyses. The protocol specified our a priori decision to consider studies with a high risk of bias for synthesis in this review only if we could not answer the KQs with the available studies with low or medium risk of bias.

Two independent reviewers assessed the risk of bias for each study; one of the two reviewers was always an experienced or senior investigator. Disagreements between the two reviewers were resolved by discussion and consensus or by consulting a third member of the team. We omitted studies deemed high risk of bias by two reviewers from our main data synthesis and main analyses; we included them only in sensitivity analyses. Appendix F details the criteria used for evaluating the risk of bias of all included studies and explains the rationale for high risk of bias ratings.

Data Synthesis

Because of the ongoing controversy about whether different interventions are efficacious at all, we assessed both evidence for the efficacy (i.e., is an intervention efficacious compared with no active treatment such as a waitlist or placebo) and the comparative effectiveness. We used this approach because our preliminary searches as well as input from experts during the topic refinement process suggested that we would find little head-to-head comparative evidence and that we might need to rely on indirect evidence to attempt to make conclusions about comparative effectiveness.

We conducted quantitative synthesis using meta-analyses of outcomes reported by multiple studies that were sufficiently homogeneous to justify combining their results. When quantitative synthesis was not appropriate (e.g., because of clinical heterogeneity, insufficient numbers of similar studies, or insufficiency or variation in outcome reporting), we synthesized the data qualitatively.

We used random-effects models to estimate pooled effects.[78] For continuous outcomes (e.g., scales for symptom reduction), we used weighted mean differences (WMD). If we had to combine multiple scales in one meta-analysis, we used the standardized mean difference (SMD), Cohen's d. For binary outcomes we calculated the relative risk of PTSD between groups. For each meta-analysis, we conducted sensitivity analyses by adding studies that we had rated as high risk of bias. We calculated the chi-squared statistic and the I^2 statistic to assess statistical heterogeneity in effects between studies.[79,80] We examined potential sources of heterogeneity by analysis of subgroups defined by subject population and variation in interventions or controls. Heterogeneity was also explored through sensitivity analyses.

For KQ 3 (subgroup analyses), we evaluated only those studies that conducted subgroup analyses on the original data. We did not perform separate stratified analyses based on subgroups because the potential for introducing confounding bias was greater than the potential insight that those analyses might yield. For example, the percentage of females in a study is likely to be associated with the type of trauma exposure. We did not perform meta-regression because the number of studies was too small.

We assessed publication bias using funnel plots. Quantitative pairwise meta-analyses were conducted using Stata® version 11.1, StataCorp., Texas, USA.

Strength of the Body of Evidence

We graded the strength of evidence (SOE) based on the guidance established for the Evidence-based Practice Center program.[81] Developed to grade the overall strength of a body of evidence, this approach incorporates four key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, strength of association (magnitude of effect), and publication bias. Table 4 defines the grades of evidence that we assigned.

We graded the SOE with respect to eight outcomes viewed as critical for decisionmaking (Table 5). We selected these outcomes a priori with input from the TEP.

Table 4. Definitions of the grades of overall strength of evidence

Grade	Definition
High	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate.
Low	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate.
Insufficient	Evidence either is unavailable or does not permit estimation of an effect.

Source: Owens et al., 2010[81]

Table 5. Outcomes viewed as critical for decisionmaking

Effectiveness of Interventions
• Incidence of PTSD • Severity of PTSD symptoms (if worsening of symptoms, outcome is relevant for adverse effects) • Quality of life • Return to work or active duty • Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide) • Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) • Incidence and severity of depressive or anxiety symptoms
Harms of Interventions
• Overall rate of harms • Dropout rate because of harms

PTSD = posttraumatic stress disorder

Two reviewers assessed each domain for each key outcome and determined an overall SOE grade based on domain ratings, and for each assessment, one of the two reviewers was always an experienced or senior investigator. In the event of disagreements on the domain or overall grade, they resolved differences by consensus discussion or by consulting with a third, senior investigator.

The principal focus in the results is on outcomes viewed as critical for decisionmaking, but we also comment on other outcomes of interest.

Appendix G includes tables showing our assessments for each domain and resulting SOE grades for each outcome, organized by KQ and intervention/comparison pair.

Applicability

We assessed applicability of the evidence following guidance from the "Methods Guide for Comparative Effectiveness Reviews."[82] We used the PICOTS framework to explore factors that

affect applicability. Some factors identified a priori that may limit the applicability of evidence include the following: age of enrolled populations, sex of enrolled populations, race or ethnicity of enrolled populations, few studies enrolling subjects with exposure to certain types of trauma, or few studies distinguishing or reporting the type of traumatic exposure for a heterogeneous population. Throughout the report, we use the terms "efficacy" and "comparative effectiveness." By efficacy, we mean the efficacy or effectiveness of an intervention tested against some type of inactive control (e.g., placebo or waitlist). By comparative effectiveness we mean the efficacy or effectiveness of an intervention compared with another intervention of interest. In this report, we did not distinguish between explanatory (i.e., efficacy) and pragmatic (i.e., effectiveness) studies.

Peer Review and Public Commentary

An external peer review was performed on this report. Peer Reviewers were charged with commenting on the content, structure, and format of the evidence report, providing additional relevant citations, and pointing out issues related to how we conceptualized the topic and analyzed the evidence. Our Peer Reviewers (listed in the front matter) gave us permission to acknowledge their review of the draft. We compiled all comments and addressed each one individually, revising the text as appropriate. AHRQ also provided review from its own staff. In addition, the Scientific Resource Center placed the draft report on the AHRQ Web site (www.effectivehealthcare.ahrq.gov/) for public review.

Results

Introduction

This chapter is organized as follows. First, we discuss general results of the literature searches and characteristics of included studies. Second, we present the available evidence by Key Question (KQ). Within each KQ we present evidence on the efficacy or risk of harms first, followed by the comparative effectiveness and risk of harms, as well as grades of the strength of evidence (SOE). Within each section on efficacy, comparative effectiveness, or absolute or comparative risk of harms, we discuss evidence on psychological interventions first, followed by studies on pharmacological interventions, and lastly by studies on emerging interventions. In addition, according to the specifications from the Agency for Healthcare Research and Quality (AHRQ) for a comparative effectiveness review (CER), within each KQ section we present key points and detailed synthesis. Table 6 lists the main questions that we address in this chapter. We focus on randomized controlled trials (RCTs) and prospective observational studies for all questions; for KQ 4 on harms, we also include retrospective observational studies. Evidence tables for all included studies, by KQ, are presented in Appendix E.

Table 6. Key Questions about interventions to prevent PTSD in adults after exposure to psychological trauma

Key Questions
KQ 1: What are the efficacy and comparative effectiveness of early interventions to prevent PTSD?
KQ 2: What is the impact of timing, intensity, or dosage of intervention on effectiveness and harms?
KQ 3: What are the efficacy, comparative effectiveness, and harms in subpopulations and different traumatic exposures?
KQ 4: What are the absolute and comparative risk of harms from early interventions to prevent PTSD?

PTSD = posttraumatic stress disorder

Reasons for exclusion were based on eligibility criteria or methodological assessments. We rated 37 studies that otherwise met eligibility criteria as having high risk of bias (Appendix F). The main reasons for rating RCTs as high risk of bias were poor randomization, high loss to followup, and lack of ITT analysis. We briefly discuss high-risk-of-bias studies in the report only if no studies of better methodological quality were available.

Studies reviewed for this report employed a notable array of diagnostic scales, some of which assess posttraumatic stress disorder (PTSD) and others that assess other outcomes of interest, such as health-related quality of life. Commonly used measures include the:

- BDI: Beck Depression Inventory;
- CAPS, CAPS-2: Clinician Administered PTSD Scales;
- HADS: Hospital Anxiety and Depression Rating Scale;
- IES, IES-R: Impact of Event Scale;
- PCL: Posttraumatic Stress Disorder Checklist;
- PDS: Posttraumatic Stress Diagnostic Scale; and
- SF-36: Medical Outcomes Study Health Survey–Short Form 36.

Results of Literature Searches

We identified 2,563 citations from searches, reviews of reference lists, and grey literature. Figure 2 documents the disposition of the 267 articles retrieved for full-text review for this report. Overall, we included 56 full-text articles (based on 55 studies) but only used 19 articles

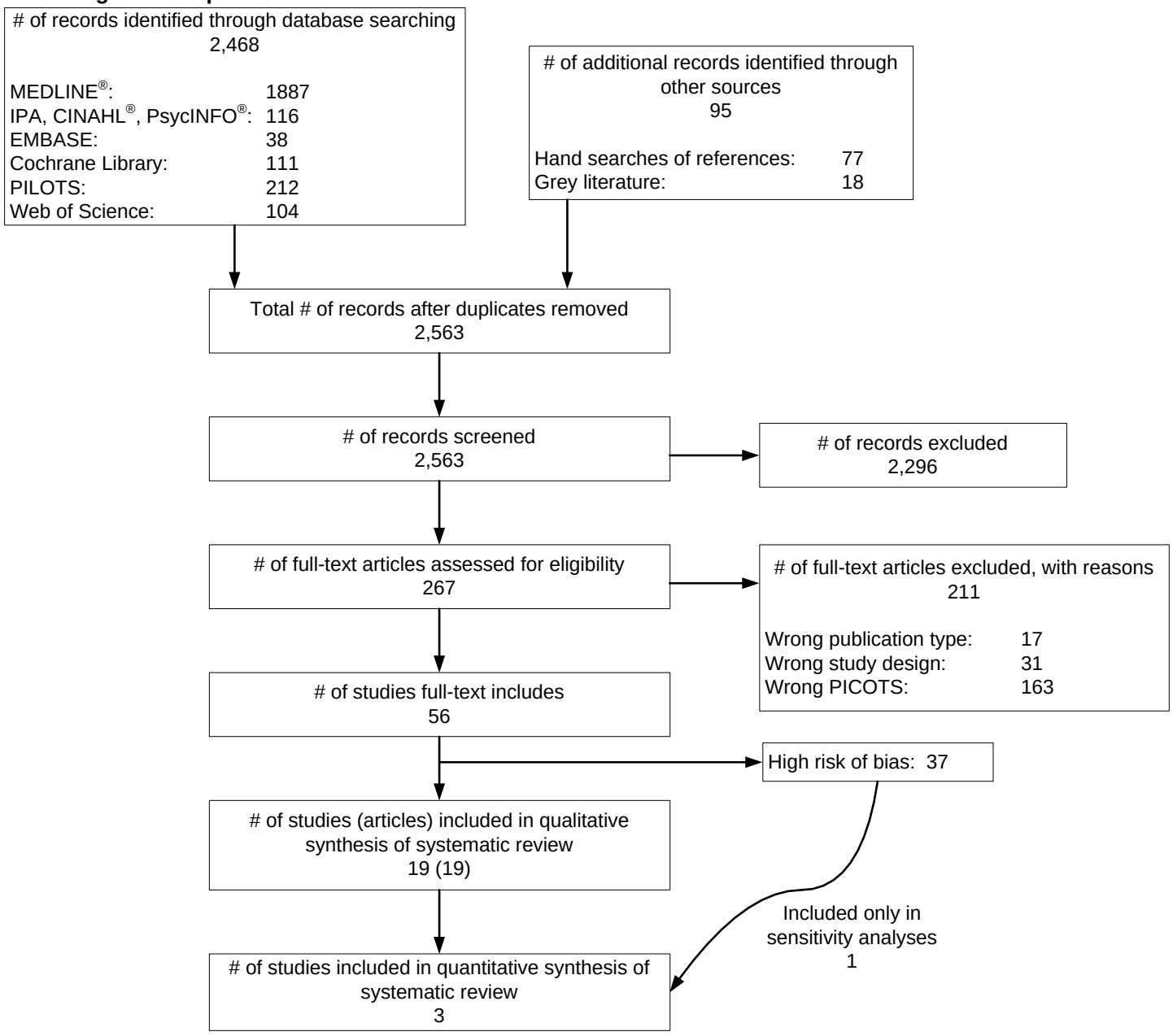
(based on 19 studies) in our main analyses, selected 106 articles for background, and excluded 211 full-text articles for various reasons. In general, the number of articles exceeds the number of studies because results of some studies were published in multiple articles. Articles excluded during full-text review are listed in Appendix D with reasons for their exclusion.

Description of Included Studies

We included 19 articles reporting on 19 studies of low or medium risk of bias in our main analyses: of the included studies, all were RCTs (Figure 2). Nine RCTs used head-to-head comparisons of early interventions; the other 10 compared active interventions with inactive comparison conditions. Evidence tables of studies with low or medium risk of bias are presented in Appendix E. In addition, we rated 37 studies that met eligibility criteria as high risk of bias (Appendix F). Table 7 presents a summary of the study designs, prevention type (i.e., universal or targeted), study comparisons, results, and methodological shortcomings of the 37 studies we rated as high risk of bias. For most interventions we had stronger, more reliable evidence to answer a particular question. When we found no evidence rated as low or medium risk of bias, we present information from high-risk-of-bias studies. When RCTs were rated as high risk of bias because of inadequate randomization, we viewed them as non-randomized studies and critically appraised them accordingly. In all cases, however, they were ultimately rated as high risk of bias non-randomized studies because they did not adequately control for differences in baseline characteristics.

If not stated otherwise, trials described in the results chapter are of medium risk of bias.

Figure 2. Disposition of articles



CINAHL = Cumulative Index to Nursing and Allied Health Literature; EMBASE = Excerpta Medica Database; IPA = International Pharmaceutical Abstracts; PICOTS = patient populations, interventions, comparators, outcomes, timing, and settings; PILOTS = Published International Literature on Traumatic Stress; PRISMA = Preferred Reporting Items for Systematic Review and Meta-analyses

Table 7. Summary of studies rated high risk of bias

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Acierno et al., 2004[83] RCT Universal	Civilians Crimes	CBT-based video intervention plus standard services vs. standard services only	Neither incidence of PTSD nor PTSD symptom severity differed between the groups.	• No baseline PTSD ratings • High overall attrition (29%) • "Completers analysis" only
Adler et al., 2009[27] RCT Universal	U.S. Army service members Combat	Stress management vs. Battlemind debriefing vs. small Battlemind training vs. large Battlemind training	PTSD symptom severity was lower in the three Battlemind groups than in the stress management group.	• Study staff masked at followup but not baseline • High overall attrition (>50%) • ITT not sufficient to account for risk of bias due to attrition
Adler et al., 2008[84] RCT Universal	U.S. Army service members Combat	CISD vs. stress management vs. survey only	PTSD symptom severity did not differ between any of the groups.	• Randomization method not described, so impossible to determine how it affects risk of bias • High overall attrition (71%) • Statistical approach to control for effect of attrition not sufficient to account for risk of bias due to attrition • No allocation concealment
Eid et al., 2001[85] Prospective cohort study Universal	First responders Fatal traffic accident	Debriefing plus stress management vs. debriefing	Combined intervention was associated with a lower frequency of posttraumatic stress symptoms.	• Cohort study with a small sample size • No reported adjustment for confounders • Further risk of bias assessment impossible due to inadequate reporting of methods
Brom et al., 1993[86] RCT Universal	Civilians MVA	SC vs. monitoring only	PTSD symptom severity did not differ between the counseling and monitoring only groups.	• Randomization process not described, so impossible to determine how it affects risk of bias • Unclear how attrition handled • Statistically significant group differences at baseline • Unclear if outcome assessors masked
Bryant et al., 1999[87] RCT Targeted	Civilians with ASD MVA or nonsexual assault	PE plus anxiety management vs. PE alone vs. SC	The combined intervention and PE alone were both associated with lower PTSD incidence and less PTSD symptom severity than SC. No differences in PTSD outcomes occurred between PE alone and PE plus anxiety management.	• High overall attrition (23%) • "Completers analysis" only

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Bryant et al., 2003[88] RCT Targeted	Civilians with ASD MVA or nonsexual assault	CBT vs. SC	The CBT group had lower incidence of PTSD rates and less PTSD symptom severity than the SC group.	• High overall attrition (49%) from end of parent studies (see Bryant et al., 1998 and Bryant et al., 1999)[87,89]
Bryant et al., 2006[90] RCT Targeted	Civilians with ASD MVA or nonsexual assault	CBT+Hypnosis vs. CBT alone vs. SC	Both the combined intervention and CBT alone were associated with lower incidence of PTSD and less PTSD symptom severity at 3-year followup than in the SC group.	• High overall attrition (39%) from end of parent study (see Bryant et al., 2005)[91]
Bugg et al., 2009[92] Targeted	Civilians with ASD symptoms Physical injury or accident	Structured writing intervention vs. information-only control	Incidence of PTSD did not differ between groups.	• High overall attrition (51% including postrandomization exclusions) • Relatively large proportion not completing all three intervention sessions (31%) • Substantial differences between groups by sex
Carlier et al., 1998[93] Retrospective cohort study Universal	First responders (police officers) Fatal civilian plane crash	CISD vs. no CISD	Findings were mixed: incidence of PTSD did not differ between groups, while the no CISD group exhibited greater PTSD symptom severity.	• Risk of recall bias because no data available until 8 months after trauma • High risk of selection bias and confounding from subjects' self-selection to treatment groups
Crespo et al., 2010[94] RCT Targeted	Civilian women with PTSD symptoms but not full PTSD diagnosis Intimate partner violence	CBT with exposure techniques vs. CBT with communication skills training instead	CBT with exposure techniques was generally associated with lower PTSD symptom severity than CBT with communication skills training. However, the communication skills group had fewer re-experiencing symptoms at posttreatment than the exposure group.	• Randomization process at high risk for bias • High overall attrition (32%) • Statistically significant baseline differences in education level, depression symptom levels, and reason for seeking treatment (Exposure group's presenting reason more often violence than communication skills group)

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Deahl et al., 2000[95] RCT Universal	British UN peacekeepers Combat in Yugoslavia	Preoperational and postoperational psychological debriefing vs. Preoperational debriefing only	Neither incidence of PTSD or PTSD symptom severity differed between groups.	• Not true randomization • High overall attrition (48%) • Baseline data collected from only 64% of the whole sample before intervention • Unclear whether study used the same truly random samples for the postbaseline outcomes as at baseline • Data not available for all participants at all times but no reasons for missing data given
Foa et al., 1995[96] Prospective cohort study Targeted	Civilian women meeting PTSD symptom criteria only Sexual or nonsexual assault	Brief CBT vs. assessment- only control	The CBT group experienced a smaller incidence of PTSD and less PTSD symptom severity than the assessment only group at posttreatment, but not at later followup.	• Nonrandomized study with small sample size (N=20) • Attrition data NR • High risk of selection bias and confounding • Participants matched on some variables but not all • Timing of outcomes differed by group
Foa et al., 2006[97] RCT Targeted	Civilian women meeting PTSD symptom criteria only Sexual or nonsexual assault	Brief CBT vs. SC vs. assessment-only control	CBT was associated with less PTSD symptom severity at posttreatment than SC, but not the assessment-only group. At later followup, all groups had similar incidence of PTSD and PTSD symptom severity.	• High overall (27%) and differential attrition (SC vs. assessment-only: 16%) • ITT not sufficient to account for risk of bias due to attrition
Frappell-Cooke et al., 2010[98] Prospective cohort study Universal	UK Royal Marines and Army returning from Afghanistan Combat	Units with experience using trauma risk management debriefing vs. Units using trauma risk management for first time	Neither incidence of PTSD nor PTSD symptom severity differed between groups.	• Nonrandomized study with high overall (24%) and differential (43%) attrition • “Completers analysis” only

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Freyth et al., 2010[99] RCT Targeted	Civilians with ASD Sexual or nonsexual assault, accidents, other (unspecified)	PE vs. SC (both groups receiving psychoeducation and progressive relaxation)	PTSD symptom severity did not differ between groups.	• Inadequate randomization • Attrition reported only for 4-year followup time point • Attrition unclear at 3-month followup time point (last data collection point for all main outcomes) • Unclear if all participants retained at posttreatment
Gelpin et al., 1996[100] Prospective cohort study Universal	Civilians admitted to the emergency room Trauma exposure NR	Benzodiazepines vs. no benzodiazepines	PTSD symptom severity did not differ between groups.	• Unclear if only "completers analysis" used • High risk of selection bias because administration of benzodiazepines based on clinician's evaluation of efficacy, side effects, distress level, and other characteristics like severity of trauma • Specific drug of choice (either alprazolam or clonazepam) administered in nonsystematic way
Gidron et al., 2001[101] RCT Targeted	MVA survivors with minimum heart rate of 95 BPM at emergency room admission (PTSD predictor) MVA	Memory Structuring Intervention (MSI) vs. supportive listening	MSI was associated with less PTSD symptom severity.	• Method of randomization unclear • Unclear attrition • Inadequate statistical analysis

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Grainger et al., 1997[102] Prospective cohort study Universal	U.S. survivors of Hurricane Andrew Natural disaster	EMDR vs. waitlist	EMDR was associated with less PTSD symptom severity.	• Only 29% of participants receiving at least 1 session of EMDR included in analysis o Only participants completing both baseline and posttreatment assessments analyzed • Inclusion criteria unclear (other than surviving Hurricane Andrew) o May have been established after treatment given to survivors • Unclear if only "completers analysis" used o Only waitlist group completers reported • Unclear how late some participants might have first received treatment
Hobbs et al., 1996[103] RCT Targeted	Civilians with posttraumatic symptoms MVA	Psychological debriefing vs. control	Neither incidence of PTSD nor PTSD symptom severity differed between groups.	• High differential attrition (16%) • Completers analysis only
Holmes et al., 2007[104] RCT Universal	Civilians Major physical trauma	Interpersonal counseling vs. treatment as usual	Neither incidence of PTSD nor PTSD symptom severity differed between groups.	• High overall (36%) and differential attrition (25%) • No ITT reported
Jotzo et al., 2005[105] Prospective cohort study Universal	Civilian mothers Premature birth of child	Structured single-session crisis intervention combined with additional psychological aid vs. standard care	The crisis intervention was associated with lower PTSD symptom severity.	• No baseline PTSD data collected • Information about attrition, ITT, blinding, or confounding largely unavailable
Kenardy et al., 2008[106] RCT Universal	Civilian parents of injured children Pediatric accidental traumatic injury	Psychoeducational information booklet vs. no intervention	Psychoeducation was associated with less PTSD symptom severity in a "completers analysis," but ITT results found no difference between groups.	• Inadequate randomization • High overall attrition (36%)

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Krauseneck et al., 2010[107] Prospective cohort study Universal	Civilian medical patients Cardiac surgery (i.e., coronary artery bypass grafting [CABG] or cardiac valve replacement)	Beta-blocker (metoprolol) vs. placebo	Women in the metoprolol group had fewer traumatic memories and less PTSD symptom severity than women in the placebo group but these outcomes did not differ among men.	• High risk of confounding due to lack of measurement or adjustment for the following potential confounders: o Beta-blockers administered postoperatively in Germany "according to a standard protocol", which is not described o Potentially important clinical reasons for not giving beta-blockers to some patients, such as preoperative characteristics or postoperative course, that could indicate illness severity after surgery o Unclear how potential confounders related to risk of PTSD symptoms
Peres et al., 2011[108] Prospective cohort study Targeted	Police officers with partial/sub-threshold PTSD Combat (gunfire attack), witnessing fellow officers dying	Exposure-based therapy and cognitive restructuring vs. waitlist	The intervention was associated with less PTSD symptom severity, but it was not reported whether between-group outcomes were statistically different.	• Not randomized • Attrition and number of subjects included in analysis NR • Impossible to determine similarity of original groups • Unclear how statistical analyses conducted
Peris et al., 2011[109] Retrospective cohort study Universal	Civilian medical patients Severe and/or critical injuries	ICU-based psychological interventions (i.e., educational, counseling, stress management, psychological support and coping strategies) vs. standard care	The intervention was associated with lower incidence of PTSD and less PTSD symptom severity.	• No randomization • High overall (44%) and differential (16%) attrition • Study groups evaluated at two different time periods • Outcome assessment not blinded

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Pitman et al., 2002[51] RCT Universal	Civilians presenting to the emergency department Traumatic events (unspecified)	Propranolol vs. placebo	Neither PTSD symptom severity nor incidence of PTSD differed between groups, although fewer patients in the propranolol group experienced physiologic responses following imagery of the traumatic event.	• High overall (41%) and differential (15%) atttrion in small sample • "Completers analysis" only
Resnick et al., 1999[110] RCT Universal	Civilian women Sexual assault	Psychoeducational video plus usual care vs. usual care alone	Differences in PTSD symptom severity between groups were not reported, and whether PTSD outcomes were compared is not clear.	• Inadequate randomization • Outcome assessment not blinded • Difficult to assess differential attrition because the number of participants in each arm completing assesments varied by assessment and time point • Noncomparability of assessment schedules for one of the conditions
Richards, 2001[111] NRCT Universal	Civilians working in a major UK financial services company Armed robberies	CISD integrated within CISM vs. CISD alone	CISD integrated within CISM was associated with lower PTSD symptom severity.	• High overall attrition (50%) • Unclear whether control group was concurrent

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Rothbaum et al., 2008[112] Prospective cohort study Universal	Civilians presenting to the emergency department Mixed (MVA, physical assault, interpersonal violence, pedestrian accident, other accident, or other unspecified trauma)	Imaginal exposure therapy vs. assessment only	PTSD symptom severity did not differ between groups.	• Nonrandomized study with small sample size (n=10) o Possible statistically significant between-group differences at baseline (e.g., age, sex) • High overall attrition (20%) • "Completers analysis" only • No attempts to adjust for potential confounding from participants' trauma histories and whether previous traumas from adulthood or childhood • Participants not screened for ASD or PTSD at baseline when eligibility assessed
Schelling et al., 2004[113] RCT Universal	Civilian medical patients with high risk for pronounced inflammatory reactions after surgery Cardiac surgery	Stress doses of hydrocortisone vs. standard postoperative care	Hydrocortisone was associated with less PTSD symptom severity, but the frequency of traumatic memories did not differ between groups.	• High overall attrition (47%) • "Completers analysis" only
Schelling et al., 2001[114] RCT Universal	Civilian medical patients Septic shock	Stress doses of hydrocortisone vs. standard postoperative care	Incidence of PTSD was lower in the hydrocortisone group, but frequency of traumatic memories did not differ between groups.	• High overall attrition (50%) • Unclear if participants blinded in intital study

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Stein et al., 2007[47] RCT Universal	Civilian medical patients Severe physical injuries requiring specialized emergency care	Propranolol (beta-blocker) vs. gabapentin (anticonvulsant) vs. placebo	Neither PTSD symptom severity nor incidence of PTSD differed between groups.	• ITT likely not conducted • No reporting of important baseline characteristics by treatment group or between-group comparisons PCL-C outcomes not reported except in line graph
Tecic et al., 2011[115] RCT Universal	Civilian medical patients Mixed (MVA, bicycle accident, pedestrian accident, collapse, assault, other trauma)	Short-term inpatient psychotherapy (using cognitive, exposure-based, SC, and relaxation elements) vs. long-term inpatient and outpatient psychotherapy (same as short-term plus outpatient therapy focused on coping with daily life after discharge)	PTSD symptom severity did not differ between groups.	• High overall (44%) and differential (22%) attrition • Unclear whether ITT used
Vaiva et al., 2003[116] Prospective cohort study Targeted	Civilian emergency department patients presenting with tachycardia MVA or physical assault	Propranolol (beta-blocker) plus standard treatment vs. standard treatment alone	The propranolol group had lower PTSD symptom severity and incidence of PTSD.	• Attrition data NR and unclear how attrition handled in the analysis • No baseline data collected about PTSD symptoms • Risk of selection bias due to participant self-selection into treatment groups, which is not addressed in analysis

Table 7. Summary of studies rated high risk of bias (continued)

Author, Year, Study Design, Prevention Type	Population, Trauma Type	Comparison	Summary of Results	Reason for Rating of High Risk of Bias
Vijayakumar and Kumar, 2008[117] Prospective cohort study Universal	Civilians Natural disaster (tsunami)	Mental health support vs. no intervention	Mental health support was associated with lower PTSD symptom severity.	• Attrition rates and method of handling dropouts NR • PTSD measure piloted for this study, but no validity data provided • Only one statistically significant baseline difference (illiteracy) taken into account in statistical analysis Outcome assessors not blinded
Zohar et al., 2011[118] RCT Targeted	Patients with threshold or subthreshold ASD symptoms Work accident, MVA, or snake bite	Hydrocortisone vs. placebo	The hydrocortisone group was less likely to develop PTSD than patients receiving placebo.	• High overall (32%) and differential (20%) attrition • Only p values for between-group CAPS score differences reported Outcomes displayed in bar graphs, but mean scores and measures of variance not reported

ASD = acute stress disorder; BPM = beats per minute; CABG = coronary artery bypass grafting; CAPS = Clinician Administered PTSD Scale; CBT = cognitive behavioral therapy; CISD = critical incident stress debriefing; CISM = critical incident stress management; COPD = chronic obstructive pulmonary disease; DSM = Diagnostic and Statistical Manual of Mental Disorders; EMDR = eye movement desensitization and reprocessing therapy; ICU = intensive care unit; ITT = intent-to-treat analysis; MSI = Memory Structuring Intervention; MVA = motor vehicle accident(s); NR = not reported; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; PE = prolonged exposure therapy; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SC = supportive counseling; UK = United Kingdom; UN = United Nations; U.S. = United States

The majority of included studies focused on psychological and pharmacological interventions. Only one study evaluated an emerging intervention.[119] For most pharmacological and emerging interventions reliable evidence was lacking. Table 8 presents the number of studies for each included intervention.

Populations enrolled in the available studies were exposed to primarily "civilian" types of trauma (e.g., domestic violence or abuse, accidents, natural events) and only secondarily "military" trauma. The majority of studies were funded by government agencies in the United States and other countries, including Australia, Israel, Switzerland, and the United Kingdom, followed by private-sector sponsors such as foundations. Only two studies were supported by academic funding[120,121] and only one by funding from a pharmaceutical company.[122]

Table 8. Number of low and medium risk-of-bias studies for each eligible intervention

Intervention Type	Intervention	Studies on Efficacy	Studies on Comparative Effectiveness	Studies on Impact of Timing, Intensity, and Dosing	Studies on Risk of Harms
Psychological Interventions	Cognitive behavioral therapy	1	3	0	0
	Cognitive processing therapy	0	0	0	0
	Coping skills therapy (including stress inoculation therapy)	0	0	0	0
	Cognitive therapy (including cognitive restructuring therapy)	2	2	0	0
	Debriefing interventions (including critical incident stress debriefing and critical incident stress management)	2	2	1	1
	Exposure-based therapies (including imaginal and in vivo exposure, as well as prolonged exposure)	3	2	0	0
	Eye movement desensitization and reprocessing	0	0	0	0
	Interpersonal therapy	0	0	0	0
	Psychoeducation	2	1	0	0
	Psychological first aid	0	0	0	0
	Other clearly defined psychological interventions (self-help materials)[a]	1	0	0	0
	Other clearly defined psychological interventions (supportive counseling)[b]	3	3	0	0
	Other clearly defined psychological interventions (Battlemind training)[c]	0	1	0	0

Table 8. Number of low and medium risk-of-bias studies for each eligible intervention (continued)

Intervention Type	Intervention	Studies on Efficacy	Studies on Comparative Effectiveness	Studies on Impact of Timing, Intensity, and Dosing	Studies on Risk of Harms
Pharmacological Interventions	Alpha blockers	0	0	0	0
	Anticonvulsants	0	0	0	0
	Benzodiazepines[d]	0	0	1	1
	Beta blockers	0	0	0	0
	Monoamine oxidase inhibitors	0	0	0	0
	Narcotics	0	0	1	1
	Nonbenzodiazepine sedatives/hypnotics	0	0	0	0
	Opioid antagonists	0	0	0	0
	Other second-generation antidepressants	0	0	0	0
	Second-generation (atypical) antipsychotics	0	0	0	0
	Selective serotonin reuptake inhibitors	1	1	0	0
	Serotonin and norepinephrine reuptake inhibitors	0	0	0	0
	Steroids	1	0	0	0
	Tricyclic antidepressants	0	0	0	0
Emerging Interventions	Complementary and alternative medicine approaches	0	0	0	0
	New models of health care delivery (collaborative care)	1	0	0	0

[a]One study evaluated the efficacy of a self-help booklet on PTSD outcomes following a new breast cancer diagnosis. Although self-help materials are not listed in Table 3, this intervention is being included as an eligible psychological intervention.
[b]Three studies evaluated the efficacy, and another three evaluated the comparative effectiveness of supportive counseling interventions on PTSD outcomes following birth-related trauma or mixed trauma, respectively. Although supportive counseling is not listed in Table 3, it is being included as an eligible psychological intervention.
[c]One study evaluated the comparative effectiveness of Battlemind training on PTSD outcomes following military deployment. Although Battlemind training is not listed in Table 3, it is being included as an eligible psychological intervention.
[d]One study evaluated the impact of sedation depth achieved by midazolam plus morphine infusion on PTSD outcomes following critical illness. Although midazolam is not listed in Table 3, it is being included as an eligible benzodiazepine.

KQ 1: Efficacy and Comparative Effectiveness of Interventions To Prevent PTSD

Description of Included Studies

Overall, 52 studies met eligibility criteria for KQ 1.[27,47,51,83-97,99-114,116-133] Of these, 35 were rated as high risk of bias,[27,47,51,83-88,90,92-97,99-114,116-118,122] and we did not include them in the main analyses reported below. Of 13 studies that identified one or more funding sources, 10 had government funding,[89,91,119,122,123,125,127-129,131] 5 had support from a private foundation or grant,[120-122,127,130] and 1 had pharmaceutical industry funding.[122] Four trials did not specify a funding source.[124,126,132,133]

Efficacy of Psychological, Pharmacological, and Emerging Interventions

Description of Included Studies

Thirteen studies addressed efficacy.[119-123,125,127-133] Of these, 11 involved psychological interventions—cognitive behavioral therapy (CBT), CBT combined with hypnosis, cognitive therapy (CT), debriefing, prolonged exposure therapy (PE), psychoeducation, self-help, and supportive counseling (SC). One study involved a stepped collaborative care intervention that incorporated care management, evidence-based pharmacotherapy and CBT components.[119] These studies were conducted in[119,125,128,133] and outside the United States.[120-123,127,129-131] They included a variety of populations such as victims of crime, motor vehicle accidents (MVAs), other types of accidents, intimate partner violence, sexual assault, and terrorist attacks; critically ill patients; and mothers experiencing traumatic childbirth or caring for a critically ill child. Two trials involved pharmacologic interventions. One studied stress doses of hydrocortisone in high-risk patients undergoing cardiac surgery[132] and one compared escitalopram with either CT, PE, placebo, or waitlist.[122]

Key Points: Efficacy

- Collaborative care is effective at reducing the severity of PTSD symptoms for civilian victims of injuries requiring inpatient surgical admission at 6-month, 9-month, and 12-month followup (low SOE).
- Debriefing is not effective in reducing either the incidence of PTSD or the severity of PTSD or depressive symptoms in civilian victims of crime, assault, or accident trauma at 6-month followup (low SOE).
- Evidence was insufficient for interventions to prevent the incidence of PTSD in the following cases:
    - CBT for civilian victims of MVAs, falls, assaults, and work-related trauma admitted to the intensive care unit
    - CT for hospitalized survivors of MVAs and terrorist attacks and for victims of nonsexual assault or MVAs
    - Debriefing for victims of crime, assault, or accident trauma at 2-week, 6-week, and 11-month followup
    - PE for hospitalized survivors of MVAs and terrorist attacks, for victims of nonsexual assault or MVAs, and for survivors of various trauma types including rape
    - Psychoeducation for victims of violent crime
    - Self-help for women recently diagnosed with breast cancer
    - SC for mothers who recently experienced traumatic childbirth, underwent and emergency cesarean section, or were caring for their critically ill child
    - Hydrocortisone in high-risk patients undergoing cardiac surgery
    - Collaborative care for civilian victims of injuries requiring inpatient surgical admission at 12-month followup
- Evidence was insufficient for interventions to reduce the severity of PTSD symptoms in all of the cases described in the previous Key Point, as well as the following:

    - Collaborative care for civilian victims of injuries requiring inpatient surgical admission at 1-month and 3-month followup
- Evidence was insufficient for interventions to reduce the severity of related psychological symptoms in the following cases:
    - CBT for reducing symptoms of anxiety or depression in victims of MVAs, falls, assaults, and work-related trauma admitted to the ICU
    - CT for reducing symptoms of anxiety or depression in hospitalized survivors of MVAs and terrorist attacks and for victims of nonsexual assault or MVAs
    - Debriefing for reducing symptoms of anxiety or depression in victims of crime, assault, or accident trauma
    - PE for reducing symptoms of anxiety or depression at the end of treatment in victims of nonsexual assault or MVAs
    - Psychoeducation for reducing symptoms of depression in victims of violent crime
    - Self-help for reducing symptoms of anxiety or depression in women recently diagnosed with breast cancer
    - SC for reducing symptoms of anxiety or depression in mothers who recently experienced traumatic childbirth, underwent an emergency cesarean section, or were caring for their critically ill child
    - Collaborative care for reducing symptoms of depression, alcohol use, or functional impairment in civilian victims of injuries requiring inpatient surgical admission

Detailed Synthesis: Psychological Interventions

Table 9 summarizes the evidence about psychological interventions for two main outcomes: preventing PTSD (incidence of PTSD) and reducing PTSD symptom severity; it also lists the SOE grade for each intervention and outcome.

Table 9. Findings and strength of evidence for the efficacy of psychological interventions to prevent PTSD and reduce PTSD symptom severity

Intervention, Population	Outcome[a]	Results	SOE[b]
Cognitive behavioral therapy, Civilian, mixed trauma types[127]	Incidence of PTSD	CBT significantly less than control at 6- and 12-month followup (CAPS: 9% vs. 55%; 21 vs. 58%, p<0.05); 1 trial (N=46)	Insufficient
	PTSD symptom severity	CBT significantly less than control at 6-month (CAPS: 31.95 vs. 52.45, p<0.05) and 12-month (CAPS: 25.26 vs. 52.50, ES (95% CI) = 1.11 (0.34 to 1.88), p<0.05) followup; 1 trial (N=46)	Insufficient
Cognitive therapy, Civilian, mixed trauma types[122,123]	Incidence of PTSD	CT significantly less than control at 5-month followup (CAPS: 20.0% vs. 58.7%, p=0.002);[122] 1 trial (n=133)	Insufficient
	PTSD symptom severity	CT not significantly different than control at the end of treatment (CAPS-2: 43.0 vs. 55.9, p=NR);[123] 1 trial (n=60) CT significantly less than control at 5-month followup (CAPS total: 29.5 vs. 50.6, p=NR);[122] 1 trial (n=133)	Insufficient

Table 9. Findings and strength of evidence for the efficacy of psychological interventions to prevent PTSD and reduce PTSD symptom severity (continued)

Intervention, Population	Outcome[a]	Results	SOE[b]
Debriefing, Civilian mixed trauma types[129,131]	Incidence of PTSD	Debriefing not significantly different than control at 2-week,[131] 6-week,[131] or 6-month (PSS-SR: 23% vs. 26%, p=NR)[129] followup,[c] data NR;[131] 2 trials (n=341)	Low
	PTSD symptom severity	Debriefing not significantly different than control at 6-month (IES: 19.7 vs. 23.3, p=NR) followup[c];[129] 1 trial (n=105) Debriefing not significantly different than control at 2-week, 6-week, or 6-month followup, respectively (SI-PTSD: emotional debriefing, 18.1, 14.4, 10.2; educational debriefing, 16.2, 11.9, 9.3; No debriefing, 15.9, 10.5, 9.6, overall between-groups p=0.33);[131] 1 trial (N=236)	Low
Exposure-based therapies, Civilian, mixed trauma types[122,123,128]	Incidence of PTSD	PE significantly less than control at the end of treatment (CAPS-2: 33% vs. 77%, p<0.001);[123] 1 trial (n=60) PE not significantly different than control at 4-week followup (PSS-I: 41% vs. 51%, p=0.60)[d];[128] 1 trial (N=137) PE significantly less than control at 5-month followup (CAPS: 21.6% vs. 57.1%, p<0.003);[122] 1 trial (n=156)	Insufficient
Psychoeducation, Civilian crime [129] and injury[133] victims	Incidence of PTSD	Psychoeducation not significantly different than control at 1-month followup (PCL > 3: 46% vs. 51%, p=0.83);[133] 1 trial (n=79) Psychoeducation not significantly different than control at 6-month followup[c] (PSS-SR: 11% vs. 26%, p=NR);[129] 1 trial (n=103)	Insufficient
Self-help materials, Women newly diagnosed with breast cancer[120]	PTSD symptom severity	Significantly greater reduction for SHB than control at 3-month followup (PSDS-SR, Cohen's d = -0.59 vs. -0.16, p=0.01) but not at 6-month followup (d = -0.47 vs. -0.13, p=NR); 1 trial (N=49)	Insufficient
Supportive counseling, Women, mixed trauma types[121,125,130]	Incidence of PTSD	SC not significantly different than control at 4 to 6 weeks postpartum [MINI-PTSD: 34% vs. 30%, RR (95% CI)=1.15 (0.66 to 2.02), p=NS] or at 3 months postpartum [MINI-PTSD 6% vs. 17%, RR (95% CI)=0.35 (0.10 to 1.23), p=NS];[121] 1 trial (N=103)	Insufficient
	PTSD symptom severity	SC not significantly different than control at 6 months (IES difference:-3.5, p=NS);[130] 1 trial (N=162) SC significantly less than control at 12 months (PHSI-P difference: -2.0, p<0.05);[125] 1 trial (N=174)	Insufficient

CAPS = Clinician Administered PTSD Scale; CBT = cognitive behavioral therapy; CT = cognitive therapy; ES = effect size; IES = Impact of Event Scale; MINI-PTSD = Mini-International Neuropsychiatric Interview Post-Traumatic Stress Disorder; N = entire sample; n = subset of sample; NR = not reported; NS = not significant; PCL = Posttraumatic Stress Disorder Checklist; PE = prolonged exposure therapy; PHSI-P = Post-Hospitalization Stress Index for Parent; PSDS-SR = Posttraumatic Stress Diagnostic Scale-Self Report; PSS-I=PTSD Symptom Scale-Interview Version; PSS-SR = Post-traumatic Stress Disorder Scale-Self Report version; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; RR = relative risk; SC = supportive counseling; SHB = self-help booklet; SI-PTSD = Structured Interview for PTSD; SOE = strength of evidence

[a]If the CAPS or CAPS-2 was the primary outcome measure, it is the only measure of PTSD symptom severity reported here. Additional outcome measures of PTSD symptom severity are reported in the subsection of the text for each intervention.

[b]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

[c]Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in this study of debriefing and psychoeducation,[129] we considered all outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.

[d]Due to high overall attrition (i.e., greater than 40% at 12-week followup) in this study of exposure-based therapy,[128] we considered all of its outcomes collected at that time point as having a high risk of bias and therefore do not report them here.

Cognitive Behavioral Therapy

Overall, one study comparing CBT with usual care met our inclusion criteria (Table 10);[127] four studies otherwise meeting inclusion criteria were omitted from our main data synthesis for high risk of bias.[83,96,97,108,127] The remaining government-funded study was conducted in Australia with male and female civilian trauma victims who sustained an injury severe enough to warrant hospitalization of greater than 24 hours (Table 10); subjects were excluded if they had a moderate to severe brain injury.[127] The investigators compared CBT (n=24) with usual care (n=22). The primary outcome measure was the Clinician Administered PTSD Scale (CAPS). Follow-up assessments were obtained at 6 and 12 months after treatment ended.

Table 10. Characteristics of included cognitive behavioral therapy trials

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
O'Donnell et al., 2012[127] Medium Targeted	Unblinded RCT, CBT (24) UC (22)	Four to 10 sessions of 90 minutes (12 months)	Civilian mixed (Transportation accidents, falls, assaults, work-related accidents, other forms of traumatic injury)	CAPS total score, CBT: 56.61 UC: 60.73	35.9[a] (range NR)	39.1[a]

CAPS = Clinician Administered PTSD Scale; CBT = cognitive behavioral therapy; n = subset of sample; NR = not reported; RCT = randomized controlled trial; UC = usual care

[a] Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Compared with patients receiving usual care, patients receiving CBT had a significantly lower prevalence of PTSD at both 6- and 12-month followup (Table 9). The CBT group also had significantly less severe PTSD symptoms as measured by the CAPS mean total score at both 6 and 12 months. Compared with usual care, the CBT group reported significantly lower symptoms of anxiety on the Hospital Anxiety and Depression Scale (HADS-A) at 6 (6.38 vs. 11.87, $p \leq 0.05$) and 12 months (7.84 vs. 11.0, $p<0.05$), as well as significantly lower symptoms of depression on the Beck Depression Index (BDI) at both followup points (12.24 vs. 31.20 and 13.95 vs. 29.00, $p<0.05$). At 6 months, the incidence of a major depressive episode was similar for the usual care and CBT groups (respectively, 9% vs. 4%, p=NS); however, at 12 months, more subjects in the usual care group met criteria for a major depressive episode than those in the CBT group (50% vs. 11%, $p<0.05$). At 6 and 12 months, the groups did not differ significantly with respect to the prevalence of anxiety disorders.

Cognitive Therapy

Table 11 summarizes the characteristics of the two CT studies meeting our inclusion criteria.[122,123] They enrolled civilian mixed trauma samples of adults recruited from either an Australian "traumatic stress clinic" (n=60)[123] or an Israeli hospital emergency department (n=133).[122] Both compared CT with a waitlist group. For both studies, individuals that conducted clinical assessments were blinded to treatment condition, but the subjects were not blinded with respect to treatment group. Both studies included men and women ranging in age from 18 to 70 years. The primary outcome measure was the CAPS[122] or the CAPS-2.[123] Follow-up assessments were conducted at 5[122] and 6 months.[123] In one of these studies,[122] the waitlist group received PE after 5-month followup, and we do not report this group's 9-month outcomes in the report

because the timing of the delayed intervention does not meet our eligibility criteria (see Table 3 in the Inclusion and Exclusion Criteria section). Both studies received government funding; one also received funding from a pharmaceutical company and a private foundation.[122] One study used ITT analysis,[123] and the other performed a "completer analysis" based on approximately 85 percent of the randomized sample.[122]

Table 11. Characteristics of included cognitive therapy trials

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Bryant et al., 2008[123] Low Targeted	Outcome assessors blinded RCT, CT (30) WL (30)	Five weekly 90-minute individual sessions (6 months)	Civilian mixed (MVAs, "other trauma," physical assault, and "other accident")	CAPS-2 total score, CT: 66.8 WL: 63.6	NR	57.8[a]
Shalev et al., 2011[122] Medium Targeted	Outcome assessors blinded RCT, CT (40) WL (93)	12 weekly 90-minute individual sessions (5 months)[b]	Civilian mixed (Terrorist attacks, MVAs, work or other accidents)	CAPS total score, CT: 71.78 WL: 71.66	NR	52.1

CAPS = Clinician Administered PTSD Scale; CAPS-2 = Clinician Administered PTSD Scale-2; CT = cognitive therapy; MVA = motor vehicle accident; n = subset of sample; NR = not reported; RCT = randomized controlled trial; WL = waitlist
[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.
[b]The WL group received PE after 5-month followup and was no longer an inactive comparison group. Because the timing of the delayed intervention does not meet our eligibility criteria, we do not report its outcomes at 9-month followup in the report.

One trial reported a significant difference in PTSD incidence between CT and waitlist groups at 5 months[122] (Table 9). The studies also reported different findings for PTSD symptom severity outcomes. One study found no significant differences between the CT and waitlist groups,[123] whereas the other study reported that CT was associated with lower PTSD symptom severity at 5 months.[122] Only one of the two studies measured symptoms of anxiety and depression, reporting no significant differences between the CT and waitlist groups in anxiety (BAI, 23.4 vs. 19.6) or depression (BDI-2 18.9 vs. 21.9) scores at the end of treatment.[123]

Coping Skills Therapy

One study otherwise meeting our eligibility criteria reported on the effectiveness of coping skills or stress inoculation therapy but was omitted from our main data synthesis for high risk of bias.[85]

Debriefing Interventions

Two studies met our eligibility criteria for a debriefing intervention.[129,131] Five studies otherwise meeting eligibility criteria were omitted from our main data synthesis for high risk of bias.[84,85,93,95,103] Table 12 summarizes the characteristics of the two included studies, which we rated as low[131] or medium risk of bias.[129]

Table 12. Characteristics of included debriefing trials

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Rose et al., 1999[129] Medium Universal	Unblinded RCT, Debriefing + psycho-education (54) Assessment only (51)	One, 1-hour individual session (6 months)[a]	Civilian crime victims (Actual or threatened physical or sexual assault; bag snatch)	PSS, Debriefing + psychoeducation: 16.8 Assessment: 15.6	35 (18-76)	24.8
Sijbrandij et al., 2006[131] Low Universal	Unblinded RCT, Emotional debriefing (76) Educational debriefing (79) No debriefing (81)	One, 45- to 60-minute individual session (6 months)	Civilian assault or accident	SI-PTSD, Emotional debriefing: 19.9 Educational debriefing: 19.9 No debriefing: 17.7	40.4[b] (range NR)	NR

n = subset of sample; NR = not reported; PSS = Post-traumatic Symptom Scale; RCT = randomized controlled trial; SI-PTSD = Structured Interview for PTSD

[a]Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in this study of debriefing and psychoeducation,[129] we considered all outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Both government-funded studies were conducted with civilian trauma samples and employed debriefing based on Mitchell's Critical Incident Stress Debriefing protocol (CISD). One study compared two forms of CISD ("emotional debriefing" [n=76] and "educational debriefing" [n=79]) with a no-debriefing control group (n=81);[131] the other study compared CISD plus education (n= 54) with assessment only (n=51).[129] The "emotional debriefing" intervention consisted of CISD minus the educational component, and the "educational debriefing" intervention consisted of CISD minus the emotional component. Timing of the debriefing ranged from 9 to 31 days[129] or 11 to 19 days[131] post-trauma. The subjects and treatment providers were not blinded with respect to treatment group assignment. Subjects were excluded if they had been assaulted by a member of their household[129] or if they had already received a debriefing session since the trauma.[131] The primary outcome measures were the Post-traumatic Symptom Scale[129] and the Structured Interview for PTSD.[131] Follow-up assessments were conducted at 2 weeks, 6 weeks, and 6 months in one study[131] and at 6 months after the debriefing in the other.[129] Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in one of the studies,[129] we considered all of its outcomes collected at that time point as having a high risk of bias and therefore do not report them here.

The debriefing intervention and the inactive comparator did not differ significantly in the number of participants meeting criteria for PTSD or in reducing PTSD symptom severity at 6-month followup[129,131] (Table 9). Both studies reported that groups did not differ significantly in severity of anxiety and depressive symptoms at followup. The mean BDI score did not differ significantly between the debriefing and assessment groups at 6-month followup (12.1 vs. 13.9, p=NR).[129] Similarly, at 6-month followup, the mean HADS-Depression score and the change in HADS-Depression score did not differ significantly (p=0.23) in the groups that received emotional debriefing (3.8, -1.6), educational debriefing (3.2, -1.5), or no debriefing (3.2, -1.4).[131] The emotional debriefing, educational debriefing, and no debriefing groups also did not differ

significantly (p=0.96) in HADS-Anxiety score (5.0, 4.4, 4.6) or change in HADS-Anxiety score from pretreatment (-2.4, -2.2, -2.1) at 6-month followup.[131]

One study reported no differences between groups on perceived helpfulness of the intervention at 6 months (p>0.10).[129]

Exposure-Based Therapies

Three studies met our inclusion criteria for exposure-based interventions;[122,123,128] two studies otherwise meeting our eligibility criteria were omitted from our main data synthesis for high risk of bias.[99,112] Table 13 summarizes the characteristics of the three studies meeting our inclusion criteria.[122,123,128]

Table 13. Characteristics of included exposure-based trials

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Bryant et al., 2008[123] Low Targeted	Outcome assessors blinded RCT, PE[a] (30) WL (30)	Five weekly 90-minute individual sessions (6 months)	Civilian mixed (MVA, other trauma, physical assault, and other accident)	CAPS-2 total score, PE: 70.6 WL: 63.6	NR	57.8[b]
Rothbaum et al., 2012[128] Medium Universal	Outcome assessors blinded RCT, PE (69) Assessment only (68)	Three 60-minute individual sessions (12 weeks)[c]	Civilian mixed (Sexual assault, nonsexual assault, MVA, other)	PSS-I[d]	31.5[b] (range NR)	65
Shalev et al., 2012[122] Medium Targeted	Outcome assessors blinded RCT, PE (63) WL (93)	12 weekly 90-minute individual sessions (5 months)[e]	Civilian mixed (Terrorist attacks, MVAs, work or other accidents)	CAPS total score, PE: 73.59 WL: 71.66	NR	52

CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; MVA = motor vehicle accident; n = subset of sample; NR = not reported; PDS = Posttraumatic Stress Diagnostic Scale; PE = prolonged exposure therapy; PSS-I = PTSD Symptom Scale-Interview version; RCT = randomized controlled trial; WL = waitlist

[a]Imaginal and/or in vivo exposure.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

[c]Because of high overall attrition (i.e., greater than 30% at 12-week followup) in this study of exposure-based therapy,[128] we considered all of its outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.

[d]PSS-I assessed at 4- and 12-week followup only; mean baseline PDS score was 18.9 in both groups.

[e]The WL group received PE after 5-month followup and was no longer an inactive comparison group. Because the timing of the delayed intervention does not meet our eligibility criteria, we do not report its outcomes at 9-month followup in the report.

All three studies compared PE with an inactive comparator of either a waitlist (WL)[122,123] or assessment only[128] in civilian mixed trauma samples. Additional details about two of these studies[122,123] are provided in the previous section on Cognitive Therapy. The third study[128] was conducted in the United States and assessed individuals ages 18 to 65 who presented to a Level I Trauma Center in a public hospital within 72 hours of experiencing a traumatic event. A total of 162 individuals were randomized to PE (30,[123] 69,[128] and 63[122]) and 191 individuals were randomized to the inactive condition (30,[123] 68,[128] and 93[122]). Because of high overall attrition

(i.e., greater than 30% at 12-week followup) in one study of exposure-based therapy,[128] we considered all of its outcomes collected at that time point as having a high risk of bias and therefore do not report them here. In addition, the waitlist group in another study received PE after 5-month followup, and we do not report this group's 9-month outcomes in the report because the timing of the delayed intervention does not meet our eligibility criteria (see Table 3 in the Inclusion and Exclusion Criteria section).[122]

The prevalence of PTSD was significantly lower in groups receiving PE compared with WL or assessment only at the end of treatment[123] and at 5-month [122] followup, but not at 4-week[128] followup (Table 9). PTSD symptom severity was significantly lower in PE compared with WL or assessment only at the end of treatment[123] and at 4-week,[128] and 5-month[122] followup (Table 9).

Compared with assessment only or WL, PE was associated with significantly lower symptoms of depression at 4 weeks (BDI-II, 15.4 vs. 21.4, $p<0.05$[128]) and at the end of treatment (BDI-2, 21.9 vs. 12.1, $p=0.003$).[123] PE was also associated with significantly lower symptoms of anxiety (BAI, 19.6 vs. 13.4, $p=0.004$) at the end of treatment.[123]

Psychoeducation

Two studies met our eligibility criteria for psychoeducation,[129,133] while one study otherwise meeting eligibility criteria was rated high risk of bias and omitted from our main data synthesis.[110] Of the included studies (Table 14), one was conducted in the UK with civilian crime victims,[110] and the other in the United States with civilians presenting to a trauma center with injuries requiring surgical intervention.[133] Subjects were excluded if they had been assaulted by a member of their household[129] or if they were in criminal custody.[133] Subjects and treatment providers were not blinded with respect to treatment group assignment. The primary outcome measures were the PSS-SR and the PCL. Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in one of the studies, we considered all of its outcomes collected at that time point as having a high risk of bias and therefore do not report them here.[129]

The incidence of PTSD did not differ significantly between the psychoeducation and control groups at 1-month[133] or at 6-month[129] followup (Table 9). The psychoeducation and control groups did not differ significantly in PTSD symptom severity at 1-month[133] or 6-month followup.[129] There was no statistically significant difference between the psychoeducation group and the assessment-only group in severity of symptoms of depression at either follow-up point (BDI at 6 months, 9.8 vs. 13.9, $p>0.10$).[129] There was no difference in perceived helpfulness of the psychoeducation intervention compared with assessment only, $p>0.10$).[129]

Table 14. Characteristics of included psychoeducation trials

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Rose et al., 1999[129] Medium Universal	Unblinded RCT, Psychoeducation (52) Assessment only (51)	One 1-hour individual session (6 months)[a]	Civilian crime victims (Actual or threatened physical or sexual assault; bag snatch)	PSS-SR, Psychoeducation: 16.0 Assessment: 15.6	35 (18-76)	24.8
Wong et al., under review[133] Medium Universal	Unblinded RCT, Psychoeducation (42) Control (37)	One 18-minute video (1 month)	Civilian mixed (Gunshot, falls, etc.) with physical injury	PCL, NR	31.2[b] (range NR)	16

n = subset of sample; NR = not reported; PCL = Posttraumatic Stress Disorder Checklist; PSS-SR = Post-traumatic Stress Disorder Scale-Self Report version; RCT = randomized controlled trial

[a]Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in this study of psychoeducation,[129] we considered all outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Self-Help Materials

One study met our eligibility criteria for self-help-based interventions;[120] one study otherwise meeting our eligibility criteria was omitted from our main data synthesis for high risk of bias.[106]

The included trial (Table 15) was conducted in Australia with 49 women ranging in age from 32 to 86 years newly diagnosed with Stage 0 to II breast cancer. This study compared a CBT-based self-help booklet (SHB) group with an information-only booklet group. The SHB (which women were encouraged to read over a 3-month period) covered topics such as relaxation and meditation; coping with side effects; emotional adjustment, including cognitive restructuring around self-blame and stress management activities; body image and identity; social support; and survivorship. Subjects and treatment providers/assessors were not blinded as to diagnosis or treatment condition. The median amount of information read by the women was 100 percent in the intervention group and 75 percent in the control group; both groups reported using the material they received for up to 15 minutes per week, and the median number of worksheets completed by the women in the SHB group was 25 percent.

Table 15. Characteristics of included self-help booklet–based trial

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Beatty et al., 2010[120] Medium Universal	Unblinded RCT, SHB (25) Information booklet (24)	NR (6 months)	Women medical (Newly diagnosed with breast cancer within previous month) (Civilian/military status not specified)	PSS-SR, 10.76[a]	55.2 (range NR)	100

n = subset of sample; NR = not reported; RCT = randomized controlled trial; PSS-SR = Posttraumatic Stress Diagnostic Scale-Self Report version; SHB = self-help booklet.
[a]Reported for the entire sample, not by treatment arm

Compared with women in the information booklet group, women in the SHB group exhibited a significantly greater reduction in PTSD symptom severity from baseline to 3 months but not from baseline to 6 months (Table 9). Symptoms of depression and anxiety were measured with the Depression and Anxiety Stress Scales (DASS). The effect sizes for change in the severity of DASS-depression were small and did not differ significantly between the SHB group and the information booklet group at 3 months (0.15 vs. 0.03, p=NR) or 6 months (0.20 vs. -0.06, p=NR). Likewise, effect sizes for change in the severity of DASS-anxiety were small and did not differ significantly between the SHB group and the information booklet group at 3 months (0.19 vs. 0.17) or 6 months (0.33 vs. 0.18). Quality of life was measured with the European Organisation for Research and Treatment of Cancer Quality of Life Core Questionnaire and Breast Cancer Module. The effect sizes for change in quality of life were small and did not differ significantly between groups at 3 months (0.10 vs. 0.18, p=NR) or 6 months (0.18 vs. 0.37, p=NR).

Supportive Counseling

Three studies met the eligibility criteria for supportive counseling (SC).[121,125,130] Three studies otherwise meeting eligibility criteria were omitted from our main data synthesis for high risk of bias.[86,105,117] Table 16 summarizes the characteristics of the three studies included in the analyses.

The three studies included women ranging in age from 18 to 76 years who recently experienced emergency cesarean section[130] or an otherwise traumatic childbirth[121] or who were caring for a critically ill child who had suffered an accidental injury.[125] The specific format of SC differed across studies and included personal storytelling,[130] a preventive educational-behavioral program to empower parents,[125] and elements of critical stress debriefing.[121] Subjects, but not the treatment providers, were blinded with respect to treatment group assignment. The researcher who conducted the 3-month follow-up assessment in one study was blinded as to group allocation.[121] One study was government funded,[125] and two were funded by private foundations.[121,130] Each study used a different primary outcome measure to assess PTSD or PTSD symptom severity: the IES,[130] the Post-Hospital Stress Index for Parents (PHSI-P),[125] and the Mini-International Neuropsychiatric Interview-Post-Traumatic Stress Disorder (MINI-PTSD).[121] Follow-up assessments were conducted at various intervals ranging from 4 weeks[121] to 12 months.[125]

Table 16. Characteristics of included supportive counseling trials

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Gamble et al., 2005[121] Medium Universal	Outcome assessor blinded RCT, SC (50) Control (53)	One 40- to 60-minute session within 72 hours of birth (4-6 weeks and 3 months postpartum)	Civilian (Traumatic childbirth)	MINI-PTSD, SC: NR Control: NR	28 (18-46)	100
Melnyk et al., 2004[125] Medium Universal	Unblinded RCT, COPE (90) Control (84)	Three-phase intervention, duration: NR (1, 3, 6, and 12 months postdischarge)	Civilian medical (Mothers of critically ill children)	PHSI-P, NR	31.2 (18-52)	100
Ryding et al., 2004[130] Medium Universal	Unblinded RCT, SC (89) Control (73)	Two 2-hour group sessions (6 months)	Civilian medical (Emergency cesarean section)	IES, SC: NR Control: NR	332 (19-44)	100

COPE = Creating Opportunities for Parent Empowerment; IES = Impact of Event Scale; MINI-PTSD = Mini-International Neuropsychiatric Interview-Posttraumatic Stress Disorder; n = subset of sample; NR = not reported; PHSI-P = Post-Hospital Stress Index for Parents; RCT = randomized controlled trial; SC = supportive counseling

Compared with standard postnatal care, SC was not more effective in preventing PTSD in mothers at 4 to 6 weeks postpartum or at 3 months postpartum (Table 9).[121] Six months after emergency cesarean section, there was no statistically significant difference in PTSD symptom severity between the group of mothers who received SC and the group who received standard postpartum care.[130] In mothers caring for a critically ill child, PTSD symptom severity did not differ between the SC and the control group at 1-month, 3-month, or 6-month followup, but it was significantly lower at 12-month followup in mothers who received SC.[125]

In mothers who experienced traumatic childbirth, the percentage of women with a diagnosis of depression did not differ significantly between the two groups at 4 to 6 weeks postpartum (32% vs. 34%); however, at 3 months postpartum, fewer women who received SC had a diagnosis of depression as compared with those in the control group (8% vs. 32%, p=0.002).[121] After emergency cesarean section, mothers who received SC did not differ from those in the control group on the severity of symptoms of depression (median Edinburgh Postnatal Depression Scale score: 6.0 vs. 6.0, p=0.1256) or in rate of depression (Edinburgh Postnatal Depression Scale score >12, 8.5% vs. 13.8%, p=NS).[130] In mothers caring for their critically ill child, symptoms of depression were significantly lower in the SC group compared with the control group at 1-month (POMS depression subscale, 2.6 vs. 4.1, p<0.05) and 6-month (POMS depression subscale, 2.0 vs. 3.9, p<0.05) followup but not at 3- or 12-month follow-up.[125] Two studies evaluated anxiety, and both reported there were no significant differences between the SC and control groups at 3-month followup (DASS-anxiety >9, 2% vs. 11% [RR (95% CI) = 0.18 (0.02 to 1.45)], p=NR;[121] STAI, 38.4 vs. 40.7, p=NR[125]) as well as at 6-month followup (STAI, 36.0 vs. 39.1, p=NR)[125] and 12-month followup (STAI, 35.8 vs. 40.9, p=NR).[125]

Finally, the perceived utility (helpfulness) of the SC intervention was rated as 8 or higher on a 10-point scale by 86 percent of women who experienced a traumatic childbirth.[121] Similarly, 71 percent of women who experienced an emergency cesarean section reported that the SC intervention completely met their expectations.[130]

All Other Psychological Interventions

One study of eye movement desensitization and reprocessing[102] and one study of interpersonal therapy[104] met the eligibility criteria but were omitted from our main data synthesis for high risk of bias. No studies of cognitive processing therapy or psychological first aid met our inclusion criteria.

High-Risk-of-Bias Studies

We rated 33 studies as high risk of bias.[27,47,51,83-88,90,92-97,99-101,103-110,112-114,116-118] In most cases, we had data from studies of either low or medium risk of bias, and we did not include these high-risk-of-bias studies in our analyses. For some psychological or related interventions or populations (e.g., veterans), however, we only found high-risk-of-bias studies; therefore, we briefly summarize them here.

Eye Movement Desensitization and Reprocessing Therapy

One unblinded, nonrandomized study compared the effect of a single session of eye movement desensitization and reprocessing (EMDR) with waitlist on PTSD symptom severity in U.S. survivors of Hurricane Andrew.[102] Controlling for pretreatment levels, the EMDR group exhibited significantly lower scores at 1 month than the waitlist group on IES total (21.6 vs. 37.9, $p<0.001$), IES avoidance (10.5 vs. 16.6, $p<0.03$) and IES intrusion (11.2 vs. 21.6, $p<0.001$). IES scores remained relatively stable at the 3-month followup for the EMDR group (total, 24.3; avoidance, 12.6; intrusions, 11.8) but were not reported for controls.

Interpersonal Counseling

One randomized study conducted in Australia compared the effect of manualized interpersonal counseling versus treatment as usual (i.e., nonspecific psychological support) on PTSD incidence and related PTSD and psychological symptoms in victims of MVAs, falls, and nonaccidental injury.[104] Interpersonal counseling focused on the impact of the trauma on interpersonal issues predating the traumatic event as well as those arising from the traumatic event in domains such as role transitioning, grief, and loss. At 6-month followup, no statistically significant differences were found between treatment groups in the incidence of PTSD or in the severity of PTSD, depression, or anxiety symptoms.

Memory Structuring Intervention

One study evaluated a novel intervention called "Memory Structuring Intervention" (MSI).[101] MSI attempts to shift processing of traumatic memory from uncontrollable somatosensory and affective processes toward more controlled linguistic and cognitive processes by providing patients organization, labeling, and causality. Seventeen MVA survivors were randomly assigned to receive MSI versus supportive listening control 48 hours after their accident. At follow-up, PDS total (8.1 vs. 18.5, $p<0.05$), PDS arousal (4.2 vs. 7.7, $p<0.05$), and PDS intrusions (1.6 vs. 5.8, $p<0.05$) were significantly lower in MSI recipients than in controls.

Debriefing Plus Stress Coping Intervention

One study evaluated a stress coping intervention with military and civilian first responders to a traffic accident with multiple fatalities.[85] The military responders received debriefing plus stress management, and the civilian responders received only debriefing. The results suggested better outcome in the military responders, as indicated by lower frequency of symptoms on the PTSS-10.

Structured Writing Intervention

One study evaluated the effectiveness of a writing intervention in 67 civilians who had experienced a traumatic physical injury or accident.[92] The perceived utility of the writing intervention was high, but it was not more effective than the information-only control condition in reducing the incidence of PTSD.

Detailed Synthesis: Pharmacological Interventions

Overall, two studies of pharmacologic interventions met eligibility criteria for KQ 1.[122,132] Eight studies otherwise meeting eligibility criteria were omitted from the main data synthesis for high risk of bias.[47,51,100,107,113,114,116,118] Both of the included studies involved civilian medical traumas, one with mixed trauma[122] and one with stress following cardiac surgery.[132] The funding was identified for only one of the studies,[122] which had both governmental and industry support.

Table 17 summarizes the available evidence of the efficacy of two included studies testing pharmacologic interventions.

Table 17. Findings and strength of evidence of the efficacy of pharmacologic interventions

Intervention, Population	Outcome	Results	SOE[a]
Escitalopram vs. waitlist control or placebo, Civilian mixed trauma types[122]	Incidence of PTSD	Escitalopram not significantly different than WL at 5-month followup (CAPS: 61.9% vs. 58.2%, p=NR); 1 trial (n=116)[b] Escitalopram not significantly different than placebo at 5-month or 9-month followup (CAPS: 61.9% vs. 55.6%, p=0.57; 42.1% vs. 47.1%, p=NR); 1 trial (n=46)[c]	Insufficient
	PTSD symptom severity	Escitalopram not significantly different than WL at 5-month followup (CAPS total: 48.7 vs. 50.6, p=NR); 1 trial (n=116)[b] Escitalopram not significantly different than placebo at 5-month or 9-month followup (CAPS total: 48.7 vs. 47.1, p=NR; 47.2 vs. 45.7, p=NR); 1 trial (n=46)[c]	Insufficient
Hydrocortisone stress dose vs. placebo, Cardiac surgery[132]	Incidence of PTSD	Hydrocortisone less than placebo at 6-month followup (PTSS-10: 7.1% vs. 21.4%, p=NR[d]); 1 trial (n=28)	Insufficient
	PTSD symptom severity	Hydrocortisone less than placebo at 6-month followup (PTSS-10: 15.5 vs. 25.5, p=0.03); 1 trial (n=28) In terms of the number and type of traumatic memories, hydrocortisone not significantly different than placebo at 6-month followup (PTSS-10: data NR, p≤0.33); 1 trial (n=28)	Insufficient

CAPS = Clinician Administered PTSD Scale; n = subset of sample; NR = not reported; PTSD = posttraumatic stress disorder; PTSS-10 = Posttraumatic Stress Symptom 10 Question Inventory; SOE = strength of evidence; WL = waitlist

[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

[b]Completers of 116 randomized.

[c]Completers of 46 randomized.

[d]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Selective Serotonin Reuptake Inhibitors (SSRIs)

Table 18 summarizes the characteristics of the one study meeting our inclusion criteria.[122]

Table 18. Characteristics of included SSRI trial

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Shalev et al., 2011[122] Medium Targeted	Double blind RCT, Escitalopram (23) Placebo (23) WL (93)	Escitalopram and placebo, 10 mg twice daily (9 months) WL: not applicable (5 months)[a]	Civilian mixed (Terrorist attacks, MVAs, work or other accidents)	CAPS total score, Escitalopram: 79.83 Placebo: 74.91 WL: 71.66	37.8[b]	48.9[b]

CAPS = Clinician Administered PTSD Scale; Mg = milligrams; MVA = motor vehicle accident; n = subset of sample; RCT = randomized controlled trial; WL = waitlist

[a]The WL group received PE after 5-month followup and was no longer an inactive comparison group. Because the timing of the delayed intervention does not meet our eligibility criteria, we do not report its outcomes at 9-month followup in the report.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

This study was conducted in Israel with a mixed civilian trauma sample. Treatment arms included escitalopram (n=23), placebo (n=23), and waitlist (93). Additional details about this study can be found in the section on Cognitive Therapy.

The incidence of PTSD did not differ between the SSRI (61.9%) and waitlist (58.2%) groups at 5-month follow-up (p=NR) (Table 17). The incidence of PTSD did not differ between the SSRI group and the placebo group at 5-month (61.9% vs. 55.6%, p=0.57) or at 9-month (42.1% vs. 47.1%, p=NR) followup. There were no differences between the SSRI and waitlist groups on mean CAPS total and PSS-SR symptom severity scores at the 5-month follow-up assessment. There were no significant differences in PTSD symptom severity between SSRI and placebo at either 5-month or 9-month followup. This study did not report on any other outcomes of interest.

Steroids

Hydrocortisone

One study assessing the efficacy of hydrocortisone to prevent PTSD met our inclusion criteria.[132] Three studies were rated as having a high risk of bias and omitted from our main data synthesis.[113,114,118] Table 19 summarizes the characteristics of the one medium risk-of-bias study.[132] One randomized, double-blind study was conducted in 36 adult German civilians who were at high risk for perioperative complications during cardiac surgery with cardiopulmonary bypass.[132] Patients were not eligible if they were pregnant, required an emergency operation, had hepatic or renal dysfunction, were HIV positive, had insulin-dependent diabetes, had an extracardial septic focus, had chronic or acute inflammatory disease, required glucocorticoids other than hydrocortisone, or could not provide informed consent. Eligible patients were randomly assigned to 4 days of either stress doses of hydrocortisone (a loading dose followed by a taper) or placebo beginning before induction of anesthesia. At 6 months postsurgery, 28 patients (ages 63 to 73 years, 32% female, 14 in each arm) were assessed by phone.

Table 19. Characteristics of included hydrocortisone trial

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Weis et al, 2006[132] Medium Targeted	Double-blind RCT, Hydrocortisone stress dose[a] (14) Placebo (14)	4 days (6 months)	Civilian medical; cardiac surgery	PTSS-10; Hydrocortisone: NR Placebo: NR	68.5[b] (63-73)	32.1[b]

mg = milligrams; n = subset of sample; NR = not reported; POD = postoperative day; PTSS-10 = Posttraumatic Stress Symptom 10 Question Inventory; RCT = randomized controlled trial

[a]Loading dose of 100 mg over 10 minutes, followed by a continuous infusion of 10 mg/hour for 24 hours (postoperative day [POD] 1). This was reduced to 5 mg/hour on POD 2, tapered to 3 X 20 mg on POD 3, and then 3 X 10 mg on POD 4.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Compared with the placebo group, the hydrocortisone group had significantly lower stress symptom scores as measured by the Posttraumatic Stress Symptom 10 Questionnaire Inventory (median of 15.5 vs. 25.5, p=0.03) and appeared less likely to have evidence of PTSD as defined by a stress symptom score > 35 (7.1% vs. 21.4%, p=NR) (Table 17). Patients did not differ significantly with regard to number and type of traumatic memories ($p \leq 0.33$). Also, patients in the hydrocortisone group had significantly higher health-related quality-of-life scores in 5 of 8 subscales and in both physical and mental summary scores ($p \leq 0.01$) on the Medical Outcomes Study Short Form (SF-36).

All Other Pharmacologic Interventions

One or more studies on the following pharmacologic therapies otherwise met inclusion criteria but were rated high risk of bias and omitted from the main data synthesis: anticonvulsants,[47] benzodiazepines,[100] and beta-blockers.[47,51,107,116] No studies of the following therapies met inclusion criteria: alpha blockers, monoamine oxidase inhibitors, narcotics, nonbenzodiazepine sedatives or hypnotics, opioid antagonists, other second-generation antidepressants, second-generation (atypical) antipsychotics, serotonin and norepinephrine reuptake inhibitors, or tricyclic antidepressants.

High-Risk-of-Bias Studies

Eight studies comparing a pharmacologic intervention with placebo that were rated as high risk of bias otherwise met our eligibility criteria.[47,51,100,107,113,114,116,118] One compared the effectiveness of two separate medications against each other and against placebo;[47] all others compared a single medication with placebo or no treatment.[51,100,107,113,114,116,118]

Anticonvulsants—Gabapentin

An RCT pilot study compared the effectiveness of a 14-day treatment with propranolol (n=17) with gabapentin (n=14) and with placebo control (n=14) in patients admitted to a level 1 surgical trauma center after a severe physical injury requiring specialized emergency care.[47] The PCL-C score decreased over time in all groups, but the treatment arms did not differ significantly at 1, 4, or 8 months; at the 4-month followup, rates of PTSD or major depressive disorder did not differ significantly across groups.

Benzodiazepines

A prospective cohort study in Israel compared the effectiveness of benzodiazepines (n=13) with no benzodiazepines (n=13) in civilians presenting to the emergency department following a traumatic event.[100] Those receiving benzodiazepines were "judged to require medication" by attending physicians, suggesting greater symptom severity than the group not receiving benzodiazepines. The two groups did not differ in PTSD or anxiety scores at either 1 or 6 months.

Beta-Blockers

Metoprolol

A prospective observational study in Germany with a treatment completer analysis compared the effectiveness of metoprolol (n=84, dispensed to patients for a varying and unclear period) with placebo (n=44).[107] Assignment between groups was at the discretion of the attending physicians. At 6-month followup, neither the number of traumatic memories nor PTSD symptom scores differed significantly between the two groups.

Propranolol

An RCT pilot study compared the effectiveness of a 14-day treatment with propranolol (n=17) with gabapentin (n=14) and with placebo control (n=14) in patients admitted to a level 1 surgical trauma center after a severe physical injury requiring specialized emergency care.[47] The PCL-C score decreased over time in all groups, but the treatment arms did not differ significantly at 1, 4, or 8 months; at the 4-month followup, rates of PTSD or major depressive disorder did not differ significantly across groups.

A nonrandomized controlled trial in France compared the effectiveness of a 7-day treatment with propranolol (n=11) with treatment without propranolol (n=8 patients who refused propranolol but agreed to participate in the study) for patients presenting to the emergency department following MVA or physical assault.[116] At 2 months after the event, patients receiving propranolol had lower severity scores on the Treatment Outcome PTSD scale and a lower risk of having a PTSD diagnosis.

A high-risk-of-bias RCT in the United States compared the effectiveness of 10 days of propranolol (n=19) with placebo (n=23) in civilians presenting to the emergency department following the experience of a traumatic event.[51] At 1-month and 3-month follow-up assessments, CAPS symptom severity and PTSD incidence did not differ significantly between groups, but there were fewer "physiologic responders during imagery of the traumatic event" in the propranolol group (0/8) than the placebo group (6/14) (p=0.04).

SteroidsHydrocortisone

An RCT in Israel compared the effectiveness of a single bolus of hydrocortisone (n=15, dose based on weight) between 1.5 and 5.5 hours after the trauma with placebo (n=10) for patients presenting to an emergency department with a variety of traumas (traffic accidents, work accidents, snake bite).[118] At 1 and 3 months, patients who received hydrocortisone were less likely to have a diagnosis of PTSD than those in the placebo arm.

An RCT in Germany compared the effectiveness of stress doses of hydrocortisone with standard postoperative care in patients after cardiac surgery.[113] At 6 months postsurgery, 48 (26 hydrocortisone, 22 standard care) of 91 randomized patients were available for assessment. The median Posttraumatic 10 Stress Symptom Inventory score was significantly lower ($p<0.05$) in

the hydrocortisone group (20.0) than in the standard care group (25.5), but the groups did not differ in traumatic memories.

An RCT in Germany compared the effectiveness of stress doses of hydrocortisone with placebo in patients with septic shock.[114] At followup (median, 31 months), the incidence of PTSD was significantly lower ($p<0.02$) in the hydrocortisone group (1/9) compared with the placebo group (7/11). There were no significant differences between the groups in the number reporting traumatic experiences.

Detailed Synthesis: Emerging Interventions

Overall, one study assessing the efficacy of an emerging intervention met eligibility criteria for KQ 1.[119] It involved civilian traumas requiring hospitalization. The study was funded by governmental support.

Table 20 summarizes the available evidence of the efficacy of the single study testing an emerging intervention.

Table 20. Findings and strength of evidence of the absolute effectiveness of collaborative care interventions

Intervention, Population	Outcome	Results	SOE[a]
Collaborative care vs. usual care, Civilian trauma requiring hospitalization[119]	Incidence of PTSD	Collaborative care not statistically different than usual care at 12 months [CAPS: OR (95% CI) = 1.39 (0.77 to 2.51)]; 1 trial (N=207)	Insufficient
	PTSD symptom severity	Collaborative care lower than usual care, as measured: • by CAPS at 6 months (42.9 vs. 56.7, $p<0.01$) and 12 months (38.6 vs. 47.2, $p<0.05$) after injury • by greater decrease in CAPS over 12 months following injury (group by time interaction, $p<0.01$) • by PCL-C at 6 months (40.6 vs. 49.9, $p<0.01$), 9 months (40.2 vs. 45.5, $p<0.01$) and 12 months (37.4 vs. 42.5, $p<0.05$) after injury) • by greater decrease in CAPS over 12 months following injury (group by time interaction, $p<0.01$ Collaborative care not statistically different than usual care at 1-month or 3-month followup after injury (PCL-C: 50.2 vs. 51.1 and 45.9 vs. 48.6, respectively, p=NR); 1 trial (N=207)	Low

CAPS = Clinician Administered PTSD Scale; CI = confidence interval; N = entire sample; NR = not reported; OR = odds ratio; PCL-C = PTSD Checklist-Civilian Version; PTSD = posttraumatic stress disorder; SOE = strength of evidence

[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

Collaborative Care

One study assessing the absolute effectiveness of collaborative care to prevent PTSD met our inclusion criteria.[119] Table 21 summarizes the characteristics of this low risk-of-bias study. This randomized, single-blind study was conducted in 207 adult civilian trauma patients requiring surgical hospitalization who screened positive for PTSD symptoms on two separate occasions within 1 month of the trauma. Patients were not eligible if they required immediate psychiatric intervention, lived over 100 miles from the trauma center, were currently incarcerated, or had recent histories of severe violence and were likely to face criminal charges. Eligible patients were randomly assigned to either 12 months of collaborative care, a stepped combination of care management, psychopharmacology, and cognitive behavioral therapy (n=104) or to a usual care control (n=103). The symptoms of PTSD and functional limitations were reassessed at 1-, 3-, 6-,

9-, and 12-month followup after the index injury admission. An ITT analysis was performed 12 months after the injury.

Table 21. Characteristics of included collaborative care trial

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Zatzick et al., in press[119] Low Targeted	Single blind RCT, CC (104) UC (103)	12 months (12 months)	Civilian medical; trauma requiring surgical admission	CAPS; CC: NR UC: NR PCL-C; CC: 50.5 UC: 50.8	38.5 (range NR)	47.8

CAPS = Clinician Administered PTSD Scale; CC = collaborative care; n = subset of sample; NR = not reported; PCL-C = PTSD Checklist-Civilian Version; RCT = randomized controlled trial; UC = usual care

Compared with usual care, the collaborative care group had significantly lower stress symptom scores beginning 6 months after injury (Table 20). Specifically, the collaborative care group had lower PTSD as measured by the Clinician-Administered PTSD Scale at followup 6 months (42.9 vs. 56.7, $p<0.01$) and 12 months (38.6 vs. 47.2, $p<0.05$) after the injury and over the course of the 12 months of treatment had a greater decrease in overall PTSD symptom severity (group-by-time interaction, $p<0.01$). Further, the collaborative care group had significantly lower stress scores as measured by the PCL-C at 6 months (40.6 vs. 49.9, $p<0.01$), 9 months (40.2 vs. 45.5, $p<0.01$), and 12 months (37.4 vs. 42.5, $p<0.05$) after injury, and a similar greater decrease in overall PTSD severity over the 12-month course (group-by-time interaction, $p<0.001$), although no significant difference was seen 1 month or 3 months after injury. The incidence of PTSD at 12 months did not differ between the groups (OR, 1.39; 95% CI, 0.77 to 2.51). Finally, patients did not differ significantly at 12-month followup with regard to symptoms of depression as measured by the PHQ-9 (8.4 vs. 10.1), alcohol use as measured by the Alcohol Use Disorders Identification Test (2.0 vs. 2.4), or functional impairment as measures by the SF-36 (43.7 vs. 41.2), although there was greater improvement in collaborative care group over the 12-month period (group-by-time interaction, $p<0.01$).

Comparative Effectiveness: Psychological Versus Psychological Interventions

Description of Included Studies

Eight studies addressed the comparative effectiveness of a psychological intervention with another psychological intervention.[89,91,122-124,126,129,131] The interventions included Battlemind training, CBT, CT, PE, debriefing, and SC. These studies were conducted outside the United States and included samples exposed to a variety of traumas, such as crime, physical assault, motor vehicle and other types of accidents, and terrorist attacks.

Key Points: Comparative Effectiveness

- In individuals with acute stress disorder a meta-analysis comparing CBT with SC found that people who received CBT had greater reductions in severity of PTSD symptoms than those who received SC (moderate SOE). Differences between CBT and SC with respect to preventing PTSD (low SOE), reducing the severity of depression symptoms (low SOE), or reducing the severity of anxiety symptoms (moderate SOE) also favored CBT; these results, however, did not reach statistical significance.
- Evidence was insufficient for preventing PTSD or for reducing the severity of PTSD symptoms in the following cases:
    - Battlemind training versus standard postdeployment debriefing in armed forces personnel from the UK
    - CBT versus CBT plus hypnosis in civilian victims of nonsexual assault or MVAs
    - CBT plus hypnosis versus SC in civilian victims of nonsexual assault
    - CT versus PE in civilian victims of nonsexual assault or MVAs, or hospitalized survivors of MVAs or terrorist attacks
    - Debriefing versus
        - A different form of debriefing in civilian victims of violent crime
        - Psychoeducation in civilian victims of violent crime
    - An SSRI (escitalopram) versus
        - CT for hospitalized survivors of MVAs and terrorist attacks
        - PE for hospitalized survivors of MVAs and terrorist attacks
- Evidence was insufficient for reducing the severity of related psychological symptoms in the following cases:
    - CBT versus CBT plus hypnosis for reducing symptoms of anxiety or depression in civilian victims of nonsexual assault or MVAs
    - CBT plus hypnosis versus SC for reducing symptoms of anxiety or depression in civilian victims of nonsexual assault or MVAs
    - CT versus PE for reducing symptoms of anxiety or depression in civilian victims of nonsexual assault or MVAs
    - Debriefing versus a different form of debriefing for reducing symptoms of anxiety or depression in civilian victims of violent crime
    - Debriefing versus psychoeducation for reducing symptoms of depression in civilian victims of violent crime
- Evidence was unavailable (no studies other than high risk of bias) for reducing PTSD incidence, PTSD symptom severity, or the severity of related psychological symptoms for any other psychological or pharmacological interventions of interest.

Detailed Synthesis: Psychological Versus Psychological Interventions

Battlemind Training

Two studies[27,126] reported on Battlemind training, one of which was omitted from our main data synthesis for high risk of bias.[27] Table 22 summarizes the characteristics of the one study meeting our inclusion criteria.[126]

The included study (Table 23) was conducted in the UK and compared an adapted version of Battlemind training with standard stress and homecoming briefs in male and female armed forces personnel returning from Afghanistan.[126] Battlemind training is described as incorporating information about common postdeployment reactions and self-help, drawing on positive psychology and cognitive behavioral techniques to reframe difficulties that personnel may encounter.[126] Treatment providers were not blinded with respect to treatment group assignment. The primary outcome measure was the PCL-C.

Table 22. Findings and strength of evidence for the comparative effectiveness of early psychological interventions to prevent PTSD and reduce PTSD symptom severity

Intervention, Population	Outcome[a]	Results	SOE[b]
Battlemind training, Military, mixed combat-related trauma types[126]	PTSD symptom severity	Battlemind training no different than standard postdeployment debriefing at 4-6 month followup (PCL-C: data=NR); 1 trial (n=2,443)	Insufficient
	Incidence of PTSD	Battlemind training no different than standard postdeployment debriefing at 4-6 month followup (PCL-C: data=NR); 1 trial (n=2,443)	Insufficient
CBT vs. CBT+Hypnosis, Civilian, mixed trauma types[91]	Incidence of PTSD	CBT not significantly different from CBT+Hypnosis at the end of treatment (CAPS-2: 36% vs. 30%, p=NR) or at 6-month followup (CAPS-2: 42% vs. 40%, p=NR); 1 trial (n=63)	Insufficient
	PTSD symptom severity	CBT+Hypnosis less than for CBT at the end of treatment (IES-I: 11.30 vs. 16.58, p<0.05) but not at 6-month followup (IES-I: 13.57 vs. 16.97, p=NR; 1 trial (n=63)	Insufficient
CBT vs. SC, Civilian, mixed trauma types with acute stress disorder[89,91,124]	Incidence of PTSD	CBT not significantly different than SC at end of treatment (CAPS-2, CIDI-PTSD: RR, 0.27, 95% CI [0.05 to 1.29]; I^2=71.8%) or at 6-month followup (CAPS-2, CIDI-PTSD: RR, 0.46, 95% CI [0.21 to 1.01]; I^2=44.9%); 3 trials (n=105)	Low
	PTSD symptom severity	Greater reduction for CBT than for SC on IES-I at the end of treatment (WMD, -7.85, 95% CI [-11.18 to -4.53]; I^2=1.3%) and at 6-month followup (WMD, -8.19, 95% CI [-11.79 to -4.58]; I^2=6.8%); 3 trials (n=105) Greater reduction for CBT than for SC on IES-A at the end of treatment (WMD, -14.04, 95% CI [-19.37 to -8.71]; I^2=53.8%) and 6-month followup (WMD, -9.94, 95% CI [-15.06 to -4.83]; I^2=44.0%); 3 trials (n=105)	Moderate
CBT+Hypnosis vs. SC, Civilian, mixed trauma types[91]	Incidence of PTSD	CBT+Hypnosis not significantly different from SC at the end of treatment (CAPS-2: 30% vs. 50%, p=NR) or at 6-month followup (CAPS-2: 40% vs. 58%, p=NR); 1 trial (n=54)	Insufficient
	PTSD symptom severity	CBT+Hypnosis lower than SC at the end of treatment (IES-I: 11.30 vs. 19.83, p<0.005) and at 6-month followup (IES-I: 13.57 vs. 20.21, p<0.05); 1 trial (n=54)	Insufficient
CT vs. exposure therapy, Civilian, mixed trauma types[122,123]	Incidence of PTSD	CT lower than PE at the end of treatment (CAPS-2: 33% vs. 63%, p=0.002) and at 6-month followup (CAPS-2: 37% vs. 63%, p=0.007); 1 trial (n=60)[123] CT not significantly different from PE at 5-month followup (CAPS: 21.4% vs. 18.2%, p=NR)[c]; 1 trial (n=89)[122] CT not significantly different from PE at 9-month followup (CAPS: 21.2% vs. 22.9%, p=NR)[c]; 1 trial (n=87)[122]	Insufficient
	PTSD symptom severity	Greater reduction for CT than for PE at 6-month followup (CAPS-2: 49.8 vs. 32.1, p=0.03); 1 trial (n=60)[123] CT not significantly different from PE at 5-month followup (CAPS: 29.5 vs. 28.6, p=NR)[c]; 1 trial (n=89)[122] CT not significantly different from PE at 9-month followup (CAPS: 27.9 vs. 27.5, p=NR)[c]; 1 trial (n=87)[122]	Insufficient

Table 22. Findings and strength of evidence for the comparative effectiveness of early psychological interventions to prevent PTSD and reduce PTSD symptom severity (continued)

Intervention, Population	Outcome[a]	Results	SOE[b]
Emotional debriefing vs. educational debriefing, Civilian, mixed trauma types[131]	Incidence of PTSD	No significant difference between the two forms of debriefing at 2-week, 6-week, or 6-month followup (SI-PTSD: data NR); 1 trial (n=155)	Insufficient
	PTSD symptom severity	No significant difference between emotional debriefing and educational debriefing at 6-month followup (SI-PTSD change scores: -7.1 and -6.4, respectively, p=0.33)[d]; 1 trial (n=155)	Insufficient
Psychoeducation vs. debriefing combined with psychoeducation, Civilian, crime victims[129]	Incidence of PTSD	Psychoeducation not significantly different than debriefing combined with psychoeducation (PSS: 11% vs. 23%, p=NR) at 6-month followup[e]; 1 trial (n=106)	Insufficient
	PTSD symptom severity	Psychoeducation not significantly different than debriefing combined with psychoeducation at 6-month followup (PSS, 10.9 vs. 13.8, p=NR; IES, 16.7 vs. 19.7, p=NR)[e]; 1 trial (n=106)	Insufficient
CT vs. SSRI (escitalopram) Civilian, mixed trauma types[122]	Incidence of PTSD	CT lower than SSRI at 5-month and 9-month followup (CAPS: 18.2% vs. 61.9%, and 22.8% vs. 42.1%, respectively, p=NR); 1 trial (n=54)[f]	Insufficient
	PTSD symptom severity	CT less than SSRI at 5-month and 9-month followup (CAPS: 29.5 vs. 48.7, and 27.9 vs. 47.2, respectively, p=NR); 1 trial (n=54)[f]	Insufficient
PE vs. SSRI (escitalopram), Civilian, mixed trauma types[122]	Incidence of PTSD	PE lower than SSRI at 5-month and 9-month followup (CAPS: 21.4% vs. 61.9% and 21.2% vs. 42.1%, respectively, p=NR); 1 trial (n=77)[g]	Insufficient
	PTSD symptom severity	PE less than SSRI at 5-month and 9-month followup (CAPS: 28.6 vs. 48.7 and 27.5 vs. 47.2, respectively, p=NR); 1 trial (n=71)[g]	Insufficient

CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; CBT = cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; CI = confidence interval; CIDI-PTSD = Composite International Diagnostic Interview PTSD; CT = cognitive therapy; IES = Impact of Event Scale; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event Scale-Intrusions subscale; n = subset of sample; NR = not reported; PCL-C = PCL-C = Posttraumatic Stress Disorder Checklist, Civilian Version; PE = prolonged exposure therapy; PSS = Posttraumatic Stress Scale; PTSD = posttraumatic stress disorder; RR = relative risk; SC = supportive counseling; SI-PTSD = Structured Interview for PTSD; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitor; WMD = weighted mean difference

[a]If the CAPS or CAPS-2 was the primary outcome measure, it is the only measure of PTSD symptom severity reported here. Additional outcome measures of PTSD symptom severity are reported in the subsection of the text for each intervention.

[b]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

[c]Completers of 103 randomized.

[d]Adjusted for baseline.

[e]Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in this study of psychoeducation and debriefing combined with psychoeducation, we considered all of its outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.

[f]Completers of 63 randomized.

[g]Completers of 86 randomized.

Table 23. Characteristics of the included Battlemind trial

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Mulligan et al., 2012[126] Medium Universal	Recruitment assessors blinded RCT, Battlemind training (1,108) Standard care (1,335)	One 45-minute group session (4 to 6 months)	Mixed combat-related traumatic events	Median PCL-C total score, Battlemind training: 21 Standard care: 20	NR	1.7[a]

n = subset of sample; NR = not reported; PCL-C = Posttraumatic Stress Disorder Checklist, Civilian Version; RCT = randomized controlled trial

[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Battlemind training was no more effective than standard postdeployment debriefing in reducing the severity of PTSD symptoms or the incidence of depression (Table 22). Most participants (> 65%) reported that they were "somewhat" or "very much" satisfied with the briefing and that they found it useful both at the end of treatment and at 4- and 6-month followup. Ratings of satisfaction and perceived utility did not differ significantly between groups.

CBT Versus CBT with Hypnosis

Table 24 summarizes the characteristics of the one study meeting our inclusion criteria.[91] This government-funded RCT was conducted in Australia with civilian trauma survivors with ASD following a nonsexual assault or MVA. The subjects were randomized to six sessions of CBT (n=33) or CBT combined with hypnosis (CBT+Hypnosis, n=30).

Table 24. Characteristics of the included cognitive behavioral therapy trial

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Bryant et al., 2005[91] Medium Targeted	Unblinded RCT, CBT (33) CBT+Hypnosis (30)	Six 50-minute sessions (6 months)	Civilian; MVAs or nonsexual assault	CAPS-2, NR	33[a] (range NR)	60.9

CAPS-2 = Clinician Administered PTSD Scale-2; CBT = cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; MVA = motor vehicle accident; n = subset of sample; NR = not reported; RCT = randomized controlled trial
[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

There was no significant difference in the incidence of PTSD between groups at the end of treatment or at 6-month followup, although PTSD symptom severity was lower in the CBT+Hypnosis group than the CBT group at the end of treatment (Table 22). There were no significant differences between the CBT and CBT+Hypnosis groups at the end of treatment or at 6-month followup, respectively, in severity of symptoms of depression (BDI-2: 13.24 vs. 11.37 and 14.61 vs. 13.57) or anxiety (BAI: 14.91 vs. 15.47 and 15.67 vs. 17.07).

CBT Versus SC

Three Australian studies directly compared the effectiveness of CBT versus SC.[89,91,124] All subjects were civilian mixed trauma survivors who met the DSM-IV or Acute Stress Disorder Interview criteria for acute stress disorder. Duration of treatment ranged from 5 to 6 weeks. Each trial included assessments at the end of treatment and at 6-month followup. The primary outcome measure was the CAPS-2[91,124] or the Composite International Diagnostic Interview PTSD (CIDI-PTSD) module.[89]

A fourth trial, otherwise meeting criteria for this section, was rated high risk of bias and omitted from our main data synthesis but included in our sensitivity analyses.[87] Table 25 summarizes the characteristics of the three studies meeting our inclusion criteria.

Table 25. Characteristics of included cognitive behavioral therapy versus supportive counseling trials

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Bryant et al., 1998[89] Medium Targeted	Unblinded RCT, CBT (12) SC (12)	Five 90-minute weekly individual sessions (6 months)	Civilian; MVAs or industrial accidents	CIDI-PTSD, NR	32.6[a] (range NR)	58.3
Bryant et al., 2003[124] Medium Targeted	Unblinded RCT, CBT (12) SC (12)	Five 90-minute weekly individual sessions (6 months)	Civilian; MVAs or nonsexual assault	CAPS-2, NR	31.2[a] (range NR)	66.7
Bryant et al., 2005[91] Medium Targeted	Unblinded RCT, CBT (33) SC (24)	Six 50-minute sessions (6 months)	Civilian; MVAs or nonsexual assault	CAPS-2, NR	34.0[a] (range NR)	60.9

CAPS-2 = Clinician Administered PTSD Scale-2; CBT = cognitive behavioral therapy; CIDI-PTSD = Composite International Diagnostic Interview PTSD Module; MVA = motor vehicle accident; n = subset of sample; NR = not reported; RCT = randomized controlled trial; SC = supportive counseling

[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

All three trials assessed the incidence of PTSD using either the CAPS-2[91,124] or the CIDI-PTSD.[89] We used random effects models to estimate the combined relative risk of PTSD at the end of treatment and at 6-month followup. Both analyses did not detect statistically significant differences between treatment groups (Table 22). Pooled findings of the risk of PTSD at the end of treatment rendered indeterminate results with wide confidence intervals (RR, 0.27; 95 CI%, 0.05 to 1.29; I^2=71.8%; Figure 3). Similarly, at 6 months, no statistically significant difference between treatments could be detected (RR, 0.46; 95 CI%, 0.21 to 1.01; I^2=44.9%; Figure 4). The results at 6 months, however, almost reached statistical significance and numerically favored patients treated with CBT than with SC. In a sensitivity analysis, we included one high-risk-of-bias trial.[87] The findings indicated a statistically significantly lower risk of PTSD for patients treated with CBT than SC at the end of treatment (RR, 0.33; 95% CI, 0.12 to 0.86; I^2=58.7%; Appendix H, Figure H1) as well as at 6-month followup (RR, 0.45; 95% CI, 0.25 to 0.82; I^2=32.0%; Appendix H, Figure H2).

Figure 3. Mean change from baseline to end of treatment in PTSD incidence rates for CBT compared with SC

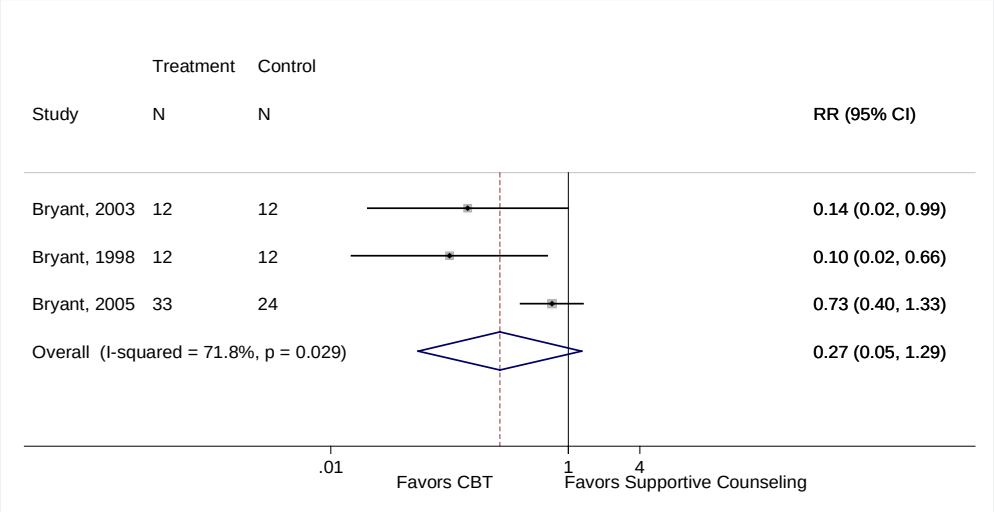
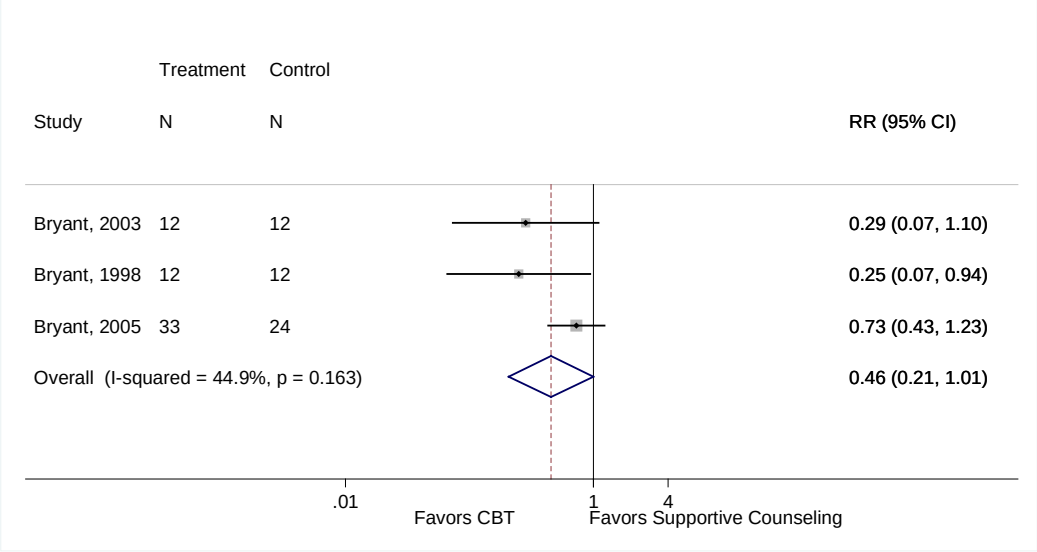


Figure 4. Mean change from baseline to 6-month followup in PTSD incidence rates for CBT compared with SC



All three studies assessed PTSD symptom severity with the IES, which consists of two subscales: intrusion (IES-I) and avoidance (IES-A). Pooled results for PTSD symptom reduction found a statistically significantly greater reduction in both subscales at the end of treatment and 6 months for subjects treated with CBT than for those who received SC (Figures 5 through 8).

Our meta-analysis shows a significantly greater reduction in IES-A scores with moderate effect size and statistical heterogeneity at the end of treatment (WMD, -14.04, 95% -8.71; CI, -19.37, I^2=53.8%; Figure 5), which was maintained but slightly smaller in magnitude at 6-month followup (WMD, -9.94; 95% CI, -15.06 to -4.83; I^2=44.0%; Figure 6). Our sensitivity analysis (n=136) including a fourth, high-risk-of-bias trial found a slightly larger benefit at the end of treatment (WMD, -14.17; 95% CI, -17.82 to -10.51; I^2=31.9%; Appendix H, Figure H3) and at 6-month followup (WMD,-11.49; 95% CI, -16.09 to -6.90; I^2=52.7%; Appendix H, Figure H4).

Figure 5. Mean change from baseline to end of treatment in IES-Avoidance subscale symptom scores for CBT compared with SC

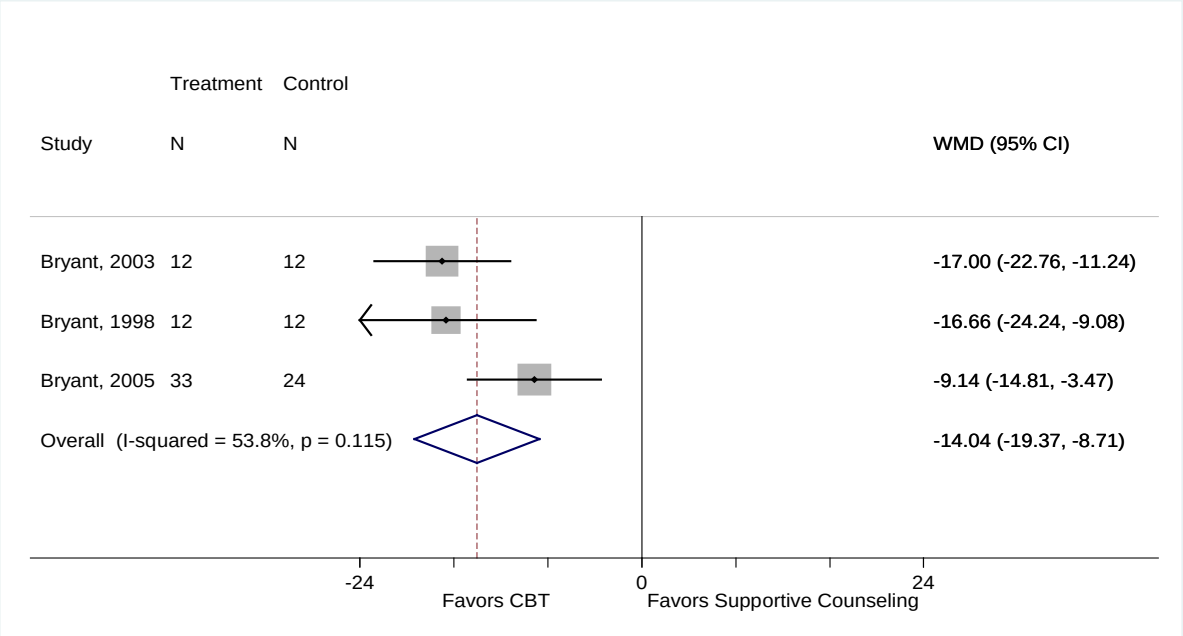
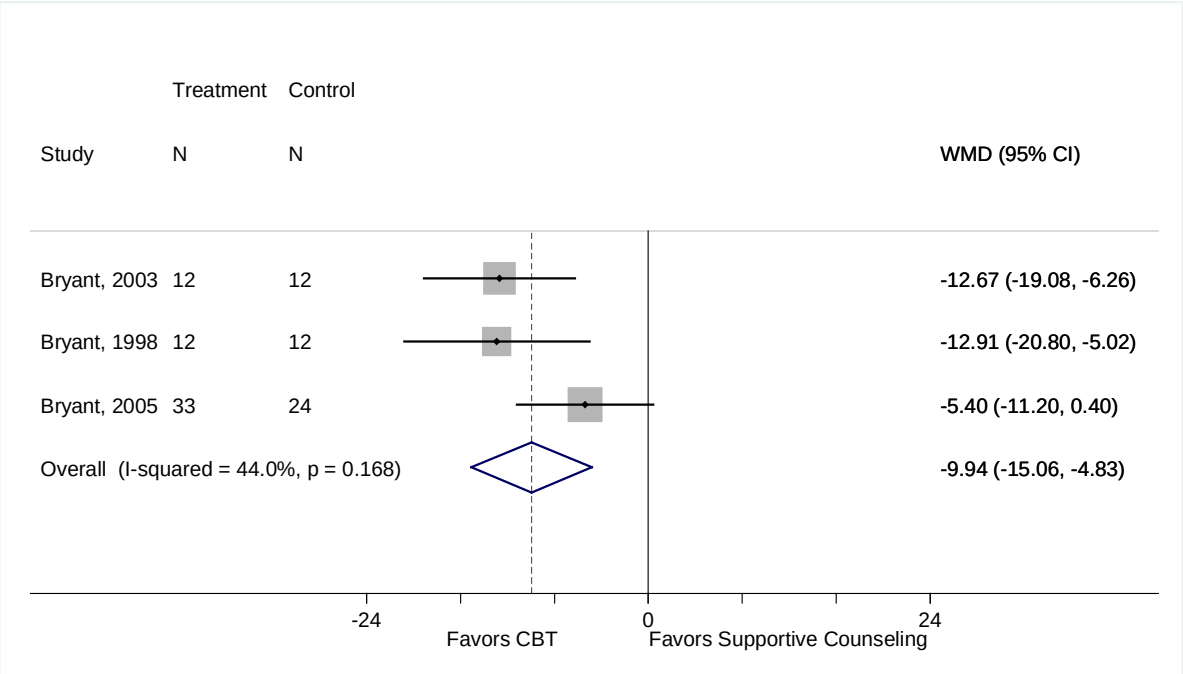


Figure 6. Mean change from baseline to 6-month followup in IES-Avoidance subscale symptom scores for CBT compared with SC



Our meta-analysis shows a significantly greater reduction in IES-I scores with a modest effect size and statistical heterogeneity at the end of treatment (WMD, -7.85; 95% CI, -11.18, -4.53; I^2=1.3%; Figure 7. Mean change from baseline to end of treatment in IES-Intrusion subscale symptom scores for CBT compared with SC), which was maintained and slightly larger in magnitude at 6-month followup (WMD, -8.19, 95% CI, -11.79 to -4.58; I^2=6.8%; Figure 8). Our sensitivity analysis (n=136) including a fourth, high-risk-of-bias trial found a slightly larger

benefit at the end of treatment (WMD, -8.39; 95% CI, -11.45 to -5.34; I^2=0.0%; Appendix H, Figure H5) but a slightly smaller benefit at 6-month followup (WMD, -7.91; 95% CI, -10.85 to -4.98; I^2=0.0%; Appendix H, Figure H6).

Figure 7. Mean change from baseline to end of treatment in IES-Intrusion subscale symptom scores for CBT compared with SC

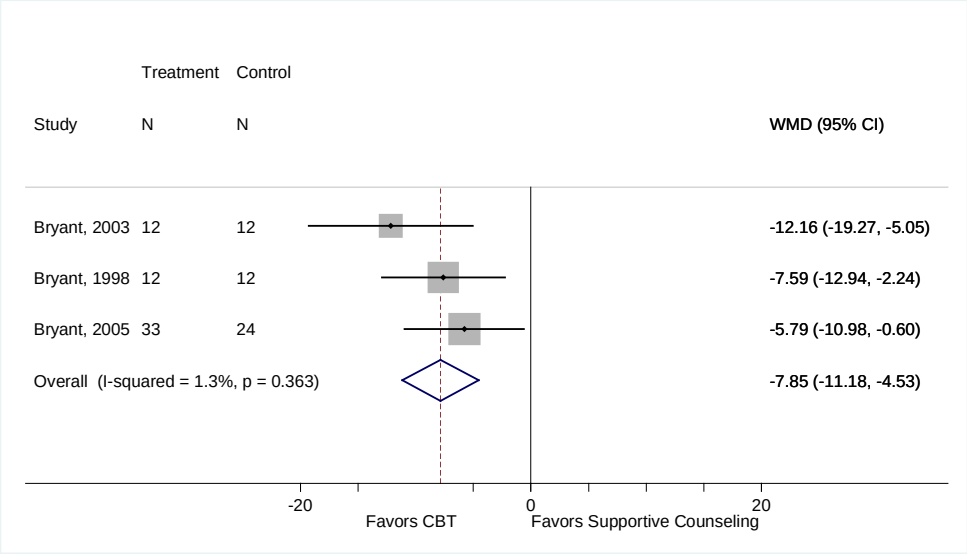
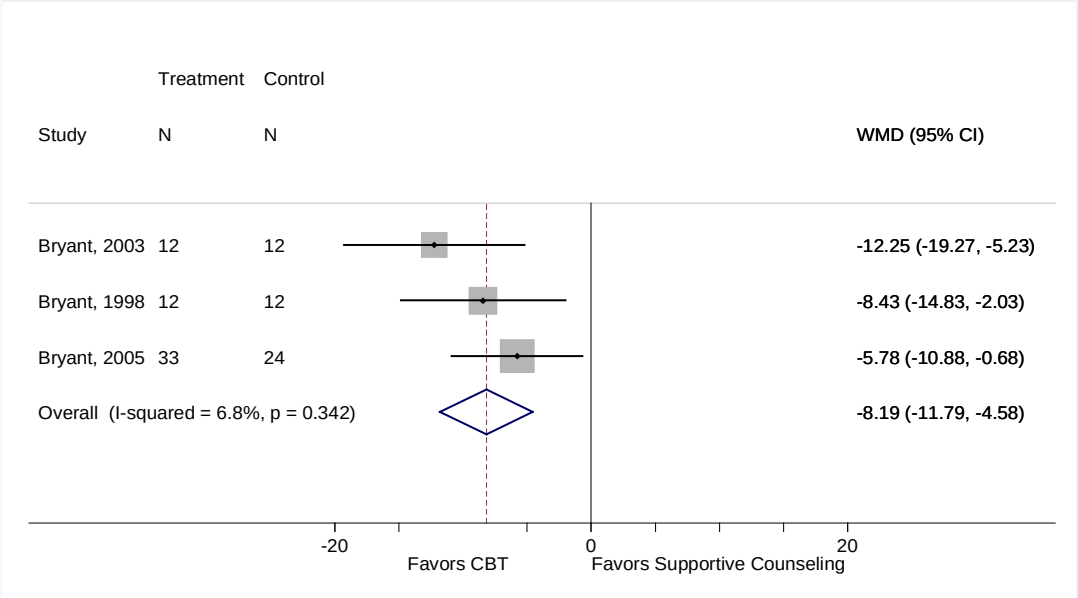


Figure 8. Mean change from baseline to 6-month followup in IES-Intrusion subscale symptom scores for CBT compared with SC



Taken together, consistent evidence (I^2 range 0.0% to 53.8%) from three medium risk-of-bias trials and a fourth high-risk-of-bias trial supports a conclusion of greater reduction of PTSD symptom severity for patients treated with CBT than for those treated with SC (moderate SOE) (Table 22).

All three included trials (n=105) evaluated the effectiveness of CBT on coexisting psychiatric conditions.[89,91,124] Three trials used the BDI or the BDI-2, two trials used the BAI,[91,124] and one trial used the STAI.[124]

Our meta-analysis showed no statistically significant difference between CBT and SC on changes in anxiety symptoms at the end of treatment (SMD, -0.25; 95% CI, -0.64 to 0.13; I^2=0.0%; Figure 9) or at 6-month followup (SMD, 95% CI, -0.28 to -0.67, 0.11; I^2=0.0%; Figure 10). Our sensitivity analysis that included one high-risk-of-bias trial[87] found a statistically significant difference between groups on changes in anxiety symptoms at the end of treatment (SMD, -0.39; 95% CI, -0.74 to -0.04; I^2=2.2%; Appendix H, Figure H7) and at 6-month followup (SMD, -0.59; 95% CI, -1.16 to -0.01; I^2=58.7%; Appendix H, Figure H8).

Figure 9. Mean change from baseline to end of treatment in anxiety symptom scores for CBT compared with SC

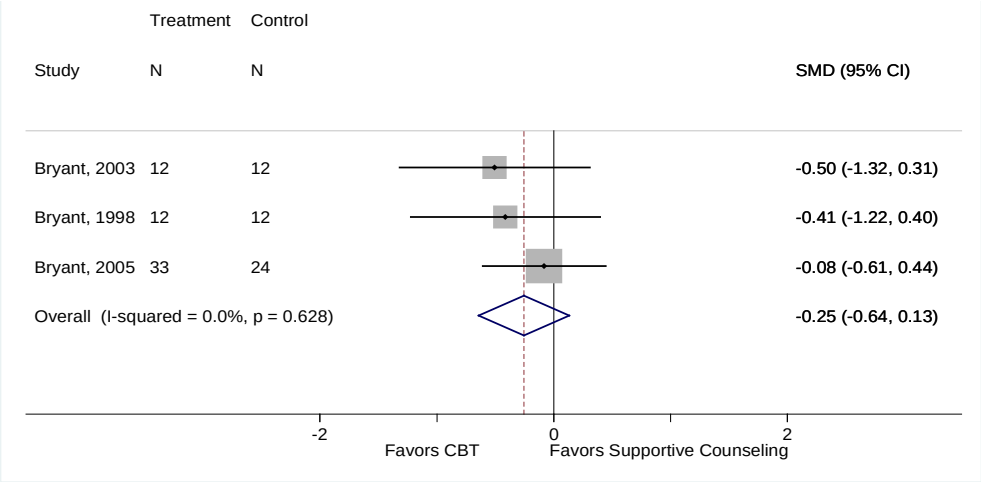
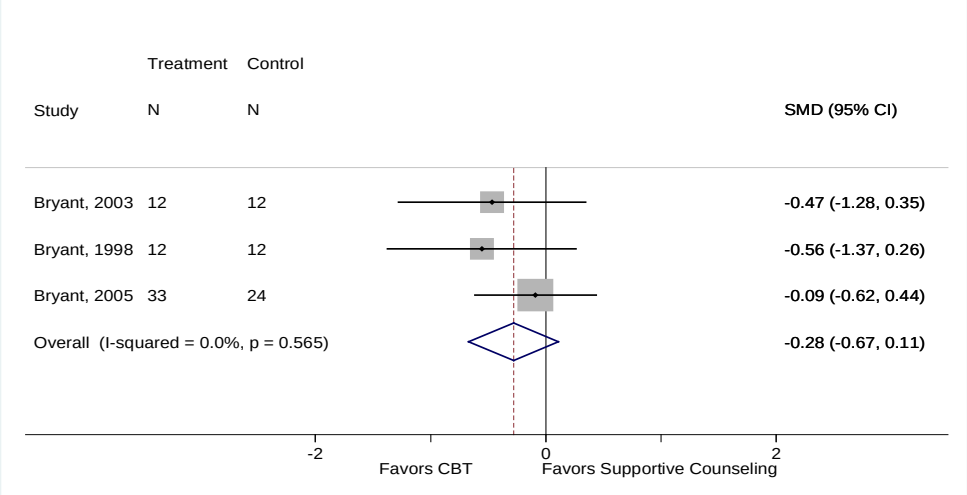


Figure 10. Mean change from baseline to 6-month followup in anxiety symptom scores for CBT compared with SC



Similarly, the pooled results rendered no statistically significant differences on changes in depression symptoms between CBT and SC at the end of treatment (SMD, -0.15; 95% CI, -0.53 to 0.24; I^2=0.0%; Figure 11) or at 6-month followup (SMD, -0.21; 95% CI, -0.70 to 0.27; I^2=30%; Figure 12). Our sensitivity analyses that included one high-risk-of-bias trial[87] did not

render any statistically significant differences on change in depression symptoms (Appendix H, Figures H-9 and H-10).

Figure 11. Mean change from baseline to end of treatment in depression symptom scores for CBT compared with SC

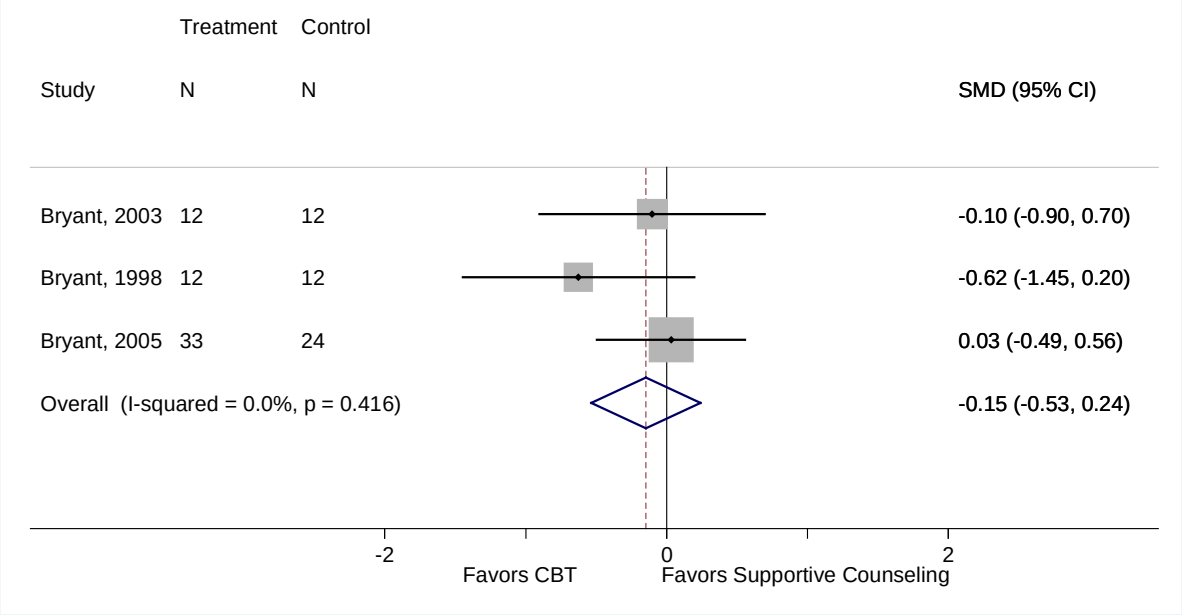
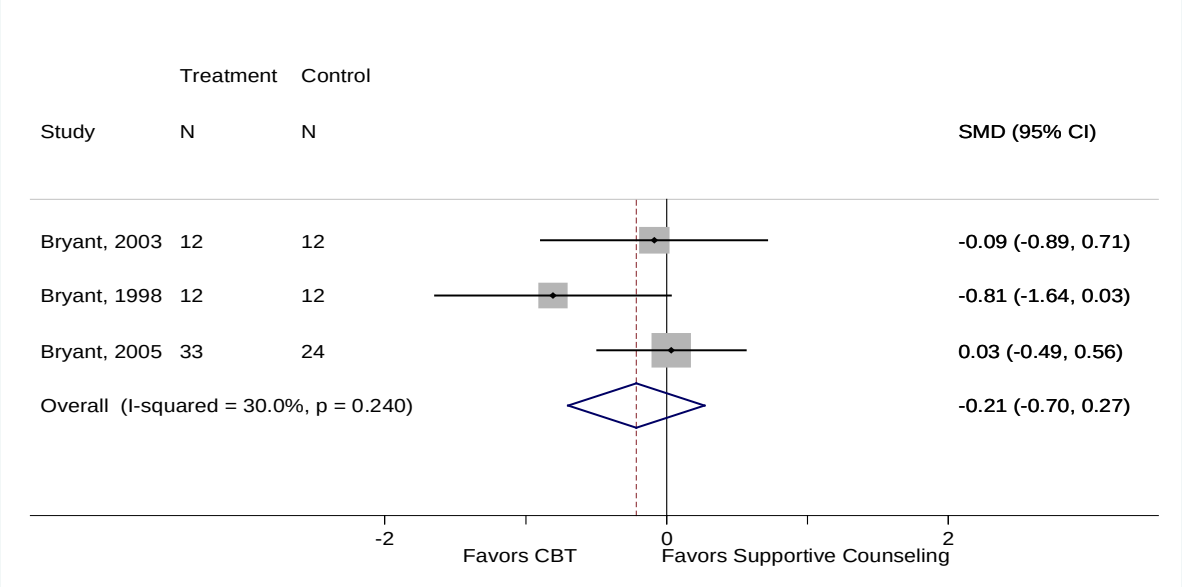


Figure 12. Mean change from baseline to 6-month followup in depression symptom scores for CBT compared with SC



CBT+Hypnosis Versus SC

Table 26 summarizes the characteristics of the one study meeting our inclusion criteria.[91] This government-funded RCT was conducted in Australia with civilian trauma survivors with acute stress disorder following a nonsexual assault or MVA who were randomized to six sessions of CBT+Hypnosis (n=30) or SC (n=24). Additional details about this study can be found in the section on the efficacy of CBT.

Table 26. Characteristics of the included cognitive behavioral therapy+hypnosis versus supportive counseling trial

Study and Risk of Bias, Prevention Type	Study design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Bryant et al., 2005[91] Medium Targeted	Unblinded RCT, CBT+Hypnosis (30) SC (24)	Six 50-minute sessions (6 months)	Civilian; MVA or nonsexual assault	CAPS-2, NR	34[a] (range NR)	60.9

CAPS-2 = Clinician Administered PTSD Scale-2; CBT+Hypnosis = combined with hypnosis; cognitive behavioral therapy; MVA = motor vehicle accident; n = subset of sample; NR = not reported; RCT = randomized controlled trial; SC = supportive counseling

[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

There was no significant difference between the rates of PTSD for the CBT+Hypnosis and SC groups at the end of treatment or at 6-month followup (Table 22). PTSD symptom severity was lower in the CBT+Hypnosis group compared with the SC group at the end of treatment and at 6-month followup. There were no significant differences between the CBT+Hypnosis and SC groups in severity of depression (BDI-2, 11.37 vs. 14.96 and 13.57 vs. 16.29) at the end of treatment or followup. Similarly, there were no significant differences between these two groups on severity of anxiety (BAI, 15.47 vs. 20.25 and 17.07 vs. 21.13).

CT Versus PE

Table 27 summarizes the characteristics of the two studies meeting our inclusion criteria for evaluating the comparative effectiveness of CT and PE.[122,123] Both studies compared CT with PE in civilian mixed trauma samples. The CT arm contained 30[123] and 40[122] subjects; the PE arm, 30[123] and 63 subjects.[122] Additional details about this study are in the section on the efficacy of cognitive therapy.

Table 27. Characteristics of included cognitive therapy versus exposure therapy trials

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Bryant et al., 2008[123] Low Targeted	Outcome assessors blinded RCT, PE (30) CT (30)	Five weekly sessions (6 months)	Civilian mixed (MVA, "other trauma," physical assault, and "other accident")	CAPS-2 total score, PE: 70.6 CT: 66.8	35.8[a]	57.8[a]
Shalev et al., 2011[122] Medium Targeted	Outcome assessors blinded RCT, PE (63) CT (40)	12 weekly 1.5-hour individual sessions (5 and 9 months)	Civilian mixed (Terrorist attacks, MVAs, work or other accidents)	CAPS total score, PE: 73.59 CT: 71.78	39.8[a]	52

CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; CT = cognitive therapy; MVA = motor vehicle accident; n = subset of sample; NR = not reported; PE = prolonged exposure therapy; RCT = randomized controlled trial

[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Compared with PE, CT was associated with a lower incidence of PTSD at the end of treatment and 6-month followup in one study,[123] but it was not significantly different at 5-month or 9-month followup in the other study[122] (Table 22). In the first study,[123] after adjusting for pretreatment levels, CAPS-2 total score, IES-I and IES-A did not differ significantly between CT and PE (p=NS) at the end of treatment. However, at 6-month followup, the CT group had significantly higher CAPS-2 total (32.1 vs. 49.8, p=0.03), IES-I (11.4 vs. 18.6, p=0.02), and IES-A (12.8 vs. 19.2, p=0.03) scores. In the second study,[122] the PE and CT groups did not differ significantly on CAPS total score at 5-month (28.6 vs. 29.5) or at 9-month (27.5 vs. 27.9) followup, reflecting no differences in the underlying subscales of re-experiencing, avoidance, and hyperarousal at either assessment time point. Likewise, the PSS-SR total score did not differ significantly between the PE and CT groups at either the 5-month (11.0 vs. 11.6) or 9-month (10.4 vs. 9.6) follow-up assessment.

One study measured depression and anxiety at the end of treatment and 6-month followup.[123] There was no significant difference between the CT and PE groups on BDI-2 scores at the end of treatment or at 6-month followup (18.9 vs. 12.1 and 20.4 vs. 12.4, p's=NS). Compared with the PE group, the CT group exhibited significantly higher BAI scores (23.4 vs. 13.4, p=0.008) at the end of treatment only.

Debriefing Versus Another Form of Debriefing

One RCT met our inclusion criteria (Table 27).[131] It compared two forms of CISD: CISD minus the psychoeducational component ("emotional debriefing," n=76) and CISD minus the emotional component ("educational debriefing," n=79) (Table 28). Additional details about this study can be found in the section on the efficacy of debriefing.

Table 28. Characteristics of the included trial of debriefing versus another form of debriefing

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Sijbrandij et al., 2006[131] Low Universal	Unblinded RCT, Emotional debriefing (76) Educational debriefing (79)	One 45- to 60-minute individual session (2 and 6 weeks; 6 months)	Civilian Assault or Accident	SI-PTSD, Emotional debriefing: 19.9 Educational debriefing: 19.9	40.4[a] (range NR)	48.7[a]

n = subset of sample; NR = not reported; RCT = randomized controlled trial; SI-PTSD = Structured Interview for PTSD
[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

The study reported that there was no significant difference between the two forms of debriefing on incidence of PTSD or the severity of PTSD symptoms (Table 22). There was no statistically significant difference between the two forms of debriefing in severity of depression or anxiety. At 6 months, HADS-Depression change scores were -1.6 and -1.5 (p=0.23) for emotional debriefing and educational debriefing, respectively. Similar results were obtained for anxiety: HADS-Anxiety change scores were -2.4 and -2.2 (p=0.96).

Psychoeducation Versus Debriefing Plus Psychoeducation

One government-funded study conducted in the UK with civilian crime victims compared psychoeducation (n= 54) with debriefing combined with psychoeducation (n=52) (Table 29).[129] Additional details about this study are reported in the section on efficacy of debriefing. Because of very high overall attrition (i.e., greater than 40% at 11-month followup), we considered all outcomes collected at that time point as having a high risk of bias and therefore do not report them here.

Table 29. Characteristics of the included trial of psychoeducation versus debriefing plus psychoeducation

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Rose et al., 1999[129] Medium Universal	Unblinded RCT, Psychoeducation (52) Debriefing + psychoeducation (54)	One 1-hour individual session (6 months)[a]	Civilian crime victims (Actual or threatened physical or sexual assault; bag snatch)	PSS-SR, Psychoeducation: 16.0 Debriefing + psychoeducation: 16.8	35.9 (18-76)[b]	24.8[b]

n = subset of sample; PSS-SR = Post-traumatic Stress Disorder Scale-Self-Report; RCT = randomized controlled trial
[a]Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in this study of psychoeducation and debriefing plus psychoeducation,[129] we considered all outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.
[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

The incidence of PTSD did not differ significantly between the psychoeducation and debriefing combined with psychoeducation groups at 6 months (Table 22). There was no significant difference in PTSD symptom severity at 6-month followup.[129] In addition, there was

no significant difference in the severity of depressive symptoms between psychoeducation and debriefing combined with psychoeducation at 6-month followup (BDI, 9.8 vs. 12.1; p=NR).[129]

Comparative Effectiveness: Psychological Versus Pharmacological Interventions

Description of Included Studies

Table 30 summarizes the characteristics of the one study meeting our inclusion criteria.[122]

This RCT was conducted in Israel with a mixed civilian trauma sample of 242 individuals admitted for emergency services. Treatment arms included PE (n=63), CT (n=40), and escitalopram (n=23). Additional details about this study are in the section on the efficacy of cognitive therapy.

Table 30. Characteristics of the included psychological versus pharmacological intervention trial

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Shalev et al., 2012[122] Medium Targeted	Outcome assessors blinded RCT, PE (63) CT (40) Escitalopram[a] (23)	PE and CT, 12 weekly 90-minute individual sessions (9 months) Escitalopram and placebo, 10 mg twice daily (9 months)	Civilian mixed (Terrorist attacks, MVAs, work or other accidents)	CAPS total score, PE: 73.59 CT: 71.78 Escitalopram: 79.83	39.8[b]	56.3[b]

CAPS = Clinician Administered PTSD Scale; CT = cognitive therapy; mg = milligrams; MVA = motor vehicle accident; n = subset of sample; PE = prolonged exposure therapy; RCT = randomized controlled trial; WL = waitlist

[a]Subjects in the pharmacological arm were blinded as to whether they were receiving escitalopram or placebo.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Key Points

- The evidence is insufficient to determine the comparative effectiveness of CT over an SSRI (escitalopram) to prevent PTSD or to reduce PTSD symptoms severity for civilians exposed to a variety of traumatic events (MVAs, physical assault, work-or other-related accidents, terrorist attacks).
- The evidence is insufficient to determine the comparative effectiveness of PE over an SSRI (escitalopram) to prevent PTSD or to reduce PTSD symptoms severity for civilians exposed to a variety of traumatic events (MVAs, physical assault, work-related or other accidents, terrorist attacks).

Detailed Synthesis: Psychological Versus Pharmacological Interventions

CT Versus SSRI

The incidence of PTSD and the severity of PTSD symptoms were significantly higher (p=NR) in the SSRI (escitalopram) group than in the CT group at 5-month and 9-month followup (Table 22).

PE Versus SSRI

The incidence of PTSD and the severity of PTSD symptoms were significantly higher (p=NR) in the SSRI (escitalopram) group than in the PE group at 5-month and 9-month followup (Table 22).

Comparative Effectiveness: Psychological Versus Emerging Interventions

No studies met inclusion criteria for this part of KQ 1.

Comparative Effectiveness: Pharmacological Versus Pharmacological Interventions

A high-risk-of-bias RCT pilot study that otherwise met inclusion criteria compared the effectiveness of a 14-day treatment with propranolol (n=17) versus gabapentin (n=14) in patients admitted to a level 1 surgical trauma center after a severe physical injury requiring specialized, emergent care (see more detailed description in the Detailed Synthesis: Pharmacological Interventions section).[47] There was no difference in effectiveness between propranolol and gabapentin as measured by PTSD severity (at 1 month, 4 months, or 8 months) or by rates of PTSD or Major Depressive Disorder at 4-month followup.

Comparative Effectiveness: Pharmacological Versus Emerging Interventions

No studies met inclusion criteria for this part of KQ 1.

Comparative Effectiveness: Emerging Versus Emerging Interventions

No studies met inclusion criteria for this part of KQ 1.

KQ 2: Impact of Timing, Intensity, or Dosing

Description of Included Studies

Two studies met eligibility criteria for KQ 2;[134,135] Two studies that otherwise met eligibility criteria were omitted from the main data synthesis for high risk of bias.[98,115] The studies covered a variety of populations, such as civil crime victims, critically ill patients, soldiers exposed to combat, and severely injured patients. Interventions included CISD, psychoeducation, psychotherapeutic treatment, trauma risk management, and pharmacological sedation. One study[135] was funded by a foundation, and we could not determine the funding source for the second included study.[134]

Key Points

- For robbery victims, the evidence was inconclusive whether immediate debriefing compared with delayed debriefing leads to fewer posttraumatic symptoms (insufficient SOE).
- For critically ill patients, the evidence was inconclusive whether light sedation compared with deep sedation leads to differences in posttraumatic symptoms, anxiety, and depression after hospital discharge (insufficient SOE).
- No studies of the impact of timing, intensity, or dosing on the risk of harms of interventions met our eligibility criteria.

Detailed Synthesis

Table 31 summarizes the available evidence of the impact of timing, intensity, or dosing on the effectiveness of interventions.

Table 31. Findings and strength of evidence of the impact of timing, intensity, and dosing on the effectiveness of interventions

Population, Treatment	Impact of Timing	Impact of Intensity	Impact of Dosing	SOE[a]
Robbery victims, Debriefing (CISD)[134]	Fewer posttraumatic symptoms with early vs. delayed CISD (PDS: 5.6 vs. 14.3; p<0.001); 1 trial (N=77) Lower PTSD symptom severity with early vs. delayed CISD (PDS: 6.9 vs. 33.1; p<0.001); 1 trial (N=77)	No evidence	Not applicable	Insufficient
Critically ill patients, Pharmacological sedation[135]	No evidence	Not applicable	Similar incidence rates of PTSD with light and deep sedation (PCL: 10% vs. 9%, p=0.83); 1 trial (N=137) Similar rates of PTSD symptom severity ranks with light and deep sedation (IES-R and PCL: PTSD scores NR, p=0.07); 1 trial (N=137)	Insufficient

CISD = Critical Incident Stress Debriefing; IES-R = Impact of Event Scale-Revised: N = entire sample; NR = not reported; PCL = PTSD Checklist; PDS = Posttraumatic Stress Diagnostic Scale; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SOE = strength of evidence

[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

Impact of Timing of Interventions

One study (Table 32) assessed the impact of timing on the effectiveness of debriefing (CISD) to prevent PTSD.[134] This RCT was conducted with 77 Australian civilians who had been exposed to a first-time robbery at their place of employment. Victims were not eligible to enter the study if they had experienced physical injuries, were threatened with a gun, or had received prior treatment or prevention of stress-related symptoms. The funding source was not reported.

Eligible victims were randomly assigned to immediate debriefing (within 10 hours of the robbery) or to delayed debriefing (48 hours or more after the robbery). Debriefings were conducted individually or in small groups. After 2 weeks, victims who received immediate debriefing had statistically significantly fewer symptoms on the PDS and significantly lower symptom severity than those in the delayed debriefing group (Table 31). Because of the lack of an inactive control group in this study, no conclusions about a greater efficacy of early debriefing can be drawn. It is conceivable that the difference between immediate and delayed intervention can be attributed to harmful effects of delayed debriefing relative to no beneficial effects of immediate debriefing.

Table 32. Characteristics of studies on impact of timing

Study and Risk of Bias, Prevention Type	Study Design, Intervention	Timing of Treatment After Trauma (N)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Campfield et al., 2001[134] Medium Universal	Unblinded RCT, CISD	Immediate CISD: <10 hours (36) Delayed CISD: >48 hours (41)	Civilian crime victims (robbery)	PDS total score and symptom severity score Baseline: NR	22.82[a] (18-32)	54.5

CISD = Critical Incident Stress Debriefing; n = subset of sample; NR = not reported; PDS = Posttraumatic Stress Diagnostic Scale; RCT = randomized controlled trial

[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Impact of Intensity of Intervention

The only available evidence on the impact of the intensity on the effectiveness of interventions were two high-risk-of-bias studies, which are summarized below.

Impact of Dosing of Pharmacological Interventions

One study (Table 33) assessed the impact of the doses of sedating medications on symptoms of PTSD, anxiety, and depression in critically ill patients.[135] This outcome assessor-blinded Swiss RCT (funded by the Swiss National Science Foundation) assigned 137 critically ill patients with endotracheal intubation to receive light sedation (i.e., sedated to be tranquil or lightly sleeping) or deep sedation (i.e., sedated to the point of being asleep but able to awaken upon physical stimulation) with midazolam and morphine. The primary endpoints were self-reported PTSD, anxiety, or depressive symptoms 4 weeks after discharge. At the 4-week followup, a similar proportion of patients in the light and deep sedation group met symptom criteria for the diagnosis of PTSD (10% vs. 9%; p=0.83) as assessed on the PTSD Checklist and the IES-R (Table 31). Likewise, patients in both treatment groups exhibited similar rates of anxiety (HADS-A: ADS-A: 12% vs. 12%) and depression (HADS-D: 8% vs. 4%), respectively. Overall, almost 20 percent of patients enrolled in this study died during the hospital stay.

Table 33. Characteristics of the study on the depth of sedation

Study and Risk of Bias	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Age Mean (Years)	Percentage Female
Treggiari et al., 2009 [135] Medium Universal	Single-blinded RCT; Light sedation (69) Deep sedation (68)	Not applicable (4 weeks postdischarge)	Civilian medical; Mechanical ventilation	IES-R and PCL: Not applicable	61.4[a]	23.5[a]

IES-R = Impact of Event Scale-Revised; n = subset of sample; PCL = PTSD Checklist; RCT = randomized controlled trial
[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

High-Risk-of-Bias Studies

Two studies rated high risk of bias otherwise met our eligibility criteria.[98,115] Because of the lack of other evidence for this key question, we briefly summarize characteristics and main findings of these studies.

Impact of Intensity of Intervention

A German RCT (N=113) compared the effectiveness of inpatient psychotherapy in severely injured patients with a combination of inpatient and continued outpatient psychotherapy.[115] After 1 year of followup of completers only, the long-term therapy group had numerically fewer posttraumatic, depressive, and anxiety symptoms than patients receiving inpatient psychotherapeutic treatment only. Differences did not reach statistical significance. Only 41 percent of all randomized patients completed the follow-up assessments.

A British nonrandomized parallel-group comparison trial compared Trauma Risk Management (TRiM) in two different groups of 180 males (Army infantry and Marine commandos) at different stages of implementation (TriM naïve and TriM experienced).[98] Subjects in the TRiM-experienced group reported lower levels of psychological distress than subjects in the TRiM-naïve group. Differences did not reach statistical significance.

KQ 3: Subgroup Analyses

Description of Included Studies

Eight studies met eligibility criteria for KQ 3;[27,107,120,126,128,129,131,134] Two of the eight were rated high risk of bias and omitted from the main data synthesis, but they are discussed separately below.[27,107] The six studies with low[131] or medium risk of bias involved survivors of a variety of trauma types: medical illness (breast cancer), violent crime, intentional and unintentional injuries, and combat. Interventions included psychological debriefing, emotional debriefing, psychoeducation, CISD, PE, a British adaptation of Battlemind training, and a self-help workbook. Three studies were funded by national government sources[128,129,131] and one by a private foundation;[120] two did not identify their funding source.[126,134]

Key Points

- For violent crime victims, the effect of early psychological interventions (debriefing, immediate vs. delayed debriefing) on PTSD symptoms did not differ between men and women at 2 weeks and 6 months (low SOE).[129,134]
- For violent crime victims, the effect of a debriefing intervention on depressive symptoms did not differ between men and women at 6 months (insufficient SOE).[129]
- For women with newly diagnosed breast cancer and survivors of civilian assault or accident, there were inconsistent findings on whether baseline severity of PTSD symptoms modified the effect of debriefing and a self-help workbook on PTSD symptoms (insufficient SOE).[120,131]
- For victims of violent crime, the effect of a debriefing intervention on PTSD symptoms did not differ between those with or without previous depression or a history of child abuse (insufficient SOE).[129]
- For United Kingdom military service members after combat deployment, the effect of Battlemind training on PTSD symptoms did not differ by the severity of combat exposure (insufficient SOE).[126]
- For survivors of mixed civilian trauma, PE was effective in reducing PTSD symptoms among survivors of sexual assault but not physical assault or motor vehicle collisions (insufficient SOE).[128]
- No study that met our inclusion criteria conducted subgroup analyses by ethnic or racial groups.

Detailed Synthesis

Table 34 summarizes the main findings on subgroups.

Of the six studies that were rated as low or medium risk of bias, two reported subgroup analyses by demographic groups (sex),[129,134] one by type of trauma,[128] one by severity of trauma exposure,[126] one by history of depression,[129] one by history of child abuse,[129] and two by severity of baseline distress[120,131] (Table 34). The number of subgroup analyses conducted ranged from one[134] to nine.[129]

All studies except one[128] used a test of interaction (intervention by group or intervention by time by group) for their subgroup analyses. Two studies[120,129] reported that the subgroup analyses were not prespecified, and four studies[126,128,131,134] did not state whether the subgroup analyses were prespecified or post hoc. Only one of the six studies adjusted for multiple comparisons[128] or reported the magnitude of the effect within levels (categories) of the subgroups being analyzed. None reported confidence intervals around estimated effects.

Table 34. Summary of evidence about subgroups

Subgroup; Interventions	PTSD Symptoms	Depression Symptoms	Quality of Life	SOE[a]
Demographic groups: sex; CBT, CISD	Sex did not modify the effect of early interventions; 2 trials (N=157; N=77)[129,134]	Sex did not modify the effect of early interventions; 1 trial (N=157)[129]	No evidence	PTSD symptoms; Low for no effect of sex Depression symptoms or quality of life: insufficient
Type of trauma; PE	Modified PE reduced PTSD symptoms among survivors of sexual, but not physical, assault and not among MVA survivors; 1 trial (N=137)[128]	No evidence	No evidence	Insufficient
Psychiatric diagnosis: previous depression; Debriefing	Previous depression did not modify effect of debriefing; 1 trial (N=157)[129]	Previous depression did not modify effect of debriefing; 1 trial (N=157)[129]	No evidence	Insufficient
History of child abuse[b]; Debriefing	History of child abuse did not modify effect of debriefing; 1 trial (N=157)[129]	History of child abuse did not modify the effect of debriefing; 1 trial (N=157)[129]	No evidence	Insufficient
Severity of exposure to trauma[b]; Battlemind training, standard postdeployment briefing	Severity of combat exposure did not modify the effect of Battlemind training; 1 trial (n=2, 443)[126]	No evidence	No evidence	Insufficient
Baseline severity of distress[b]; Debriefing, self-help workbook	Inconsistent findings; 2 trials (N=49; N=236);[120,131] one reported that high baseline arousal symptoms increased PTSD symptoms among those randomized to debriefing while the other reported that a self-help workbook reduced PTSD symptoms to a greater extent in those with high baseline PTSD symptom severity	No evidence	No evidence	Insufficient

CBT = cognitive behavioral therapy; CISD = Critical Incident Stress Debriefing; MVA = motor vehicle accident; N = entire sample; n = subset of sample; PE= prolonged exposure therapy; PTSD = posttraumatic stress disorder; SOE = strength of evidence

[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

[b]Personal risk factor for PTSD.

Table 35. Characteristics of included trials for subgroup analyses

Study and Risk of Bias Subgroups Analyzed	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Beatty et al., 2010[120] Medium Severity of baseline distress (high vs. low)[a]	Unblinded RCT, SHB (25) Information only (24)	NR (3 and 6 months)	Women newly diagnosed with breast cancer (within previous month)	PSS-SR: 10.76 (pooled for both groups)	55.2 (range NR)	100
Campfield et al., 2001[134] Medium Sex	Unblinded RCT, <10 hour (36) >48 hour (41)	One session, median duration 1-2 hours (2 and 4 days; 2 weeks)	Crime victims (robbery)	PDS total score, NR	22.82[b] (18-32)	55
Mulligan et al., 2011[126] Medium Severity of combat exposure	Unblinded RCT, Battlemind training (797) Standard postdeployment briefing (819)	One large group session lasting < 1 hour (4 to 6 months)	UK military service members; combat trauma	PCL-C, Battlemind: 21 Standard briefing: 20	NR	1.7[b]
Rose et al., 1999[129] Medium Sex; previous depression, history of child abuse	Unblinded RCT, Debriefing (54) Psycho-education (52) Assessment (51)	One individual session of 1 hour (6 months)[c]	Crime victims (actual or threatened physical or sexual assault; bag snatch)	IES, Debriefing: 28.5 Psychoeducation: 24.2 Assessment: 28.0 PSS-SR, Debrief: 16.8 Psychoeducation: 16.0 Assessment: 15.6	35.9[b] (18-76)	24.8c
Rothbaum et al., 2012[128] Medium Type of trauma	Unblinded RCT, Modified (early) PE (69) Assessment only (68)	Three individual 1-hour sessions (1 and 3 months)	Physical and sexual assault, or MVA	PSS-I, NR	31.5 (range NR)	65

Table 35. Characteristics of included trials for subgroup analyses (continued)

Study and Risk of Bias Subgroups Analyzed	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Sijbrandij et al., 2006[131] Low Severity of baseline distress, based on presence of 3 PTSD symptom clusters at baseline[d]	Unblinded RCT, Emotional debriefing (76) Educational debriefing (79) No debriefing (81)	One individual, 45- to 60-minute session (2 and 6 weeks; 6 months)	Assault or accident	SI-PTSD, Emotional debriefing: 19.9 Educational debriefing: 19.9 No debriefing: 17.7	40.4[b] (range NR)	48.7[c]

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; IES = Impact of Event Scale; MVA = motor vehicle accident; n = subset of sample; NR = not reported; PCL-C = PTSD Checklist, Civilian version; PDS = Posttraumatic Stress Diagnostic Scale; PSS-I = Posttraumatic Stress Diagnostic Scale-Interview version; PSS-SR = Posttraumatic Stress Diagnostic Scale-Self Report version; PE = prolonged exposure therapy; PSS-I = PTSD Symptom Scale-Interview version; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SHB = self-help book; SI-PTSD = Structured Interview for PTSD; UK = United Kingdom

[a]Baseline distress was based on dichotomous (above median vs. below median) baseline score for each outcome. For example, for PTSD, baseline distress is based on dichotomized PTSD score at baseline.

[b]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

[c]Because of very high overall attrition (i.e., greater than 40% at 11-month followup) in this study of debriefing and psychoeducation, we considered all outcomes collected at that time point as having a high risk of bias and therefore do not report them here or in Appendix G.[129]

[d]Presence of each PTSD symptom cluster was based on DSM-IV criteria. For reexperiencing, one of five DSM-IV criteria at baseline was required; for arousal, two of five were required; and for avoidance/numbing, three of seven were required. Severity was defined as high vs. low for each of the three PTSD symptom clusters (reexperiencing, arousal, and avoidance), where high is defined as meeting DSM-IV criteria for that cluster.

Subgroups by Demographic Characteristics

Sex

Two trials evaluated whether sex modified the effect of early psychological interventions on PTSD symptoms; one trial (N=157) tested debriefing versus psychoeducation among victims of violent crime,[129] and the other (N=77) tested immediate versus delayed debriefing for robbery victims (Table 35).[134] These two trials reported consistent findings that the effect of early psychological interventions in reducing PTSD symptoms did not differ between men and women (Table 33).[134] However, neither study reported the magnitude of the estimated effect (i.e., the coefficient of the interaction term) or the precision of the estimate.

One study[129] reported no differences between men and women in the effects of early intervention on depressive symptoms. Based on this single study, we concluded that the evidence was insufficient to determine if there are differences between men and women in reducing depressive symptoms. The evidence was insufficient for all other outcomes.

Age and Ethnic and Racial Groups

No study addressed effectiveness of interventions in subgroups defined by age, race, or ethnicity.

Subgroups by Type of Trauma

One study[128] reported that type of trauma modified the effect of modified PE, initiated less than 1 day after trauma, on PTSD symptoms. Survivors of sexual assault, but not survivors of physical assault or MVAs, had clinically and statistically significant declines in PTSD symptoms compared with those in the assessment-only group (Table 34). An overall group by trauma type by time interaction effect was not assessed. Because this was the only study that reported a subgroup analysis by trauma type, there is insufficient evidence that the effect of modified PE on PTSD symptoms was different among survivors of sexual assault and survivors of other trauma types.

Subgroups by Psychiatric Comorbidity

Previous Depression

One study reported that previous depression did not modify the effect of the debriefing for PTSD symptoms or depression symptoms (Table 34).[129] For their models for PTSD symptoms and depression symptoms as outcomes, they did not report either estimated magnitude of effect for the interaction terms (intervention-by-time-by-previous depression) or precision of those estimates. The evidence was insufficient to determine the impact of previous depression on the incidence of PTSD or PTSD symptom severity.

Previous Anxiety Disorder Other Than PTSD

No study addressed effectiveness of interventions in subgroups defined by previous anxiety disorder other than PTSD.

Personal Risk Factors for Developing PTSD

History of Child Abuse

Rose and colleagues reported that history of child abuse did not modify the effect of debriefing for PTSD symptoms or symptoms of depression (Table 34).[129] The authors did not report the estimated magnitude of effects for the intervention by time or by history of child abuse interaction terms or the precision of their estimates.

Severity of Trauma Exposure

One study[126] reported that the severity of combat exposure, entered into regression models as either linear or quadratic interaction terms, did not modify the effect of Battlemind training that was adapted for use in the UK (Table 34). The magnitude of interaction effects and their precision were not reported. The evidence was insufficient to conclude whether there are differences in the effect of Battlemind training across varying levels of severity of trauma exposure.

Baseline Severity of Distress

Two trials (one low risk of bias) performed subgroup analyses on baseline severity of distress.[120,131] Sijbrandij and colleagues evaluated the impact of debriefing on PTSD symptoms, depressive symptoms, and anxiety symptoms, among survivors of a single traumatic event, of any kind, that occurred 2 weeks before study entry.[131] They reported a significant ($p=0.005$) interaction for intervention by time by level of baseline arousal symptoms (high versus low): at 6

weeks, individuals in the debriefing group had increased PTSD symptoms compared with controls in the high baseline hyperarousal group but not in the low baseline hyperarousal group (Table 34). The authors did not report magnitude of the effect or precision. Beatty and colleagues evaluated the impact of a psychoeducational SHB on PTSD symptoms, among women with a recent diagnosis of breast cancer.[120] For PTSD symptoms, the interaction for intervention by baseline PTSD severity was significant ($p<0.01$) at 3 months. Compared with controls, the women with high baseline symptoms who received the SHB experienced decreased PTSD symptoms to a greater extent than did women with low baseline PTSD symptoms. The magnitude of the interaction effect and its precision were not reported. The discrepant findings between these two trials may arise from differences in any or all of the following: (1) composition of the sample (including type of trauma and percentage of women), (2) intervention (debriefing vs. workbook), (3) timing of followup assessment, (4) definition of baseline distress, or (5) measure of PTSD symptoms.

High-Risk-of-Bias Studies

The two studies omitted from the main data synthesis for high risk of bias are briefly described here.[27,107]

Exposure to Combat-Related Events

Adler and colleagues randomly assigned, at the platoon level, U.S. soldiers who had been deployed to Iraq to stress education (n=527), Battlemind debriefing (n=582), small group Battlemind training (n=562), and large group Battlemind training (n=616).[27] Attrition was very high (53.9%) at the follow-up survey at 4 months, primarily because of Army reassignment of personnel; the only difference between the baseline and follow-up samples was a higher loss to followup among noncommissioned officers than junior-ranking soldiers. They reported that the interaction between intervention and exposure to combat-related events (entered as a quadratic term) was strong (with PTSD symptoms as the outcome). Among soldiers with low levels of combat exposure, PTSD symptoms did not differ for soldiers randomized to any of the four interventions. However, among soldiers with very high levels of combat exposure, all three of the active interventions resulted in substantially lower PTSD symptoms at 4 months than stress education.

Sex

Krauseneck and colleagues,[107] previously described in KQ 1, conducted a prospective cohort study of the effect of beta-adrenergic blockade with metoprolol on traumatic memories and PTSD symptoms among cardiac surgery patients 1 day before surgery and at 1 week and 6 months after surgery. Baseline and treatment medical characteristics (such as duration of surgery) did not differ between those who did or did not receive metoprolol. The authors did not report on psychological characteristics that might confound the association between beta-blockers and PTSD symptoms upon followup. For PTSD symptoms, they reported a significant interaction of treatment (metoprolol vs. no metoprolol) by time by sex: at 6 months, women treated with metoprolol had lower PTSD symptoms than women not treated with metoprolol, whereas men treated with metoprolol had the same PTSD symptoms as men not treated with metoprolol.

KQ 4: Risks of Harms

Description of Included Studies

Overall, we identified four studies assessing harms for early interventions to prevent PTSD.[84,93,131,135] Two otherwise eligible studies were rated high risk of bias and omitted from the main data synthesis but are discussed below.[84,93] The two included studies involved civilian medical trauma, assault or accident,[131] and mechanical ventilation.[135] Interventions for these two studies involved different forms of psychological debriefing (emotional or educational)[131] and use of light versus deep sedation.[135]

Key Points

- For patients with early hyperarousal, the evidence was inconclusive whether emotional debriefing leads to increased PTSD symptoms compared with no debriefing (insufficient SOE).
- For critically ill patients, the evidence was inconclusive whether there was a difference in mortality between light and deep sedation groups (insufficient SOE).

Detailed Synthesis

Table 36 summarizes the available evidence of the absolute and comparative risks of harms from early interventions to prevent PTSD for the two studies with either low or medium risk of bias. For absolute risk, the SOE was determined to be insufficient because the data are from a single study and results are mixed across assessment points. For comparative risk, the SOE was found to be insufficient because the data are from a relatively small sample from a single study.

Table 36. Findings and strength of evidence about harms

Intervention, Population	Outcome	Results	SOE[a]
Emotional debriefing vs. educational debriefing vs. no debriefing, Civilian medical (psychological trauma)[131]	Absolute risk: PTSD severity (in subgroup with hyperarousal)	For patients with early hyperarousal, the evidence was inconclusive whether emotional debriefing leads to increased PTSD symptoms compared with no debriefing; 1 trial (N=236).	Insufficient
Light sedation vs. deep sedation), Mechanical ventilation[135]	Comparative risk: Mortality	The evidence was inconclusive whether there was a difference in mortality between light and deep sedation groups; 1 trial (N=137).	Insufficient
	Comparative risk: Incidence of adverse events	The evidence was inconclusive whether there was a difference in the incidence of organ dysfunction, hypertension, or tachycardia between light and deep sedation groups; 1 trial (N=137).	Insufficient

N = entire sample; PTSD = posttraumatic stress disorder; SOE = strength of evidence

[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

One trial provided limited data about the absolute risk of early interventions to prevent the onset of PTSD,[131] while a second study provided limited data about the comparative risks of such interventions.[135] Table 37 summarizes the characteristics of these studies.

Table 37. Characteristics of the included studies evaluating risk of harms from interventions to prevent PTSD

Study and Risk of Bias, Prevention Type	Study Design, Intervention (n)	Treatment Duration (Followup Duration)	Population and Trauma Type	Primary Outcome Measure and Baseline Score	Mean Age and Age Range (Years)	Percentage Female
Sijbrandij et al., 2006[131] Low Universal	Unblinded RCT, Emotional debriefing (76) Educational debriefing (79) No debriefing (81)	One 45- to 60-minute session (6 months)	Civilian medical, psychological trauma	SI-PTSD Emotional debriefing: 19.9 Educational debriefing: 19.9; Control 17.7	40.4[a] (range NR)	48.7[a]
Treggiari et al., 2009[135] Medium Universal	Single-blinded RCT; Light sedation (69) Deep sedation (68)	7 days (1 month)	Civilian medical, mechanical ventilation	IES-R & PCL: not applicable	61.4[a] (range NR)	23.5[a]

IES-R = Impact of Event Scale-Revised; n = subset of sample; NR = not reported; PCL = PTSD Checklist; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SI-PTSD = Structured Interview for PTSD

[a]Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

One trial (low risk of bias), previously described in KQ 1, was conducted in 236 adult Dutch civilians who had experienced psychological trauma (Table 37).[131] Eligible patients were randomly assigned to one of three groups: (1) emotional debriefing, (2) educational debriefing, or no debriefing within 2 weeks of the trauma. In a subgroup analysis, the authors reported that for participants with early hyperarousal, those receiving emotional debriefing experienced higher PTSD scores than the control group at 6 weeks (test for interaction, p=0.005) (Table 36). This difference was not found at the two other assessment points (2 weeks or 6 months), and no other differences between the groups were noted.

A second study (medium risk of bias), previously described in KQ 2, provided data relevant to comparative risks (Table 37).[135] In this randomized open label study of 137 adult Swiss patients being placed on mechanical ventilation for at least 12 hours, patients were randomly assigned to receive either light or deep sedation. There were no differences in mortality (14% ICU deaths in each arm; 18% vs. 17% death during stay hospital stay, p=0.65) or in the incidence of adverse events (as measured by organ dysfunction, hypertension, and tachycardia) (Table 36).

High-Risk-of-Bias Studies

Two studies otherwise meeting our eligibility criteria were omitted for high risk of bias.[84,93]

Critical Incident Stress Debriefing

The other study was a nonrandomized retrospective cohort study in the Netherlands with high potential for selection bias; it compared the effectiveness of one session of debriefing (n=46) with no debriefing (n=59) for police officer first responders to a large plane crash.[93] At 18-month followup, but not at 8-month followup, the officers who had been debriefed were significantly more likely to exhibit disaster-related hyperarousal symptoms than those not debriefed.

Critical Incident Stress Debriefing and Stress Management

One tested the comparative effectiveness of CISD versus a stress management class versus a group that received no intervention but completed assessment tools at the follow-up periods.[84] More information about this study's characteristics is available above in the KQ 3 (Subgroup Analyses) section. At 4-month followup, CISD was not more distressing or arousing than a stress management class or no intervention.

Discussion

We conducted a systematic review of the efficacy and comparative effectiveness and harms of psychological, pharmacological, and emerging interventions for the prevention of PTSD in adults exposed to psychological trauma. Because of the ongoing controversy about whether different treatments are efficacious at all, we first assessed evidence for the efficacy of the treatments of interest and then proceeded to assess comparative effectiveness. We used this approach because our preliminary searches and input from experts during the topic refinement process suggested that we would find little head-to-head comparative evidence; we realized that we would likely need to rely on indirect evidence to attempt to draw conclusions about comparative effectiveness.

Below, we summarize the main findings and strength of evidence (SOE) by Key Question (KQ). We then discuss the findings in relationship to what is already known, applicability of the findings, implications for decisionmaking, limitations, research gaps, and conclusions.

Key Findings and Strength of Evidence

KQ 1: Efficacy and Comparative Effectiveness

The evidence for the effectiveness of psychological, pharmacological, and emerging interventions to prevent PTSD is limited. Overall, 52 studies met eligibility criteria for KQ 1.[27,47,51,83-97,99-114,116-133] Of these, 35 were rated as high risk of bias and omitted from the main data synthesis.[27,47,51,83-88,90,92-97,99-114,116-118] Tables 38 and 39 summarize the main findings and the SOE for KQ 1.

We identified trials that reported on one or more of eight different psychological interventions: debriefing, cognitive behavioral therapy (CBT), CBT combined with hypnosis, cognitive therapy (CT), prolonged exposure therapy (PE), psychoeducation, self-help materials, and supportive counseling (SC). We included two trials that reported on two different medications: hydrocortisone and escitalopram. In addition, we identified one trial reporting on an emerging intervention: collaborative care. All these studies evaluated the efficacy of the intervention against an inactive control such as a waitlist, usual care, or placebo.

From these studies, we concluded that debriefing is not effective in preventing PTSD or reducing the severity of PTSD symptoms in civilian victims of crime, assault, or accident trauma at 6-month followup (low SOE) (Table 38). We had insufficient data (single study) to determine the efficacy of debriefing at 2- or 6-week followup, as well as at 11-month followup. From a single study involving civilian trauma patients requiring surgical hospitalization, we concluded that collaborative care produces a greater decrease in PTSD symptom severity at 6, 9, and 12 months after injury compared with usual care (low SOE). However, data addressing whether there was a difference in PTSD diagnosis 12 months after injury were not conclusive (insufficient SOE). For most interventions—namely, CBT, CBT combined with hypnosis, CT, PE, psychoeducation, self-help material, SC, and the two pharmaceuticals—we had single studies with small treatment arms (generally fewer than 80 subjects). This paucity of information led us to conclude that the evidence was insufficient to support their efficacy in preventing PTSD or reducing the severity of PTSD symptoms. When assessed, we arrived at the same conclusion for the effectiveness of these interventions in reducing comorbid symptoms of anxiety and depression.

Table 38. Summary of findings and strength of evidence for the efficacy of psychological, pharmacological, and emerging interventions to prevent PTSD and reduce PTSD symptom severity

Intervention, Population	Outcome	Results	SOE
Cognitive behavioral therapy, Civilian, mixed trauma types[127]	Incidence of PTSD	Inconclusive, single trial (N=46)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=46)	Insufficient
Cognitive therapy, Civilian, mixed trauma types[122,123]	Incidence of PTSD	Inconclusive, single trial (n=133)	Insufficient
	PTSD symptom severity	Inconclusive, 2 trials (n=193), inconsistent findings at different assessment intervals	Insufficient
Collaborative care Civilian, mixed trauma types requiring hospitalization[119]	Incidence of PTSD	Inconclusive, single trial (N=207)	Insufficient
	PTSD symptom severity	Collaborative care produces a greater decrease in PTSD symptom severity at 6, 9, and 12 months after injury compared to usual care, single trial (N=207)	Low
Debriefing, Civilian mixed trauma types[129,131]	Incidence of PTSD	Debriefing not significantly different than control at multiple followup assessment intervals across 2 trials (n=341)	Low
	PTSD symptom severity	Debriefing not significantly different than control at multiple followup assessment intervals across 2 trials (n=341)	Low
Exposure-based therapies, Civilian, mixed trauma types[122,123,128]	Incidence of PTSD	Inconclusive, 3 trials (n=355), inconsistent findings at different assessment intervals	Insufficient
	PTSD symptom severity	Inconclusive, 3 trials (n=355) with different assessment intervals that prevent direct comparisons	Insufficient
Hydrocortisone stress dose, Civilians undergoing high-risk cardiac surgery[132]	Incidence of PTSD	Inconclusive, single trial (n=28)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=28)	Insufficient
Psychoeducation, Civilian, crime [129] and injury[133] victims	Incidence of PTSD	Inconclusive, 2 trials (n=182) with different assessment intervals that prevent direct comparisons	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=103)	Insufficient
Self-help materials, Women, newly diagnosed with breast cancer[120]	PTSD symptom severity[a]	Inconclusive, single trial (N=49)	Insufficient
SSRI (escitalopram), Civilian, mixed trauma types[122]	Incidence of PTSD	Inconclusive, single trial (n=139)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=139)	Insufficient
Supportive counseling, Women, mixed trauma types[121,125,130]	Incidence of PTSD	Inconclusive, single trial (N=103)	Insufficient
	PTSD symptom severity	Inconclusive, 2 trials (N=336), inconsistent findings at different assessment intervals using different outcome measures	Insufficient

N = entire sample; n = subset of sample; PTSD = posttraumatic stress disorder; SSRI = selective serotonin reuptake inhibitor; SOE = strength of evidence

[a]Incidence of PTSD not reported.

Table 39. Summary of findings and strength of evidence for the comparative effectiveness of psychological, pharmacological, and emerging interventions to prevent PTSD and reduce PTSD symptom severity

Intervention, Population	Outcome	Results	SOE
Battlemind training vs. standard brief, UK military service members[126]	PTSD symptom severity	Inconclusive, single trial (n=2,443)	Insufficient
CBT vs. CBT+Hypnosis Civilian, mixed trauma types[91]	Incidence of PTSD	Inconclusive, single trial (n=63)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=63)	Insufficient
CBT vs. SC, Civilian, mixed trauma types with acute stress disorder[89,91,124]	Incidence of PTSD	CBT not significantly different than SC at end of treatment (RR, 0.27; 95% CI [0.05 to 1.29]; I^2=71.8%) or at 6 months (RR, 0.46; 95% CI [0.21 to 1.01]; I^2=44.9%); 3 trials (n=105)	Low
	PTSD symptom severity	Greater reduction for CBT than for SC on IES-I at the end of treatment (WMD, -7.85; 95% CI [-11.18 to -4.53]; I^2=1.3%) and at 6 months (WMD, -8.19; 95% CI [-11.79 to -4.58]; I^2=6.8%); 3 trials (n=105) Greater reduction for CBT than for SC on IES-A at end of treatment (WMD, -14.04; 95% CI [-19.37 to -8.71]; I^2=53.8%) and 6 months (WMD, -9.94; 95% CI [-15.06 to -4.83]; I^2=44.0%); 3 trials (n=105)	Moderate
CBT+Hypnosis vs. SC, Civilian, mixed trauma types[91]	Incidence of PTSD	Inconclusive, single trial (n=54)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=54)	Insufficient
CT vs. PE, Civilian, mixed trauma types[122,123]	Incidence of PTSD	Inconclusive, 2 trials (n=163), inconsistent findings at different assessment intervals; 1 trial used a completer analysis	Insufficient
	PTSD symptom severity	Inconclusive, 2 trials (n=163), inconsistent findings at different assessment intervals; 1 trial used a completer analysis	Insufficient
CT vs. SSRI (escitalopram), Civilian, mixed trauma types[122]	Incidence of PTSD	Inconclusive, single trial (n=54)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=54)	Insufficient
Emotional debriefing vs. Educational debriefing, Civilian, mixed trauma types[131]	Incidence of PTSD	Inconclusive, single trial (n=155)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=155)	Insufficient
PE vs. SSRI (escitalopram), Civilian, mixed trauma types[122]	Incidence of PTSD	Inconclusive, single trial (n=71)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=71)	Insufficient
Psychoeducation vs. debriefing combined with psychoeducation, Civilian, crime victims[129]	Incidence of PTSD	Inconclusive, single trial (n=106)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=106)	Insufficient

CBT = cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; CI = confidence interval; CT = cognitive therapy; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event Scale-Intrusions subscale; n = subset of sample; PE = prolonged exposure therapy; PTSD = posttraumatic stress disorder; RR = relative risk; SC = supportive counseling; SSRI = selective serotonin reuptake inhibitor; UK = United Kingdom; WMD = weighted mean difference

A small number of studies evaluated the comparative effectiveness of two or more psychological interventions with one another or with a pharmacological intervention. Our meta-analyses of trials that compared CBT with SC in a sample of participants with acute stress disorder found that, at both the end of treatment and at 6-month followup, CBT was no more effective than SC for preventing PTSD (low SOE), reducing symptoms of anxiety (moderate

SOE), or reducing symptoms of depression (low SOE) (Table 39). By contrast, related meta-analyses of the CBT compared with SC trials found that, at both the end of treatment and at 6-month followup, CBT was more effective than SC in reducing the severity of PTSD symptoms as measured by the IES (moderate SOE).

For many interventions, we had insufficient evidence to draw conclusions about efficacy. This, coupled with the fact that this knowledge base largely comprises single studies with small sample sizes, we concluded that the evidence was insufficient to determine the comparative effectiveness of most of the psychological interventions in preventing PTSD or reducing PTSD symptom severity. This includes whether Battlemind training is more effective than standard postdeployment debriefing for military personnel in the UK, CBT plus hypnosis is more effective than CBT or SC for civilian victims of nonsexual assault or motor vehicle accidents (MVA), various forms of debriefing, alone or in combination with psychoeducation for crime victims, and CT compared with PE for hospitalized survivors of MVAs or terrorist attacks. Only one study compared psychological interventions (CT and PE) with a medication (escitalopram), so we could not draw any conclusion about the comparative effectiveness of an selective serotonin reuptake inhibitors (SSRI) with a psychological intervention. No study evaluated the comparative effectiveness of two or more medications with each other. Finally, when assessed, we drew the same conclusion (insufficient evidence) for the comparative effectiveness of these interventions in reducing comorbid symptoms of depression and anxiety.

KQ2: Timing, Intensity, or Dosing

The evidence on the impact of timing, intensity, or dosing on the effectiveness or risk of harms of interventions used for the prevention of PTSD is scarce. Overall, four studies addressed timing and dosing questions;[98,115,134,135] two of these were rated as high risk of bias.[98,115] We found no studies on the impact of intensity of intervention for any psychological or emerging interventions. Table 40 summarizes the main findings and the SOE for KQ 2.

Table 40. Summary of evidence of the impact of timing, intensity, and dosing on the effectiveness of interventions and strength of evidence

Intervention, Population	Outcome	Results	SOE[a]
Debriefing (CISD) timing (early vs. late), Robbery victims[134]	PTSD symptom severity	Inconclusive, single trial (N=77)	Insufficient
Pharmacological sedation depth (light vs. deep), Critically ill patients[135]	Incidence of PTSD	Inconclusive, single trial (N=137)	Insufficient

CISD = critical incident stress debriefing; N = entire sample; PTSD = posttraumatic stress disorder; SOE = strength of evidence
[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.

One randomized controlled trial (RCT) addressed the impact of timing of a psychological intervention. Immediate debriefing (within 10 hours) compared with late debriefing (after 48 hours) led to victims experiencing significantly fewer posttraumatic symptoms (insufficient SOE) (Table 40). No evidence was available on the impact of timing for any other psychological, pharmacological, or emerging interventions or any other outcomes.

In one RCT, dosing of sedation (light vs. deep) in critically ill patients did not affect either posttraumatic symptoms or symptoms of depression or anxiety (insufficient evidence). We did

not find any eligible evidence on the effect of dosing for any other pharmacological or emerging interventions to prevent PTSD.

KQ 3: Subgroups

Evidence is also sparse on whether the effect of early interventions differs across demographic groups, psychiatric diagnoses, or personal risk factors for developing PTSD. Six studies that met our inclusion criteria[27,107,120,129,131,134] included subgroup analyses; two were rated high risk of bias.[27,107] Table 41 summarizes the main findings and the SOE for KQ 3.

Table 41. Summary of evidence and strength of evidence for the effect of early interventions in various subgroups

Subgroup; Intervention, Population	Outcome	Results	SOE
Demographic groups: sex; CBT, CISD; Crime victims[129,134]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Sex did not modify the effect of CBT or CISD; consistent findings, 2 trials (N=234)	Low
Type of trauma; PE, Mixed civilian trauma[128]	Incidence of PTSD	Inconclusive, single trial (N=137)	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=137)	Insufficient
Psychiatric diagnosis: previous depression; Debriefing, Crime victims[129]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=157)	Insufficient
History of child abuse[b]; Psychoeducation vs. debriefing combined with psychoeducation; Crime victims[129]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconclusive, single trial (N=157)	Insufficient
Severity of baseline distress[b]; Debriefing, self-help workbook; Crime victims; women with breast cancer[120,131]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconsistent findings, 2 trials (N=285)	Insufficient
Severity of combat exposure[b]; UK military service members[126]	Incidence of PTSD	No evidence	Insufficient
	PTSD symptom severity	Inconclusive, single trial (n=2,443)	Insufficient

CBT = cognitive behavioral therapy; CISD = critical incident stress debriefing; N = entire sample; n = subset of sample; PE = prolonged exposure therapy; PTSD = posttraumatic stress disorder; SOE = strength of evidence; UK = United Kingdom
[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.
[b]Personal risk factor for PTSD.

Two trials assessed whether sex modified the effect of early psychological interventions on PTSD symptoms.[129,134] Both reported consistent results that the effects of early psychological interventions on PTSD symptoms were similar for men and women (Table 41). However, because neither trial reported the magnitude of the estimated effect or its precision, we graded the SOE as low.

One trial tested the effect of a debriefing intervention on subgroups defined by sex, history of depression, and history of child abuse, but it did not report magnitude or precision of effects (SOE insufficient in all cases).[129] No differences were found for any of these subgroup comparisons for the effect of debriefing.

Two trials provided inconsistent findings on whether baseline severity of PTSD symptoms modified the effect of early psychological interventions (SOE insufficient).[120,131]

KQ 4: Harms

Little evidence exists addressing the absolute risks and/or comparative risks of harms from early interventions to prevent PTSD. Four studies assessed harms;[84,93,131,135] two were rated as high risk of bias.[84,93] Table 42 summarizes the main findings and the SOE for KQ 4.

Table 42. Summary of findings and strength of evidence about harms

Intervention, Population	Outcome	Results	SOE[a]
Emotional debriefing vs. no debriefing, Civilian, medical trauma[131]	PTSD symptom severity	For subgroup with hyperarousal, inconclusive, single trial (N=236), inconsistent findings at different assessment intervals	Insufficient
Pharmacological sedation (light vs. deep),[b] Critically ill patients[135]	Mortality	Inconclusive, single trial (N=137)	Insufficient
	Incidence of adverse events	Inconclusive, single trial (N=137)	Insufficient

N = entire sample; PTSD = posttraumatic stress disorder; SOE = strength of evidence
[a]For more detailed information about the rationale for SOE grading, please refer to Appendix G.
[b]Open label study.

A three-armed RCT (low risk of bias) considered absolute risk in patients presenting to an outpatient psychiatric clinic after assault or an accident.[131] In a subgroup of patients with early hyperarousal, those receiving emotional debriefing experienced higher PTSD severity at 6 weeks than those not receiving such debriefing (Table 42). The investigators did not find this difference in this subgroup at either 2 weeks or 6 months or in any other subgroups (insufficient evidence). We found no other trials of psychological or pharmacological interventions that provided information on risks of early interventions.

One randomized open-label study considered comparative risk of harms from light versus deep sedation for patients requiring mechanical ventilation.[135] The two groups did not differ with regard to rates of mortality (whether during their stays in the intensive care unit or their overall hospitalization) or in the incidence of adverse events (organ dysfunction, hypertension, and tachycardia). The evidence was insufficient (single study) for us to draw any conclusions about harms for this intervention.

Findings in Relationship to What Is Already Known

As stated in the introductory chapter of this review, variability of types of trauma, contexts in which they occur, and individual differences of those exposed to traumatic events are likely to prohibit a "one size fits all" model for preventive intervention. Preventing PTSD is not easy in part because each individual responds to stress differently; thus, predicting who will develop PTSD is similarly difficult. Other challenges include identifying people at risk for PTSD and, from a logistics perspective, conducting "early" interventions in the aftermath of a traumatic event.

Our results found insufficient evidence to support the effectiveness of most psychological, pharmacological, and emerging interventions that have been studied to prevent PTSD. The two primary reasons are that (1) we generally had only one or two studies that addressed each intervention and (2) most of these studies had relatively small sample sizes.

Departments of Veterans Affairs and Defense Guidelines

Clinical practice guidelines published in October 2010 by the U.S. Department of Veterans Affairs and Department of Defense (VA/DoD)[136] listed several possible early interventions: crisis intervention and stress management, the PIE (proximity, immediacy, and expectations) model for combat stress reactions, brief CBT, debriefing, and pharmacological interventions (benzodiazepines and sedatives). However, these guideline developers concluded that, among these, only time-limited CBT (four or five sessions) is the most effective in preventing PTSD in samples of survivors of sexual assault, nonsexual assault, and accidents.

We concluded that short- term CBT (5 to 6 weeks) is no more effective than SC in preventing PTSD for samples of civilian trauma survivors (motor vehicle accidents [MVAs], industrial accidents, and nonsexual assault) with acute stress disorder. We did find, however, that CBT was more effective than SC in reducing PTSD symptom severity (moderate SOE) with these same trauma samples.

Consistent with the VA/DoD guidelines, we concluded that debriefing was not effective in preventing PTSD or reducing PTSD symptom severity. The guidelines note that short-term use of benzodiazepines improved sleep and PTSD symptoms but that long-term use was associated with a higher incidence of PTSD at 6 months. One of the prospective cohort studies that met our eligibility criteria (but rated high risk of bias),[100] which examined the efficacy of early intervention with benzodiazepines, reported that the treatment and control groups were not significantly in PTSD or anxiety symptoms at 1-month and 6-month followup. These guidelines also stated that no studies (in their evidence base) had evaluated the effectiveness of antidepressants for preventing PTSD. We identified one study that compared an SSRI with placebo and other psychological interventions,[122] but it provided insufficient evidence to determine the absolute and comparative effectiveness of an SSRI compared with either CT or PE for preventing PTSD or for reducing PTSD symptom severity.

Finally, the VA/DoD guidelines stated that the effectiveness of PIE has not been confirmed and that there is some evidence that it is not effective in preventing PTSD. Our literature search did not identify any studies that used the PIE (proximity, immediacy, and expectations) model, so we cannot comment on this intervention or method of intervention.

National Center for Posttraumatic Stress Disorder

The National Center for Posttraumatic Stress Disorder and the VA/DoD identify psychological first aid as an appropriate post-trauma early intervention strategy.[136] In general, psychological first aid is seen as a mental health correlate of physical first aid and not as a therapeutic or preventive intervention for PTSD. Guidelines published by the VA/DoD reported that there is insufficient evidence to recommend for or against the use of psychological first aid to address post-trauma symptoms beyond 4 days. Our search of the literature did not identify any studies on the effectiveness of psychological first aid in preventing PTSD.

Other Sources

Our literature searches did not identify a large number of studies that reported on prevention interventions after the 2001 World Trade Center disasters (WTCD) in the United States. Two studies of employees at the worksite after the WTCD were identified did not meet our eligibility criteria because of lack of objective information about the interventions used.[137,138] The only data available about the interventions from this team of investigators were based on participant self-

report; this precluded our categorizing them in our analyses or results. Although evidence from these studies is insufficient to draw any conclusions about the effectiveness of whatever crisis intervention strategies they had used, the studies were methodologically sound and were the only studies we found that reported on data on this traumatic event. Given this, we briefly summarize characteristics and main findings of these studies.

Both studies pertain to a prospective cohort of English- or Spanish-speaking adults living in New York City on the day of the WTCD identified using random-digit dialing. The first cohort was contacted 1 year after the WTCD, and the second 2 years after the event. In telephone interviews, the investigators asked subjects whether they had attended brief sessions related to coping with the WTCD and questions about alcohol use and mental health status including PTSD symptom severity. Compared with subjects who had not attended any intervention sessions, subjects who received two to three sessions experienced a reduction in PTSD symptom severity (OR, 0.36; $p<0.05$) at 1 year after the WTCD[137] and lower PTSD symptom severity (0.8 percentage points lower, $p<0.05$) during the month before the assessment.[138] At the 2-year followup, 80 percent of the sample reported that the brief sessions were helpful for coping with the disaster.[138]

Despite the limitations of these studies (i.e., lack of randomization, inability to contact subjects without a telephone, excluding individuals who did not speak English or Spanish), their results suggest brief postdisaster crisis interventions may be effective after mass exposure to psychologically traumatic events. The reasons for the effectiveness of these interventions are unclear and warrant further investigation. Whether the findings of this intervention would generalize to other types of disasters and trauma samples also remains unclear.

Implications for Clinical and Policy Decisionmaking

Treatment guidelines from the VA/DoD outline a four-stage framework for early responses to traumatic events[15]: (1) provide concrete help, food, warmth, and shelter; (2) soothe and reduce states of extreme emotion and increase controllability; (3) assist survivors with distressing and repetitive reappraisals of the trauma; and (4) treat specific syndromes and disorders such as acute stress disorder, depression, and anxiety.

The first step in this framework is clear, but clinical uncertainty exists about what interventions to use to address the other three. Initially, practical considerations, such as presence or lack of availability of trained personnel or resources to implement treatment, will likely guide treatment decisions in the immediate aftermath of a traumatic event. Once safety and basic needs stabilization has occurred, which early psychological or pharmacological interventions would be most effective and the least harmful in preventing PTSD cannot be specified from our results. If individuals have access to a variety of early interventions and they do not have a preference for a particular type of intervention, our findings would support the use of brief CBT interventions over SC for possibly reducing PTSD symptom severity; this was the intervention for which we had the most information to support efficacy (although low SOE). If an individual prefers medication, our results did not identify any class of drugs that has been shown to be effective in preventing PTSD.

Evidence on the impact of timing, intensity, or dosing on the effectiveness or risk of harms of interventions used for preventing PTSD is extremely scarce. The single trial of critical incident stress debriefing (CISD) timing indicated that early CISD was more effective than late CISD in reducing the number of posttraumatic symptoms in victims of robbery.[134] However, because of the lack of an inactive control group in this study, no firm conclusions about a greater efficacy of

early debriefing can be drawn. It is conceivable that the difference between immediate and delayed intervention can be attributed to harmful effects of delayed debriefing relative to no beneficial effects of immediate debriefing.

With respect to subgroups, we had similarly very little evidence. Clinicians may not need to take the sex of a patient into consideration when choosing a preventive intervention for at least some types of traumas, for example, nonsexual assault crime or robbery victims (low SOE). Whether that would generalize to other types of trauma, such as sexual assault, is unclear. We found no evidence about which early interventions are more or less effective for various other subgroups of interest (defined by sociodemographic characteristics, history of psychological conditions such as depression, or history of traumas that might put victims at increased risk of PTSD).

Evidence addressing the absolute risks and/or comparative risks of harms from early interventions for the prevention of PTSD was similarly insufficient. Of note, concern has been raised as to whether emotional debriefing might worsen symptoms associated with PTSD. The one study addressing this question found higher PTSD scores with emotional debriefing than with no debriefing (test of interaction, p=0.005) at 6-week followup but no differences at 2 weeks or 6 months.[131]

We would like to emphasize though that these results do not apply to the treatment of PTSD, a topic that is not covered in this report.

Applicability

The scope of this review was limited to studies that enrolled adults exposed to psychological trauma who were at risk for PTSD. We did not attempt to review literature on preventive interventions for PTSD in children exposed to psychological trauma.

The included studies covered diverse populations exposed to a wide range of traumas. Nevertheless, we had little or no evidence about terrorist attacks, sexual assault, natural disaster, or combat. Many studies were conducted in civilian populations outside the United States; the applicability of their results to patients or victims within this country is uncertain. The mean age of subjects was generally in the 30s to 40s, but some studies enrolled slightly older populations. Some studies screened participants for posttraumatic symptoms before enrollment and generally included them in their samples. Although these participants did not have a diagnosis of PTSD per se (because their symptoms had lasted less than 1 month), results from studies in such selected populations with acute stress symptoms might have little applicability to average populations exposed to psychological trauma who may not have acute stress symptoms at the time of the intervention. Furthermore, most studies were conducted in clinical settings. Results from samples of patients attending a clinic might not apply to members of the general community who suffered traumatic experiences of the same type. Therefore, evidence, in general, was insufficient to determine whether findings are applicable to all those at risk for PTSD from this heterogeneous set of traumatic events or, possibly, applicable only to certain groups.

Similarly, we did not find evidence to confirm or refute whether treatments are more or less efficacious for various subgroups: patients characterized by sex, race, or ethnicity; refugee status; first responders; victims of either natural or manmade disasters; or individuals with coexisting psychiatric conditions or with a history of events that might have put them at risk of PTSD. The samples used in many studies had some subjects with the aforementioned subgroup characteristics, even if the main focus was on a different population. For instance, the trials may have included individuals with a history of multiple past traumas, service-connected disability, or

coexisting psychiatric conditions such as depression. Three drawbacks posed challenges for this review and limit anything we might say about applicability: we had only a single study per intervention/population combination, many studies did not publish details about some attributes of their subjects (e.g., race or ethnicity), and generally investigators did not report whether interventions were efficacious for individuals in subgroups that they may have in fact included.

For the few interventions for which we did have low or moderate SOE for effectiveness (collaborative care over usual care and CBT over SC for people with acute stress disorder, for instance), we could not say with confidence that these results could be generalized to other patient populations or other types of trauma.

In addition, many studies were conducted outside the United States with civilian populations (not U.S. military abroad). For example, all three trials comparing CBT with SC were conducted by the same research group in Australia. Whether and how differences in ethical or cultural backgrounds and health systems affect the applicability of results to U.S. populations remains uninvestigated and unanswered.

Finally, for many interventions we lacked sufficient (or indeed any) evidence to draw conclusions about either absolute or comparative effectiveness. Consequently, we cannot draw any conclusions about applicability.

Limitations of the Comparative Effectiveness Review Process

To find relevant studies, we employed an intensive search process in multiple electronic databases; we also conducted searches for grey literature. Because of time and monetary limitations, however, we limited eligible studies to those published in English. Methods research indicates that such an approach can introduce language bias; however, in general, it may also lead to overestimates of the effectiveness of interventions.

For KQs 1 through 4, we included RCTs and prospective cohort studies. For KQ 4, focused on harms, we also reviewed retrospective cohort studies or case-control studies without any sample size limits. We chose this broad approach because preliminary searches indicated that, for many interventions, no evidence from controlled trials is available. Nevertheless, these eligibility criteria might still have led us to exclude some observational studies that might have provided useful information, particularly for generating hypotheses for future studies with more rigorous study designs.

For harms, studies conducted in other populations (i.e., those without PTSD) might have yielded useful information. Such studies could, for instance, could provide important information about adverse effects of medications that might be used to prevent PTSD or its symptoms.

If information in full-text articles was unclear or missing, we attempted to contact authors for clarification. The yield of this effort, however, was small. Despite multiple attempts to contact authors, few replied or were able to provide missing information. Lack of information regarding the timing of interventions, in particular, makes evaluating preventive interventions for PTSD difficult; the main reason is that only interventions administered within the first 3 months after the exposure to psychological trauma qualify as preventive interventions.

Finally, publication bias and selective outcome reporting are potential limitations. Although we searched for grey and unpublished literature, the extent and impact of publication and reporting bias in this body of evidence is impossible to determine.

Limitations of the Evidence Base

Overall, two major limitations characterize this body of evidence. First, no eligible evidence was available assessing the efficacy or comparative effectiveness or risk of harms of many of our eligible interventions. Despite our broad eligibility criteria, including observational studies for effectiveness and harms, we could not draw conclusions for or against benefits and harms for the majority of our interventions of interest. Even when studies assessing the effectiveness of an intervention were available, they often did not assess harms. For example, we included 17 studies for KQ 1 on the efficacy and comparative effectiveness of interventions, but only two studies of low or medium risk of bias provided data on the risk of harms. Although lack of evidence cannot be equated with lack of effectiveness or harms, incautious use of interventions without proven net benefit has the potential of causing more harms than benefits. Important questions, for instance, whether particular interventions such as single-session emotional or educational debriefing might worsen symptoms, remain unanswered.

Second, available evidence was frequently fraught with methodological shortcomings. Of the 56 studies meeting our eligibility criteria, we rated 37 as high risk of bias and only 3 as low risk of bias. Studies assessed as high risk of bias have significant flaws of various types (e.g., stemming from serious errors in design, conduct, or analysis) that may invalidate their results. Consequently, the evidence base for most critical outcomes was insufficient to draw conclusions. The evidence for only a few outcomes could be rated as low or moderate; the latter indicates reasonable confidence in effect estimates of those studies.

Research Gaps

For KQ 1, we have a long way to go before we can conclude which psychological and pharmacological interventions are effective in preventing PTSD. We had insufficient data for the majority of psychological and pharmacological interventions that have been used to prevent PTSD; moreover, many studies that we did identify were rated as high risk of bias. For the few interventions for which we did have low (collaborative care over usual care for individuals with traumatic injuries requiring surgical hospitalization) or moderate SOE for effectiveness (CBT over SC for individuals with ASD), whether these results would generalize to other trauma types or samples is simply unknown. The studies that compared CBT with SC in individuals with ASD were all conducted in Australia by the same group of researchers. Ideally, these studies would be replicated in other samples by other researchers in order to determine the generalizability of these findings. Consistent with other reviews,[32,36,38] we also concluded that psychological debriefing is not useful for preventing PTSD. One of these reviews also concluded that debriefing could actually be harmful to participants and should cease;[38] this is not something we can conclude from our evidence base.

Surprisingly, we had essentially no studies reporting on preventing PTSD in the aftermath of natural disasters; those that did were rated as high risk of bias. Whether this lack of studies reflects logistical difficulty of providing treatment immediately after a natural disaster or some other barrier warrants further examination. Most of the studies included in our analyses were not conducted with samples in the United States, although every year thousands of people living in the United States are exposed to tornados, hurricanes, floods, MVAs, crime, and so on. What this reflects—lack of financial support for prevention intervention, poorly designed or conducted research, fear of prematurely offering medication because of possible adverse side effects, or other issues—is not clear. Groups with strong interests in the mental health of U.S. citizens could

use the results of this report to advocate for increased attention, efforts, and resources targeted at PTSD prevention.

As noted, many of the studies we identified were rated as high risk of bias. Specific and important methods flaws that we identified included the following:

- Inadequate randomization procedures
- High rates of loss to followup
- Inadequate statistical approaches for data analysis (e.g., lack of intention-to-treat [ITT] analysis, or lack of statistical adjustment for significant between-group differences at baseline)

An important task of systematic reviews is to assess design and conduct of included studies and whether they provide adequate protection against bias. The methodological shortcomings of many studies conducted for the prevention of PTSD substantially limit our confidence that results accurately reflect the truth. Therefore, the focus of this report is on evidence from studies rated as having low or medium risk of bias. We summarize findings of high-risk-of-bias studies if no other evidence is available, but readers have to be aware that we have no confidence in the estimates of effect from such studies.

The inherent nature of conducting research in the immediate aftermath of a traumatic event may make addressing some of the methods problems difficult. For example, loss to followup in the wake of a natural disaster, when subjects may be living in temporary housing and then relocate during the course of the study, can be especially challenging. By contrast, other flaws are more readily addressed or under the investigators' control, such as adjusting for between-group differences at baseline. Future research of prevention interventions for PTSD should strive to minimize these types of flaws to increase the efficacy and generalizability of their results. This gap might best be bridged through active interdisciplinary consultation with statisticians, clinical epidemiologists, and other experts in the public health sector.

For KQ 2, on timing, intensity, and dosing of interventions, eligible evidence was generally entirely missing or of high risk of bias. Even considering two studies of medium risk of bias, we could draw no conclusions about these for any of the eligible interventions. Focusing on timing, intensity, and dosing may be premature given the lack of robust support for the efficacy of any psychological or pharmacological intervention to prevent PTSD. We may not be able to answer the issues posed with KQ 2 until we have identified which interventions are effective, with which populations, trauma types, and so forth. Once we have answered this question, the field will be in a better position to address the more nuanced questions of timing, intensity, and dosing. If the ultimate goals are to prevent PTSD, reduce the severity of PTSD, and improve quality of life, we are not there yet. Issues of timing, intensity, and dosing overlap with considerations of risk, harms, and delivery of interventions in an ethical and cost-effective way. Although one cannot divorce these considerations from the preliminary question of which interventions are effective, perhaps their consideration is not so crucial at this time.

Likewise, for KQ 3, we could draw no conclusions about the impact of characteristics of traumatic exposure or subgroups defined by various personal or medical characteristics. Thus, more rigorous research is warranted with respect to the impact that demographic factors, psychiatric comorbidities, or personal risk factors might have on the effectiveness or risk of harms of interventions. This is an area of research where the VA/DoD could expand its research efforts in such a way as to benefit not only military personnel but also civilian trauma survivors. Military personnel can—and do—experience traumatic events that are not the result of direct or even indirect combat exposure. Examples even for members of the military include subgroups

comprising many of the following: military police; medics and health care providers in military health care centers located outside combat zones; and victims of physical and or sexual assault, domestic violence, or even natural disasters.

More generally, other individual and personal risk factors could also be evaluated when possible. History of trauma and psychiatric comorbidity is a case in point. Such information could further advance our knowledge and understanding of how best to intervene with certain subgroups of individuals both in and outside the military culture to prevent PTSD or reduce PTSD symptom severity.

For KQ 4, the scarce data highlight the absence of any evidence basis for the potential harms of preventive interventions. In short, a full half of the intricate calculus of weighing therapeutic harms and benefits is missing. Considerations about using any of the interventions—psychological, psychological, pharmacological, or combinations—requires a thorough understanding of the possible risks of early interventions. It is imperative that investigators who conceptualize their interventions in terms of both benefits and harms identify and specify potential harms a priori and measure them adequately. Although this might be seemingly more important (or easier) for pharmaceutical interventions, for which adverse drug events may be better known, those studying psychological interventions are not immune from this expectation and ethical consideration.

Psychological first aid has gained rapid acceptance as a universal intervention for people in the acute aftermath of trauma, but no studies of psychological first aid met inclusion criteria for our review. Although psychological first aid was not designed as an intervention to reduce the incidence of PTSD, it may have beneficial or adverse effects on mental health among trauma survivors.[139,140] Rigorous studies of psychological first aid should be conducted.

One of the key research gaps for studies of targeted prevention is the limited ability to identify people who are at high risk of developing PTSD shortly after they have been exposed to trauma. Some targeted prevention studies have focused on acute stress disorder as a marker of high risk for development of PTSD. However, only 50 percent of people who meet criteria for acute stress disorder go on to develop PTSD, and more than 50 percent of people who develop PTSD never meet criteria for acute stress disorder. Focusing on acute stress disorder to identify people at high risk for developing PTSD is, therefore, not a reasonable strategy for targeted prevention.[141] Other studies have tried to identify people at high risk of developing PTSD by using screening instruments for PTSD symptoms. However, those instruments are unlikely to be helpful shortly after trauma when the vast majority of trauma survivors have some symptoms of PTSD, but few of whom go on to develop the disorder of PTSD.

The development of a clinical prediction rule to identify, shortly after exposure to trauma, those who will develop PTSD and the even smaller number who will develop chronic disabling PTSD, would be an enormous help to the field. The National Institutes of Health announced a Request for Application for development of a clinical prediction rule for PTSD, but the request was limited to research on existing longitudinal datasets. Prediction rules developed from existing datasets may have limited predictive power if key variables that predict PTSD were not measured in the original dataset. A recent study reported that a clinical prediction rule for PTSD had a sensitivity of 87 percent, a specificity of 65 percent, positive predictive value of 18 percent, and negative predictive value of 98 percent (in a population with a prevalence of PTSD at 12 months of 8 percent).[142] This prediction rule would therefore seem to be promising for identifying people who will not develop PTSD, but less useful for identifying people who will develop PTSD. It is this latter group that needs to be identified for targeted prevention of PTSD

to be effective. We recommend that additional work be devoted to developing a clinical prediction rule based on including all key variables predictive of PTSD (i.e., pretrauma factors, event characteristics, and peri-event responses).

Conclusions

Evidence supporting the efficacy of most interventions used to prevent PTSD is lacking. If available in a given setting, brief trauma-focused CBT might be the preferable choice for reducing PTSD symptom severity in people with acute stress disorder, collaborative care may be helpful for reducing PTSD symptom severity postinjury, and debriefing is not an effective prevention intervention.

Our findings highlight the inherent difficulties of conducting research on prevention interventions, which is often more challenging when conducting research on mental-health-related problems compared with medical or other health-related issues. Our body of evidence was highly limited because of the paucity of methodologically sound studies. Although disappointing, our findings underscore the need for ongoing research efforts in the field of PTSD prevention. Our findings lead us to conclude that the development of a clinical prediction algorithm to identify those who are at high risk of developing PTSD post-trauma exposure is perhaps a more crucial next step in the field of PTSD prevention, before determining which interventions are more effective than others. The ability to identify those most at risk for developing PTSD and then evaluating the effectiveness of prevention interventions in those individuals should be the focus of future clinical and research efforts.

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Appendix A. PTSD Outcome Measures and Instruments

Abbreviated Name	Complete Name	Description	Range/Meaning of Possible Scores	Improvement Indicated by
CAPS	Clinician-Administered PTSD Scale	Structured interview administered by a trained professional that assesses symptoms, impact on functioning, response validity, lifetime diagnosis, and overall PTSD severity. Includes 30 items that correspond to the DSM-IV diagnostic criteria for PTSD. Time frame for assessment includes past week, month, or worst month since trauma.	0 to136	Decrease
CIDI-PTSD	PTSD module of the Composite International Diagnostic Interview	Structured diagnostic interview that based on ICD-10 and DSM-IV PTSD criteria. Once exposure to at least one such traumatic event is established, lifetime symptoms of PTSD are assessed.	CIDI-PTSD	PTSD module of the Composite International Diagnostic Interview
IES	Impact of Event Scale	15-item self-report measure that assesses the frequency of experiences of intrusions, avoidance, and emotional numbing related to stressful events in the last week. A total distress score is calculated by summing all 15 item responses.	0 to 75	Decrease
IES-R	Impact of Event Scale-Revised	22-item self-report measure of subjective distress caused by traumatic events. Includes 7 additional items regarding hyperarousal symptoms of PTSD. Items correspond directly to 14 of the 17 DSM-IV symptoms of PTSD. Subscale scores can be computed for Intrusion, Avoidance, and Hyperarousal.	0 to 88	Decrease
MINI-PTSD	PTSD module of the MINI International Neuropsychiatric	Structured interview includes 6 areas of diagnostic criteria corresponding to DSM-IV and ICD-10. The module begins with screening questions to determine if criterion A of the DSM-IV met and follows with questions about PTSD symptoms and interference.	NA	NA
PCL	PTSD Checklist	17-item self-report measure of the 17 DSM-IV symptoms of PTSD. The PCL has been used to screen individuals for PTSD, diagnose PTSD, and monitor symptom change during and after treatment. There are three versions of the PCL: PCL-M (military), PCL-C (civilian), and PCL-S (specific).	17 to 85	Decrease
PDS or PTDS	Posttraumatic Diagnostic Scale	49 item self-report measure of PTSD symptom severity related to a single identified traumatic event. Assesses all DSM-IV criteria (A-F) in the past	0 to 51	Decrease

Abbreviated Name	Complete Name	Description	Range/Meaning of Possible Scores	Improvement Indicated by
		month (time frame can be adjusted) using 4 sections: trauma checklist, description of traumatic event, assessment of 17 PTSD symptoms, and interference of symptoms. Total severity score reflecting frequency of 17 PTSD symptoms.		
PHSI-P	Post-Hospital Stress Index for Parents	A 20–item self-report questionnaire of symptoms based on DSM-IV PTSD criteria.	0 to 20	Decrease
PSS	PTSD Symptom Scale	17-item semi-structured interview or scale that assesses the presence and severity of DSM-IV PTSD symptoms related to a single identified traumatic event in individuals with a known trauma history. Each item is assessed with a brief, single question. There are two versions of the PSS: PSS-I (interview that asks about symptoms experienced in the past 2 weeks) and PSS-SR (self-report).	0 to 51	Decrease
PTSS-10	Posttraumatic Stress Symptom 10 Question Inventory	10-item self-report questionnaire that assesses the presence and intensity of post-traumatic stress symptoms based on the DSM-III. Patients rate the presence and severity of each symptom during the past 7 days.	10 to 70	Decrease
SI-PTSD	Structured Interview for PTSD	Assesses the 17 PTSD symptoms as well as survival and behavioral guilt. For each item, the interviewer assigns a severity rating that reflects both frequency and intensity. Responses can be used to make a determination about whether client's symptoms meet DSM criteria B, C, and D for PTSD	0 to 68	Decrease

Abbreviations: DSM-III-R= Diagnostic and Statistical Manual Criteria, third edition; DSM-IV= Diagnostic and Statistical Manual Criteria, fourth edition; ICD-10 = International Classification of Diseases, tenth revision; NA = not applicable; PTSD = posttraumatic stress disorder.

Appendix B. Literature Search Strategies

MEDLINE®:

Search	Query	Items found
	Search “Traumatizing”[tiab] OR “Traumatising”[tiab] OR “Trauma”[tiab] OR “Traumatic”[tiab] OR “Traumas”[tiab] OR “Traumatization”[tiab] OR “Traumatisation”[tiab] OR “Traumatized”[tiab] OR “Traumatised”[tiab] OR "peritraumatic"[tiab]	207835
	Search "Stress Disorders, Traumatic"[Mesh] OR "PTSD"[tiab] OR "post-traumatic stress disorders"[tiab] OR "post-traumatic stress disorder"[tiab] OR "posttraumatic stress disorders"[tiab] OR "posttraumatic stress disorder"[tiab]	21591
	Search "Social Problems/psychology"[Mesh]	39134
	Search "Life Change Events"[Mesh]	17145
	Search "Stress, Psychological"[Mesh]	77741
	Search "Wounds and Injuries/psychology"[Mesh]	12844
	Search "Disasters"[Mesh]	53875
	Search "survival/psychology"[Mesh]	367
	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	390089
	Search #9 Limits: Humans, English, All Adult: 19+ years	145273
	Search "Anesthetics, Dissociative"[Pharmacological Action] OR "Opiate Alkaloids"[Mesh] OR "Benzodiazepines"[MeSH] OR "Tranquilizing Agents"[Pharmacological Action] OR "Antipsychotic Agents"[Pharmacological Action] OR "Adrenergic Agents"[Pharmacological Action] OR "Anticonvulsants"[Pharmacological Action] OR "Monoamine Oxidase Inhibitors"[Pharmacological Action] OR "Antidepressive Agents"[Pharmacological Action] OR "Psychotropic Drugs"[Mesh]	691213
	Search #10 AND #11	4622
	Search "Psychotherapy"[Mesh] OR "Complementary Therapies"[Mesh] OR "Therapeutics/psychology"[Mesh] OR "Adaptation, Psychological"[Mesh] OR "Mental Health Services"[Mesh]	425466
	Search #10 AND #13	20742
	Search "prevention and control" [Subheading]	890704
	Search "prevention"[tiab] OR "prevent"[tiab] OR "preventive"[tiab] OR "preventative"[tiab]	567453
	Search "early intervention"[tiab]	7594
	Search "Emergency Treatment/psychology"[Mesh]	1043
	Search "Crisis Intervention"[Mesh]	4917
	Search "Resilience, Psychological"[Mesh]	667
	Search "Preventive Health Services"[MeSH]	373860
	Search "Preventive Medicine"[Mesh]	31385
	Search "immediate treatment"[tiab]	1682
	Search #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23	1517709
	Search (#12 OR #14) AND #24	5026
	Search "Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Single-Blind Method"[Mesh] OR "Double-Blind Method"[Mesh] OR "Random Allocation"[Mesh]	464580
	Search "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields]	52267
	Search "Comparative Study"[Publication Type] OR "comparative study" OR case control stud* OR "Case-Control Studies"[Mesh]	2006988
	Search ("review"[Publication Type] AND "systematic"[tiab]) OR "systematic review"[All Fields] OR ("review literature as topic"[MeSH AND "systematic"[tiab])	45060
	Search "Cohort Studies"[Mesh] OR “cohort effect”[MeSH Term] OR cohort*[tiab]	1210509
	Search #26 OR #27 OR #28 OR #29 OR #30	2970190
	Search #25 AND #31	1810
	Search "Stress Disorders, Post-Traumatic/prevention and control"[Mesh]	834
	Search #31 AND #33	158
	Search #34 Limits: Humans, English, All Adult: 19+ years	101
	Search #32 OR #35	1855

PILOTS Database Search:

PILOTS search done January 5, 2012 using the following search criteria; 188 unique results found.

DE="adults" and DE="prevention" and DE="ptsd"

English Only

Cochrane:

ID	Search	Hits
#1	"Traumatizing"[tiab] OR "Traumatising"[tiab] OR "Trauma"[tiab] OR "Traumatic"[tiab] OR "Traumas"[tiab] OR "Traumatization"[tiab] OR "Traumatisation"[tiab] OR "Traumatized"[tiab] OR "Traumatised"[tiab] OR "peritraumatic"[tiab]	9433
#2	"Stress Disorders, Traumatic"[Mesh] OR "PTSD"[tiab] OR "post-traumatic stress disorders"[tiab] OR "post-traumatic stress disorder"[tiab] OR "posttraumatic stress disorders"[tiab] OR "posttraumatic stress disorder"[tiab]	1218
#3	"Social Problems/psychology"[Mesh]	2
#4	"Life Change Events"[Mesh]	381
#5	"Stress, Psychological"[Mesh]	2934
#6	"Wounds and Injuries/psychology"[Mesh]	33
#7	"Disasters"[Mesh]	104
#8	"survival/psychology"[Mesh]	4
#9	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)	12820
#10	"Anesthetics, Dissociative"[Pharmacological Action] OR "Opiate Alkaloids"[Mesh] OR "Benzodiazepines"[MeSH] OR "Tranquilizing Agents"[Pharmacological Action] OR "Antipsychotic Agents"[Pharmacological Action] OR "Adrenergic Agents"[Pharmacological Action] OR "Anticonvulsants"[Pharmacological Action] OR "Monoamine Oxidase Inhibitors"[Pharmacological Action] OR "Antidepressive Agents"[Pharmacological Action] OR "Psychotropic Drugs"[Mesh]	13154
#11	(#1 AND #10)	269
#12	"Psychotherapy"[Mesh] OR "Complementary Therapies"[Mesh] OR "Therapeutics/psychology"[Mesh] OR "Adaptation, Psychological"[Mesh] OR "Mental Health Services"[Mesh]	10506
#13	(#1 AND #12)	572
#14	(#11 OR #13)	777
#15	"prevention"[tiab] OR "prevent"[tiab] OR "preventive"[tiab] OR "preventative"[tiab]	100796
#16	"early intervention"[tiab]	1157
#17	"Emergency Treatment/psychology"[Mesh]	2
#18	"Crisis Intervention"[Mesh]	263
#19	"Resilience, Psychological"[Mesh]	21
#20	"Preventive Health Services"[MeSH]	443
#21	"Preventive Medicine"[Mesh]	2727
#22	"immediate treatment"[tiab]	246
#23	(#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22)	101847
#24	(#14 AND #23)	266
#25	"Adult"[Mesh]	270874
#26	(#24 AND #25)	155
#27	(#26)	148

IPA, CINAHL, PsychINFO:

#	Query	Limiters/Expanders	Results
S11	S10	Limiters - English Language; Human; Language: English; Age Groups: All Adult; Language: English; Articles about Human Studies; English; Language: English; Age Groups: Adulthood (18 yrs & older), Young Adulthood (18-29 yrs), Thirties (30-39 yrs), Middle Age (40-64 yrs), Aged (65 yrs & older), Very Old (85 yrs & older); Population Group: Human; Exclude Dissertations Search modes - Boolean/Phrase	124
S10	S8 and S9	Search modes - Boolean/Phrase	456
S9	"prevention" OR (MH "Early Intervention+")	Search modes - Boolean/Phrase	516323
S8	S5 or S7	Search modes - Boolean/Phrase	2562
S7	S3 and S6	Search modes - Boolean/Phrase	1672
S6	DE "Drug Therapy"	Search modes - Boolean/Phrase	96635
S5	S3 and S4	Search modes - Boolean/Phrase	902
S4	DE "Psychotherapeutic Techniques" OR DE "Animal Assisted Therapy" OR DE "Autogenic Training" OR DE "Cotherapy" OR DE "Dream Analysis" OR DE "Ericksonian Psychotherapy" OR DE "Guided Imagery" OR DE "Mirroring" OR DE "Morita Therapy" OR DE "Motivational Interviewing" OR DE "Mutual Storytelling Technique" OR DE "Paradoxical Techniques" OR DE "Psychodrama"	Search modes - Boolean/Phrase	25870
S3	S1 or S2	Search modes - Boolean/Phrase	163590
S2	"Injuries" OR DE "Burns" OR DE "Electrical Injuries" OR DE "Head Injuries" OR DE "Spinal Cord Injuries" OR DE "Wounds"	Search modes - Boolean/Phrase	119613
S1	"Posttraumatic Stress Disorder" OR DE "Reactive Psychosis" OR DE "Stress Reactions" OR DE "Psychological Stress" OR DE "Acute Stress Disorder" OR DE "Emotional Trauma"	Search modes - Boolean/Phrase	45455

EMBASE:

No.	Query	Results
#1	'posttraumatic stress disorder'/exp	26,817
#2	'psychotherapy'/exp	174,672
#3	'drug therapy'/exp	1,526,816
#4	#2 OR #3	1,688,791
#5	#1 AND #4	5,638
#6	'prevention'/exp OR 'early intervention'/exp	934,844
#7	#5 AND #6	202
#8	'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'systematic review'/exp OR 'cohort analysis'/exp OR 'meta analysis'/exp OR 'comparative study'/exp OR 'case control study'/exp	1,448,799
#9	#7 AND #8	37

Web of Science:

Set	Results	Query
# 12	108	#11 AND #8 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 11	336,240	#10 OR #9 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 10	50,812	(TS=(early intervention)) AND Language=(English) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 9	291,955	(TS=(prevention)) AND Language=(English) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 8	1,418	#7 AND #4 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 7	54,820	#6 OR #5 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 6	15,172	TS=(pharmacotherapy) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 5	41,223	TS=(Psychotherapy) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 4	39,541	#3 OR #2 OR #1 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 3	12,815	TS=("post trauma*") Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 2	27,812	TS=(posttraumatic) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 1	11,784	TS=(PTSD) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On

Total references identified by the main searches, minus duplicates = 2364

Total references from main and handsearches, minus duplicates = 2438

The following update searches were conducted on July 30, 2012

MEDLINE®:

Search	Query	Items found
#1	Search “Traumatizing”[tiab] OR “Traumatising”[tiab] OR “Trauma”[tiab] OR “Traumatic”[tiab] OR “Traumas”[tiab] OR “Traumatization”[tiab] OR “Traumatisation”[tiab] OR “Traumatized”[tiab] OR “Traumatised”[tiab] OR "peritraumatic"[tiab]	215392
#2	Search "Stress Disorders, Traumatic"[Mesh] OR "PTSD"[tiab] OR "post-traumatic stress disorders"[tiab] OR "post-traumatic stress disorder"[tiab] OR "posttraumatic stress disorders"[tiab] OR "posttraumatic stress disorder"[tiab]	22750
#3	Search "Social Problems/psychology"[Mesh]	40575
#4	Search "Life Change Events"[Mesh]	17610
#5	Search "Stress, Psychological"[Mesh]	80886
#6	Search "Wounds and Injuries/psychology"[Mesh]	13375
#7	Search "Disasters"[Mesh]	55059
#8	Search "Survival/psychology"[Mesh]	379
#9	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8	403607
#10	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 Filters: Humans	342462
#11	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 Filters: Humans; English	278680
#12	Search #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 Filters: Humans; English; Adult: 19+ years	151076
#13	Search "Anesthetics, Dissociative"[Pharmacological Action] OR "Opiate Alkaloids"[Mesh] OR "Benzodiazepines"[MeSH] OR "Tranquilizing Agents"[Pharmacological Action] OR "Antipsychotic Agents"[Pharmacological Action] OR "Adrenergic Agents"[Pharmacological Action] OR "Anticonvulsants"[Pharmacological Action] OR "Monoamine Oxidase Inhibitors"[Pharmacological Action] OR "Antidepressive Agents"[Pharmacological Action] OR "Psychotropic Drugs"[Mesh]	701274
#14	Search #12 and #13	4732
#15	Search "Psychotherapy"[Mesh] OR "Complementary Therapies"[Mesh] OR "Therapeutics/psychology"[Mesh] OR "Adaptation, Psychological"[Mesh] OR "Mental Health Services"[Mesh]	438499
#16	Search #12 and #15	21625
#17	Search "prevention and control" [Subheading]	919536
#18	Search "prevention"[tiab] OR "prevent"[tiab] OR "preventive"[tiab] OR "preventative"[tiab]	591226
#19	Search "early intervention"[tiab]	8083
#20	Search "Emergency Treatment/psychology"[Mesh]	1083
#21	Search "Crisis Intervention"[Mesh]	4974
#22	Search "Resilience, Psychological"[Mesh]	850
#23	Search "Preventive Health Services"[MeSH]	385136
#24	Search "Preventive Medicine"[Mesh]	31611
#25	Search "immediate treatment"[tiab]	1745
#26	Search #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25	1570081
#27	Search (#14 OR #16) AND #26	5239
#28	Search "Randomized Controlled Trial"[Publication Type] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Single-Blind Method"[Mesh] OR "Double-Blind Method"[Mesh] OR "Random Allocation"[Mesh]	481850
#29	Search "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields]	57134
#30	Search "Comparative Study"[Publication Type] OR "comparative study" OR case control stud* OR "Case-Control Studies"[Mesh]	2059195
#31	Search ("review"[Publication Type] AND "systematic"[tiab]) OR "systematic review"[All Fields] OR ("review literature as topic"[MeSH AND "systematic"[tiab])	49778
#32	Search "Cohort Studies"[Mesh] OR “cohort effect”[MeSH Term] OR cohort*[tiab]	1264820
#33	Search #28 or #29 or #30 or #31 or #32	3065032
#34	Search #27 and #33	1914
#35	Search "Stress Disorders, Post-Traumatic/prevention and control"[Mesh]	870
#36	Search #33 and #35	170
#37	Search #33 and #35 Filters: Humans	167
#38	Search #33 and #35 Filters: Humans; English	163
#39	Search #33 and #35 Filters: Humans; English; Adult: 19+ years	108

Search	Query	Items found
#40	Search #34 OR #39	1962
#41	Search #40 AND (2011/12:2012/07[edat])	33

PILOTS:

PILOTS search limited to Date Range= 2011-2012 using the following search criteria; 40 unique results.

DE="adults" and DE="prevention" and DE="ptsd"

English Only

Cochrane Library:

ID	Search	Hits
#1	"Traumatizing"[tiab] OR "Traumatising"[tiab] OR "Trauma"[tiab] OR "Traumatic"[tiab] OR "Traumas"[tiab] OR "Traumatization"[tiab] OR "Traumatisation"[tiab] OR "Traumatized"[tiab] OR "Traumatised"[tiab] OR "peritraumatic"[tiab]	10124
#2	"Stress Disorders, Traumatic"[Mesh] OR "PTSD"[tiab] OR "post-traumatic stress disorders"[tiab] OR "post-traumatic stress disorder"[tiab] OR "posttraumatic stress disorders"[tiab] OR "posttraumatic stress disorder"[tiab]	1304
#3	"Social Problems/psychology"[Mesh]	2
#4	"Life Change Events"[Mesh]	392
#5	"Stress, Psychological"[Mesh]	3096
#6	"Wounds and Injuries/psychology"[Mesh]	34
#7	"Disasters"[Mesh]	113
#8	"Survival/psychology"[Mesh]	4
#9	(#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8)	13678
#10	"Anesthetics, Dissociative"[Pharmacological Action] OR "Opiate Alkaloids"[Mesh] OR "Benzodiazepines"[MeSH] OR "Tranquilizing Agents"[Pharmacological Action] OR "Antipsychotic Agents"[Pharmacological Action] OR "Adrenergic Agents"[Pharmacological Action] OR "Anticonvulsants"[Pharmacological Action] OR "Monoamine Oxidase Inhibitors"[Pharmacological Action] OR "Antidepressive Agents"[Pharmacological Action] OR "Psychotropic Drugs"[Mesh]	13673
#11	(#1 AND #10)	354
#12	"Psychotherapy"[Mesh] OR "Complementary Therapies"[Mesh] OR "Therapeutics/psychology"[Mesh] OR "Adaptation, Psychological"[Mesh] OR "Mental Health Services"[Mesh]	11130
#13	(#1 AND #12)	682
#14	(#11 OR #13)	939
#15	"prevention"[tiab] OR "prevent"[tiab] OR "preventive"[tiab] OR "preventative"[tiab]	105103
#16	"early intervention"[tiab]	1308
#17	"Emergency Treatment/psychology"[Mesh]	2
#18	"Crisis Intervention"[Mesh]	293
#19	"Resilience, Psychological"[Mesh]	25
#20	"Preventive Health Services"[MeSH]	462
#21	"Preventive Medicine"[Mesh]	2953
#22	"immediate treatment"[tiab]	276
#23	(#15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22)	106214
#24	(#14 AND #23)	392
#25	"Adult"[Mesh]	279877
#26	(#24 AND #25)	232
#27	(#26), from 2011 to 2012	70

IPA, CINAHL, PsycINFO:

Search ID#	Search Terms	Search Limits	Results
S1	"Posttraumatic Stress Disorder" OR DE "Reactive Psychosis" OR DE "Stress Reactions" OR DE "Psychological Stress" OR DE "Acute Stress Disorder" OR DE "Emotional Trauma"		47098
S2	"Injuries" OR DE "Burns" OR DE "Electrical Injuries" OR DE "Head Injuries" OR DE "Spinal Cord Injuries" OR DE "Wounds"		125584
S3	S1 or S2		171131
S4	DE "Psychotherapeutic Techniques" OR DE "Animal Assisted Therapy" OR DE "Autogenic Training" OR DE "Cotherapy" OR DE "Dream Analysis" OR DE "Ericksonian Psychotherapy" OR DE "Guided Imagery" OR DE "Mirroring" OR DE "Morita Therapy" OR DE "Motivational Interviewing" OR DE "Mutual Storytelling Technique" OR DE "Paradoxical Techniques" OR DE "Psychodrama"		26493
S5	S3 and S4		918
S6	DE "Drug Therapy"		100216
S7	S3 and S6		1748
S8	S5 or S7		2653
S9	"prevention" OR (MH "Early Intervention+")		539111
S10	S8 and S9		475
S11	S10	Limiters - English Language; Human; Language: English; Age Groups: Adult: 19-44 years, Middle Aged: 45-64 years, Aged: 65+ years, Aged, 80 and over, All Adult; Language: English; Articles about Human Studies; English; Language: English; Age Groups: Adulthood (18 yrs & older), Young Adulthood (18-29 yrs), Thirties (30-39 yrs), Middle Age (40-64 yrs), Aged (65 yrs & older), Very Old (85 yrs & older); Population Group: Human; Exclude Dissertations	132
S12	S11	Limiters - Published Date from: 20111201-20120731	5

Note: The number of available results reflects the removal of duplicates.

EMBASE:

No.	Query	Results
#1	'posttraumatic stress disorder'/exp	28,724
#2	'psychotherapy'/exp	180,063
#3	'drug therapy'/exp	1,606,636
#4	#2 OR #3	1,773,200
#5	#1 AND #4	6,041
#6	'prevention'/exp OR 'early intervention'/exp	976,054
#7	#5 AND #6	230
#8	'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'systematic review'/exp OR 'cohort analysis'/exp OR 'meta analysis'/exp OR 'comparative study'/exp OR 'case control study'/exp	1,516,832
#9	#7 AND #8	44
#10	#9 AND [1-12-2011]/sd NOT [30-7-2012]/sd	8

Web of Science:

Set	Results	Query
# 1	12,757	TS=(PTSD) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 2	29,614	TS=(posttraumatic) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 3	13,588	TS=("post trauma*") Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 4	42,065	#3 OR #2 OR #1 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 5	42,555	TS=(Psychotherapy) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 6	16,068	TS=(pharmacotherapy) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 7	56,975	#6 OR #5 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 8	1,546	#7 AND #4 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 9	308,926	(TS=(prevention)) AND Language=(English) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 10	54,447	(TS=(early intervention)) AND Language=(English) Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 11	356,307	#10 OR #9 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
# 12	118	#11 AND #8 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=All Years Lemmatization=On
#13	18	#12 Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=2011-2012 Lemmatization=On

Appendix C. Abstract and Full-Text Form Fields

The following are lists of fields used in the abstract and full-text review forms. Please see the Evidence Tables (Appendix E) for fields used in the data abstraction forms.

Table C1. Abstract review form fields

REF ID
Author
Year
Title
Abstract
Exclude (Select an option from the dropdown list)
Include
Background? (To suggest an abstract that would otherwise be excluded from the review for use as background information, mark it with BKG, along with EXC and the exclusion number/code. Use BKG judiciously!)
Comments: Please include a comment if you included an abstract, but did so do to a lack of clarity within the abstract. Explain why you think the FT will reveal that the study should be excluded.

Table C2. Full text review form fields

Ref ID
Authors
Year
Title
Inclusion/Exclusion Code
Should article be included as background? ('X')
Design
Subpopulations
Psychological Interventions ('X')
Pharmacological Interventions ('X')
CAM Interventions ('X')
Group 1 (Main treatment group)
Group 2 (First comparison group)
Group 3 (Second comparison group, if applicable)
Group 4 (Third comparison group, if applicable)
KQ 1 ('X')
KQ 2 ('X')
KQ 3 ('X')
KQ 4 ('X')
Comments
Does the study belong to a set of Companion Studies? (Yes/No)
Include citations of any Companion Studies here

Appendix D. Studies Excluded at the Full-Text Level

Excluded for Ineligible Publication Type

1. Andre C, Lelord F, Legeron P, et al. Effectiveness of early intervention on 132 bus drivers victims of aggressions: A controlled study. Encephale-Revue De Psychiatrie Clinique Biologique Et Therapeutique. 1997 Jan-Feb;23(1):65-71.
2. Cuijpers P, Van Straten A, Smit F. Preventing the incidence of new cases of mental disorders: a meta-analytic review. J Nerv Ment Dis. 2005 Feb;193(2):119-25. PMID: 15684914.
3. Donovan JM, Bennett MJ, McElroy CM. The crisis group--an outcome study. Am J Psychiatry. 1979 Jul;136(7):906-10. PMID: 453351.
4. Dreman S. Children of victims of terrorism in Israel: coping and adjustment in the face of trauma. Isr J Psychiatry Relat Sci. 1989;26(4):212-22. PMID: 2632457.
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Appendix E. Evidence Tables

Evidence Table 1. Characteristics of included trials

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Beatty, 2010[1] Australia	Randomized: 49 G1: 25 G2: 24 Analyzed: 49 G1: 25 G2: 24	RCT Outpatient, urban public hospitals 6 months	PSS-SR Baseline, 3 months, & 6 months	Academic
Bryant, 2008[2] Australia	Randomized: 90 G1: 30 G2: 30 G3: 30 ITT Analyzed: 90 G1: 30 G2: 30 G3: 30 Analyzed (Completers Analysis): 69 G1: 25 G2: 23 G3: 21	RCT Outpatient, special MH 6 months	CAPS-2, Baseline, 5 weeks, 6 months	Government
Bryant, 2003[3] Australia	Randomized: 24 G1: 12 G2: 12 Analyzed: 24 G1: 12 G2: 12	RCT Inpatient 6 months	CAPS-2 & IES Baseline, 1 week, & 6 months	Government
Bryant, 1998[4] * Australia *Study design changed from NRCT to RCT	Randomized: 24 G1: 12 G2: 12 Analyzed: 24 G1: 12 G2: 12	RCT Outpatient, special MH 6 months	IES Baseline CIDI PTSD & IES 6 weeks & 6 months	Government

Evidence Table 1. Characteristics of included trials (continued)

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Bryant, 2005[5] Australia	Randomized: 87 G1: 33 G2: 30 G3: 24 ITT Analyzed: 87 G1: 33 G2: 30 G3: 24 Analyzed (Completers Analysis): 69 G1: 24 G2: 23 G3: 22	RCT Outpatient, special MH 6 months	IES Baseline IES & CAPS-2 5 weeks, 6 months	Government
Campfield, 2001[6] Australia	Randomized: 77 G1: 36 G2: 41 Analyzed: 77 G1: 36 G2: 41	RCT Outpatient, special MH 2 weeks	PDS Debriefing, 2 days post debriefing, 4 days post-debriefing, 2 weeks post-trauma	NR
Gamble, 2005[7] Australia	Randomized: 103 G1: 50 G2: 53 Analyzed (Completers Analysis): 103 G1: 50 G2: 53	RCT Inpatient and Home 3 months	MINI-PTSD 4-6 weeks, 3 months	Foundation and academic
Melnyk, 2004[8] NA	Randomized: 174 G1: 90 G2: 84 ITT Analyzed: 174 G1: 90 G2: 84 Analyzed (Completers Analysis): 163 G1: 87 G2: 76	RCT Inpatient 12 months	Post-Hospital Stress Index for Parents (post treatment) 1 month, 3 months, 6 months, & 12 months	Government

Evidence Table 1. Characteristics of included trials (continued)

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Mulligan, 2012[9] United Kingdom	Randomized: 2523 G1: 1144 G2: 1379 Analyzed 4-6 month ITT: 2443 G1: 1108 G2: 1335 Analyzed 4-6 month completers analysis: G1: 797 G2: 819	RCT Outpatient, military 4-6 months	PCL-C Baseline, 4-6 months	NR
O'Donnell, 2012[10] Australia	Randomized: 46 G1: 24 G2: 22 Analyzed 6 & 12 month ITT: 46 G1: 24 G2: 22 Analyzed (6 month completers analysis): 42 G1: 22 G2: 20 Analyzed 12 month completers analysis): 31 G1: 19 G2: 12	RCT Outpatient, special MH 12 months	CAPS Baseline, 6 months, 12 months	Government and Foundation

Evidence Table 1. Characteristics of included trials (continued)

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Rose, 1999[11] United Kingdom	Randomized: 157 G1: 54 G2: 52 G3: 51 Analyzed (completers analysis): 92 G1: NR G2: NR G3: NR ITT Analyzed: 157 G1: 54 G2: 52 G3: 51	RCT Community 6 months [a]	PSS-SR & IES Baseline, 6 months[a]	Government
Rothbaum, 2012[12] United States	Randomized: 137 G1: 69 G2: 68 Analyzed 4 weeks ITT:[b] 137 G1: 69 G2: 68	RCT Inpatient and outpatient 4 weeks [b]	PDS & PSS-I Baseline, 4 weeks [b]	Government
Ryding, 2004[13] Sweden	Randomized:162 G1: 89 G2: 73 Analyzed: 147 G1: 82 G2: 65	RCT Inpatient 6 months	IES 6 months	Foundation/non-profit

Evidence Table 1. Characteristics of included trials (continued)

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Shalev, 2011[14] Israel	Randomized: 242 G1: 63 G2: 40 G3: 23 G4: 23 G5: 93 Analyzed: 180 G1: 52 G2: 35 G3: 19 G4: 17 G5: 57	RCT Outpatient, special MH 9 months	CAPS Baseline, 5 months, & 9 months	Foundation, Pharmaceutical, and Government
Sijbrandij, 2006[15] Netherlands	Randomized: 236 G1: 76 G2: 79 G3: 81 ITT Analyzed: 236 G1: 76 G2: 79 G3: 81	RCT Outpatient, special MH 6 Months	SI-PTSD Baseline, 2 weeks, 6 weeks, & 6 months	NR
Treggiari, 2009[16] Switzerland	Randomized: 137 G1: 69 G2: 68 Analyzed:129 G1: 65 G2: 64	RCT Inpatient 4 weeks	PCL & IES-R Baseline & 4 weeks	Foundation
Weis, 2006[17] Germany	Randomized: 36 G1: NR G2: NR Analyzed: 28 G1: 14 G2: 14	RCT Inpatient 6 months	PTSS-10 6 months	NR

Evidence Table 1. Characteristics of included trials (continued)

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Wong, Under review[18] United States	Randomized: 99 G1: 52 G2: 47 Analyzed 1 month completers analysis: 79 G1: 42 G2: 37	RCT Inpatient 1 month	PCL Baseline, 1 month	NR
Zatzick, In press[19] United States	Randomized: 207 G1: 104 G2: 103 Analyzed 1 month ITT: 207 G1: 104 G2: 103 Analyzed 1 month completers analysis: 176 G1: 86 G2: 90 Analyzed 3 months ITT: 207 G1: 104 G2: 103 Analyzed 3 months completers analysis: 164 G1: 81 G2: 83 Analyzed 6 months ITT: 207 G1: 104 G2: 103 Analyzed 6 months completers analysis: 162 G1: 86 G2: 76	RCT Inpatient and outpatient 12 months	CAPS & PCL-C Baseline, 1 month, 3 months, 6 months, 9 months, & 12 months	Government

Evidence Table 1. Characteristics of included trials (continued)

Author, Year Country	Group Sample Size	Study Design Study Setting Study Duration	Primary Outcome & Timing of Assessment	Funding Source
Zatzick, In press[19] (continued)	Analyzed 9 months ITT: 207 G1: 104 G2: 103 Analyzed 9 months completers analysis: 155 G1: 83 G2: 72 Analyzed 12 months ITT: 207 G1: 104 G2: 103 Analyzed 12 months completers analysis: 167 G1: 87 G2: 80			

[a] Followup was also conducted at 11 months, but we rated all 11-month outcomes as having a high risk of bias because of high overall attrition (>30%) at that timepoint and therefore do not report any of those outcomes.

[b] Followup was also conducted at 12 weeks, but we rated all 12-week outcomes as having a high risk of bias because of high overall attrition (>30%) at that timepoint and therefore do not report any of those outcomes.

Abbreviations: CAPS = Clinician Administered PTSD Scale; CAPS-2 = Clinician Administered PTSD Scale-2; CIDI PTSD = Composite International Diagnostic Interview PTSD module; G = group; IES = Impact of Event Scale; IES-R = Impact of Event Scale-Revised; ITT = intent-to-treat analysis; MH = mental health; MINI-PTSD = Mini-International Neuropsychiatric Interview-Post-Traumatic Stress Disorder Module; NA = not applicable; NR = not reported; NRCT = nonrandomized controlled trial; PCL = Posttraumatic Stress Disorder Checklist; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; PDS = Posttraumatic Stress Diagnostic Scale; PTSD = posttraumatic stress disorder; PSS-I = Posttraumatic Stress Scale-Interview version; PSS-SR = Posttraumatic Stress Scale-Self-Report version; PTSS-10 = Posttraumatic Stress Symptom 10 Question Inventory; RCT = randomized controlled trial; SI-PTSD = Structured Interview for PTSD

Evidence Table 2. Characteristics of samples from included trials

Author, Year	Population Trauma Type	Baseline PTSD	% Without PTSD Diagnosis	Mean Age (Age Range if reported)	% Female	% Nonwhite
Beatty, 2010[1]	Female Medical trauma	PSDS-SR, mean (SD) Overall: 10.76 (NR) G1: NR G2: NR	NR	NR	Overall: 55.2 G1: 56.0 G2: 54.5	Overall: 100 G1: 100 G2: 100
Bryant, 2008[2]	Male and Female Mixed: non-sexual assault or MVA	CAPS-2 total, mean (SD) Overall: 67.0[a] (NR) G1: 70.6 (17.7) G2: 66.8 (19.0) G3: 63.6 (18.3)	NR	Overall: 35.4[a] G1: 37.9 G2: 33.7 G3: 34.7	Overall: 57.7[a] G1: 63 G2: 60 G3: 50	Overall: 13.3[a] G1: 10 G2: 13 G3: 17
Bryant, 2003[3]	Male and Female Mixed: MVA or nonsexual assault	IES-intrusion (IES-I) and avoidance (IES-A) subscales, mean (SD) Overall: 26.16[a] (NR), 18.42[a] (NR) G1: 27.83 (5.31), 20.58 (5.02) G2: 24.50 (8.20), 16.25 (7.42)	NR	Overall: 31.21[a] G1: 29.42 G2: 33.0	Overall: 66.7 G1: 66.7 G2: 66.7	NR
Bryant, 1998[4]	Male and Female Mixed: MVA or industrial accidents	IES-I and IES-A, mean (SD) Overall: 24.62[a] (NR), 29.00[a] (NR) G1: 24.17 (7.45), 29.33 (12.23) G2: 25.08 (5.56), 28.67 (7.08)	NR	Overall: 32.62[a] G1: 32.25 G2: 33.00	Overall: 58.3 G1: 58.3 G2: 58.3	NR
Bryant, 2005[5]	Male and Female Mixed: Nonsexual assault or MVA	IES-I and IES-A, mean (SD) Overall: 25.48[a] (NR), 21.98[a] (NR) G1: 24.73 (8.06), 24.43 (9.49) G2: 27.12 (7.46), 21.58 (9.66) G3: 24.58 (8.21), 19.92 (9.79)	NR	Overall: 33.69[a] G1: 33.09 G2: 32.97 G3: 35.00	Overall: 60.9 G1: NR G2: NR G3: NR	NR
Campfield, 2001[6]	Male and Female Interpersonal violence	NR	NR	Overall: 22.82(18-32) G1: 22.61 G2: 23.02	Overall: 54.5 G1: 52.8 G2: 56.1	NR

Evidence Table 2. Characteristics of samples from included trials (continued)

Author, Year	Population Trauma Type	Baseline PTSD	% Without PTSD Diagnosis	Mean Age (Age Range if reported)	% Female	% Nonwhite
Gamble, 2005[7]	Female Traumatic birth	NR	NR	Overall: 28 (18-46) G1: NR G2: NR	Overall: 100	Caucasian/ European G1: 96 G2: 90.6 Aboriginal/ Torres Strait Islander NR Asian G1: NR G2: 1.9 Other G1: NR G2: 5.7
Melnyk, 2004[8]	Female Medical trauma - other (Child hospitalized with PICU admission)	NR	NR	Overall: 31.2 G1: 32.0 G2: 30.1	Overall: 100	Overall: 28.8 G1: 25.3 G2: 32.9
Mulligan, 2012[9]	Male and Female Combat	PCL-C, full study sample, median (IQR): Overall: 20.5[a] (NR) G1: 21 (18-26) G2: 20 (17-26)	Overall: 97.6[a] G1: 97.1 G2: 98	Overall: 44% sample < 25; 95% < 40 G1: NR G2: NR	Overall: 1.7[a] G1: 1.1 G2: 2.2	NR
O'Donnell, 2012[10]	Male and Female Injury	CAPS total score, mean (SD): Overall: 58.67[a] (NR) G1: 56.61 (NR) G2: 60.73 (NR)	Overall: 28 G1: 33 G2: 23	Overall: 35.9[a] G1: 34.67 G2: 37.14	Overall: 39.1[a] G1: 50 G2: 28	NR
Rose, 1999[11]	Male and Female Assault	PSS, IES, mean (SD) Overall: 16.1[a] (NR), 26.9[a] (NR) G1: 16.8 (13.9), 28.5 (18.4) G2: 16.0 (13.2), 24.2 (19.0) G3: 15.6 (12.6), 28.0 (19.3)	NR	Overall: 35.9[a] (18-76) G1: 35.4 G2: 34.9 G3: 37.3	Overall: 24.8[a] G1: 31.5 G2: 25.0 G3: 17.6	NR

Evidence Table 2. Characteristics of samples from included trials (continued)

Author, Year	Population Trauma Type	Baseline PTSD	% Without PTSD Diagnosis	Mean Age (Age Range if reported)	% Female	% Nonwhite
Rothbaum, 2012[12]	Male and Female Rape, nonsexual assault, MVA, other (unspecified)	PDS score, mean (SE) Overall: 19.18 [a] (NR) G1: 18.90 (1.80) G2: 19.46 (1.78) No baseline PSS-I data available	NR	Overall: 31.48 [a] G1: 30.17 (12.08) G2: 32.78 (11.12)	Overall: 65 [a] G1: 63.8 G2: 66.2	Black Overall: 78.8 [a] G1: 81.2 G2: 76.5 Native American Overall: 2.9 [a] G1: 2.9 G2: 0 Other Overall: 6.6 [a] G1: 8.7 G2: 4.4
Ryding, 2004[13]	Female Emergency c-section	NR	NR	Overall: 32 G1: 32 G2: 32	Overall: 100	NR
Shalev, 2011[14]	Male and Female Mixed: MVA (83%), terrorist attack (11%), other (6%)	CAPS total, mean (SD) Overall: 74.35 [a] (SD) G1: 73.59 (21.34) G2: 71.78 (15.18) G3: 79.83 (15.60) G4: 74.91 (14.69) G5: 71.66 (15.22)	100	Overall: 38.6 [a] G1: 40.1 G2: 39.54 G3: 39.83 G4: 36.26 G5: 37.28	Overall: 52.1 G1: 44.4 G2: 75.0 G3: 56.5 G4: 43.5 G5: 58.1	NR
Sijbrandij, 2006[15]	Male and Female Mixed	SI-PTSD, mean (SD) Overall: 19.17 [a] (NR) G1: 19.9 (NR) G2: 19.9 (NR) G3: 17.7 (NR)	100	Overall: 40.4 [a] G1: 41.7 G2: 38.3 G3: 41.2	Overall: 48.7[a] G1: 47.4 G2: 54.4 G3: 44.4	NR
Treggiari, 2009[16]	Male and Female ICU ventilation	NR	NR	Overall: 61.4 [a] G1: 63.0 G2: 59.8	Overall: 23.5[a] G1: 25 G2: 22	Overall: 2.5 G1: 2 G2: 3
Weis, 2006[17]	Male and Female Cardiac surgery	NR	NR	Overall: 68.5 [a] G1: 68 G2: 69	Overall: 32.1[a] G1: 28.6 G2: 35.7	NR

Evidence Table 2. Characteristics of samples from included trials (continued)

Author, Year	Population Trauma Type	Baseline PTSD	% Without PTSD Diagnosis	Mean Age (Age Range if reported)	% Female	% Nonwhite
Wong, Under review[18]	Male and Female Injury	NR	% without probable PTSD G1: 86.5 G2: 91.5 Between-groups p=.53	Overall: 31 G1: 28.8 (9.05) G2: 33.7 (12.3) Between-groups p=.03[b]	Overall: 16 G1: 17.3 G2: 14.9	African American Overall: 12.1[a] G1: 13.5 G2: 10.6 Asian American Overall: 9.8[a] G1: 15.4 G2: 4.3 Hispanic Overall: 59 G1: 55.8 G2: 61.7 Other Overall: 3.0[a] G1: 3.9 G2: 2.1

Evidence Table 2. Characteristics of samples from included trials (continued)

Author, Year	Population Trauma Type	Baseline PTSD	% Without PTSD Diagnosis	Mean Age (Age Range if reported)	% Female	% Nonwhite
Zatzick, In press[19]	Male and Female Injury	PCL-C total score, mean (SD) Overall: 50.6 (10.5) G1: 50.5 (10.5) G2: 50.8 (10.5) N (%) with pre-injury PTSD symptoms Overall: 130 (62.8) G1: 66 (63.5) G2: 64 (62.1)	NR	Overall: 38.5 (13.1) G1: 39.4 (13.4) G2: 37.7 (12.8)	Overall: 47.8 G1: 51.9 G2: 43.7	Black Overall: 18.4 G1: 20.2 G2: 16.5 American Indian Overall: 13.0 G1: 13.4 G2: 12.6 Asian Overall: 5.8 G1: 3.9 G2: 7.8 Hispanic Overall: 2.9 G1: 1.9 G2: 3.9

[a] Data not directly provided by the study authors. Data provided here are calculated by authors of this report.

[b] The study authors state that no differences between groups were significant at baseline, although the p value suggests a statistically significant difference in age.

Abbreviations: C-section = Cesarean section; CAPS = Clinician Administered PTSD Scale; CAPS-2 = Clinician Administered PTSD Scale-2; G = group; ICU = intensive care unit; IES = Impact of Event Scale; IES-R = Impact of Event Scale-Revised; IQR = interquartile range; MVA = motor vehicle accident(s); N = number of participants; NR = not reported; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; PDS = Posttraumatic Stress Diagnostic Scale; PICU = pediatric intensive care unit; PSS-I = Posttraumatic Stress Scale-Interview version; PSS-SR = Posttraumatic Stress Scale-Self-Report version; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SD = standard deviation; SI-PTSD = Structured Interview for PTSD

Evidence Table 3. Treatment and control arms from included trials

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Beatty, 2010[1] Active vs. inactive	Self-help workbook with suggestions, worksheets, and CD Self-help Workbook to be read over a 3-month period	"Information control" group (see Comments) Self-help Workbook to be read over a 3-month period	NA	NA	NA	Unclear NA	G2 group: Received same workbook as G1 but without suggestions, worksheets or CD
Bryant, 2008[2] Head-to-head trial	Prolonged exposure therapy (PE) (mixed imaginal and in vivo) Face-to-face (F2F) individual Five weekly 90-min sessions	Cognitive therapy (CT) / cognitive restructuring F2F individual Five weekly 90-min sessions	Waitlist NA Assessment at baseline and at 6 weeks	NA	NA	No NA	
Bryant, 2003[3] Head-to-head trial	CBT-mixed (see components in Comments) F2F individual Five 90-min sessions once a week	Supportive control F2F individual Five 90-min sessions once a week	NA	NA	NA	No NA	G1 CBT components: Education about trauma reactions, progressive muscle relaxation traning, imaginal exposure, cognitive restructuring, graded in vivo exposure. G2 Supportive control components: Educational, general problem-solving skills.

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Bryant, 1998[4] Head-to-head trial	CBT-mixed (see components in Comments) F2F individual Five 90-min sessions with clinical psychologist, once per week	Supportive control F2F individual Five 90-min sessions with clinical psychologist, once per week	NA	NA	NA	No NA	G1 CBT components: Education about trauma reactions, muscle relaxation training, imaginal exposure, cognitive restructuring of fear-related beliefs, and graded in vivo exposure G2 Supportive control components: provider offered unconditional supportive role and education about trauma including homework.
Bryant, 2005[5] Head-to-head trial	CBT-mixed (see components in Comments) F2F individual Five once-weekly 90-min sessions	CBT-mixed combined with hypnosis (see components in Comments) F2F individual Five once-weekly 90-min sessions	Supportive control F2F individual Five once-weekly 90-min sessions	NA	NA	NA	G1 CBT components: Education about trauma reactions, breathing control, imaginal exposure, cognitive restructuring, graded in vivo exposure, relapse-prevention strategies. G2 CBT+Hypnosis components: Identical to G1 CBT except that hypnotic induction used prior to each imaginal exposure exercise.
Campfield, 2001[6] Head-to-head trial	Psychological debriefing F2F individual and group One 1-2 hr debriefing within 10 hrs of robbery	Psychological debriefing F2F individual and group One 1-2 hr debriefing after 48 hrs of robbery	NA	NA	NA	NA	

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Gamble, 2005[7] Active vs. inactive	Supportive counseling incorporated CISD elements and issues relevant to childbearing context Multiple (F2F and phone) (see Comments) Two sessions lasting 40-60 mins total	Usual care Other (see Comments) Standard postnatal care	NA	NA	NA	Unclear NA	G1: F2F component delivered by a research midwife. G2: No other data provided.
Melnyk, 2004[8] Active vs. inactive	Psychoeducation (see Comments) Self-help Three sessions (6-16 hrs after PICU admission; 2-6 hrs after transfer to general pediatric unit; 2-3 days after children discharged)	Inactive control (see Comments) Self-help Three sessions (6-16 hrs after PICU admission; 2-6 hrs after transfer to general pediatric unit; 2-3 days after children discharged)	NA	NA	NA	No NA	G1 intevention: COPE program, which was an education-behavioral intervention program delivered by audiotapes and matching written information followed by 2 booster sessions that introduced a workbook with parent-child activities designed to enhance child coping. G2: Also received audiotaped information and a workbook, but both were non-specific.

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Were Cointerventions Allowed? If Yes, Describe	Comments
Mulligan, 2012[9] Head-to-head trial	Battlemind training (see Comments) F2F group Single session of 45 min	Standard post-deployment brief (see Comments) F2F group Single session of 35 min	NA	NA	NA	Unclear NA	G1 received Anglicized postdeployment Battlemind training. G2 received a standard postdeployment stress and homecoming brief.
O'Donnell, 2012[10] Active vs. inactive	CBT-mixed (see Comments) F2F individual 4-10 sessions of 90 min (Note: >4 sessions provided if HADS scores were 11 or greater after 4th session)	Usual care NA Varied but NR	NA	NA	Unclear NR	Unclear NA	G1 CBT was conducted by masters-level clinical psychologists. Treatment was manualized, evidence-based, and specifically tailored to the clinical symptom-cluster profile of each patient and involved structured homework activities.
Rose, 1999[11] Head-to-head trial; active vs. inactive	Psychological debriefing F2F individual Single 1 hr debriefing session within 30 days of assault	Psychoeducation F2F individual Single 30 min educational session with leaflet within 30 days of assault	No intervention NA NA	NA	NA	No NA	Co-intervention allowed after 6-month outcome measurement, so NR here.
Rothbaum, 2012[12] Active vs. inactive	Modified PE (see Comments for components) F2F individual Three 1 hr sessions distributed about 1 week apart	Assessment only NA	NA	NA	NA	Unclear NA	Modified PE components: imaginal exposure, identification of behavioral exposures, brief psychoeducation, breathing retraining, and homework assignments

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Ryding, 2004[13] Active vs. inactive	Supportive counseling (see Comments) F2F group Two 2-hour sesssions at 1-2 months post-partum	Usual care (see Comments) NA NA	NA	NA	NA	Unclear NA	G1 Supportive counseling components: Focused on personal storytelling in unstructured sessions G2 usual care: Midwife's and doctor's standard procedure of visiting mother in maternity ward to exchange information about the birthing experience (Note: not all patients in the usual care group received it)
Shalev, 2011[14] Head-to-head trial; Active vs. inactive	PE (see components in Comments) F2F individual 12 weekly 90-min sessions	CT F2F individual 12 weekly 90-min sessions	Escitalopram NA Initial dose of 10 mg daily was increased to 20 mg (10 mg twice daily) after 2 weeks of treatment. Trained psychiatrists provided 4 weekly sessions (weeks 1-4) followed by 4 biweekly sessions (weeks 6-12).	Placebo NA Initial dose of 1 tablet daily was increased to 2 daily tablets after 2 weeks of treatment. Trained psychiatrists provided 4 weekly sessions (weeks 1-4) followed by 4 biweekly sessions (weeks 6-12) (see Comments)	Waitlist NA NA	Unclear NA	G1 PE components: Psychoeducation, training in breathing control, prolonged imaginal exposure and in vivo exposure (Note: concealment was broken at the end of the study, and 8 participants with PTSD who received placebo were invited to receive PE, which was accepted by 5 of them.)

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Sijbrandij, 2006[15] Head-to-head trial; active vs. inactive	Psychological debriefing F2F individual Single 45-60 min session	Psychological debriefing F2F individual Single 45-60 min session	No intervention NA NA	NA	Unclear NA NA	Unclear NA	
Treggiari, 2009[16] Head-to-head trial	Light pharmacological sedation NA Light sedation group targeting a Ramsay level of 1-2 by giving intermittant injection of midazolam	Deep pharmacological sedation NA Deep sedation group targeting Ramsay level of 3-4 by giving continuous infusion of midazolam	NA	NA	NA	Unclear NA	

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Weis, 2006[17]	Hydrocortisone	Placebo	NA	NA	NA	No	
Active vs. inactive	NA	NA				NA	
	Started with loading dose of 100 mg over 10 min IV before anesthesia, followed by continuous infusion of 10 mg/hr for 24 hrs which was reduced to 5 mg/hr on day 2 and then 3x20mg IV on day 3 and 3x10mg IV on day 4	NA					

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Wong, Under review[18] Active vs. inactive	Psychoeducation Other (see Comments) Single 18-min viewing session	Wound care education Other (see Comments) Single 10-min viewing session	NA	NA	NA	Unclear NA	Psychoeducation was provided using a video viewing session and included information about traumatic event causes/identity, consequences, controllability, and timeline regarding when to seek treatment. Wound care education included information about medical treatment for lacerations, the healing process, and home care.

Evidence Table 3. Treatment and control arms from included trials (continued)

Author, Year Comparison Type	Group 1 Mode Duration and Number of Treatments/ Dose and Frequency	Group 2 Mode Duration and Number of Treatments/ Dose and Frequency	Group 3 Mode Duration and Number of Treatments/ Dose and Frequency	Group 4 Mode Duration and Number of Treatments/ Dose and Frequency	Group 5 Mode Duration and Number of Treatments/ Dose and Frequency	Cointerventions Allowed If Yes, Describe	Comments
Zatzick, In press[19] Active vs. inactive	Collaborative care (see Comments) Other (see Comments) Care managers: median (IQR) of 13.2 (13.3) hours with each patient	Usual care (see Comments) Other (see Comments) NR	NA	NA	NA	Unclear NA	G1 received a stepped collaborative care intervention from a trauma center-based mental health team. The main components were delivered F2F and by phone, including care management and evidence-based pharmacotherapy and CBT. G2 received usual care, which the authors describe as routine outpatient surgical and primary care visits, as well as occasional specialty mental health service usage.

Abbreviations: CBT = cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; CD = compact disc; CISD = Critical incident stress debriefing; COPE = Creating Opportunities for Parent Empowerment; CT = Cognitive therapy; F2F = face-to-face; G = group; HADS = Hospital Anxiety and Depression Rating Scale; hr = hour; IQR = interquartile range; IV = intravenous; mg = milligrams; min(s) = minute(s); N = number of participants; NA = not applicable; NR = not reported; NS = not significant; PE = prolonged exposure therapy; PICU = pediatric intensive care unit; PTSD = posttraumatic stress disorder

Evidence Table 4. PTSD incidence and symptom severity scale outcomes

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Beatty, 2010[1]	NA	**PSDS-SR** Mean (SE) @ 3 months G1: 5.43 (0.91) G2: 9.46 (0.98) p=.01 @ 6 months G1: 6.78 (1.07) G2: 8.98 (1.10) p=NS	NR	Only overall baseline PSDS-SR provided so unable to calculate mean change.
Bryant, 2008[2]	**CAPS-2 total score** Mean (SD) - ITT sample @ Baseline G1: 70.6 (17.7) G2: 68.8 (19.0) G3: 63.6 (18.3) @ Post-treatment (6 weeks) G1: 31.5 (27.3) G2: 43.0 (27.6) G3: 55.9 (23.1) G1<G3, p <.001 G2<G3, p=NS @ 6 months Follow-up G1: 32.1 (29.1) G2: 49.8 (29.4) G3: NA G1<G2, p=.03	**IES-Intrusion and Avoidance subscales** Mean (SD) - ITT sample @ Baseline G1: 26.9 (8.5), 26.9 (9.3) G2: 26.3 (8.2), 23.6 (9.9) G3: 23.5 (9.1), 24.0 (8.7) @ Post-treatment (6 weeks) G1: 12.4 (12.5), 11.7 (12.4) G2: 17.7 (11.3), 17.1 (12.4) G3: 22.1 (9.8), 22.6 (10.8) Intrusion: G1<G3, p=.001, G2 vs. G3, p=NS Avoidance: G1<G3, p <.001, G2 vs. G3, p=NS @ 6 months Follow-up G1: 11.4 (11.2), 12.8 (13.5) G2: 18.6 (11.4),19.2 (12.0) G3: NA, NA Intrusion: G1<G2, p=.02 Avoidance: G1<G2, p=.03	**CAPS-2** Patients meeting PTSD criteria, N (%) - ITT sample @ Post-treatment (6 weeks) G1: 10 (33%) G2: 19 (63%) G3: 23 (77%) G1 vs. G2: OR (95% CI): 2.52 (1.28 to 4.93), p=.002 G1 vs. G3: OR (95% CI): 3.40 (1.73 to 6.67), p <.001 @ 6 months Follow-up G1: 11 (37%) G2: 19 (63%) G3: NA G1 vs. G2: OR (95% CI): 2.10 (1.12 to 3.94), p=.007 NNT=3.75	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Bryant, 2008[2] (continued)	**CAPS-2 score** Mean (SD) - Completers analysis results Baseline G1: 71.4 (18.0) (N=25) G2: 66.9 (17.8) (N=23) G3: 61.3 (18.2) (N=21) @ Post-treatment (6 weeks) G1: 24.4 (23.1) G2: 35.8 (24.7) G3: 50.1 (22.9) G1<G3, p<.001; G2<G3, p=.03 @ 6 months Follow-up G1: 21.4 (24.1) G2: 44.3 (28.5) G3: NA	**IES-Intrusion and Avoidance subscales** Mean (SD) - Completers analysis results Baseline G1: 26.2 (9.0), 26.6 (10.1) G2: 26.8 (8.0), 23.4 (10.6) G3: 22.7 (9.8), 23.2 (10.1) @ Post-treatment (6 weeks) G1: 8.8 (10.3), 8.4 (10.5) G2: 15.2 (10.8), 14.6 (12.6) G3: 20.7 (10.6), 21.0 (12.4) Post hoc Tukey comparisons: G1<G3, p <.002 (Intrusion); p <.001 (Avoidance) G1<G2, p=.03 (Intrusion) G2<G3, p=NS (Intrusion); p=NS (Avoidance) @ 6 months Follow-up G1: 6.9 (7.4), 7.6 (7.7) G2: 15.0 (10.7),16.3 (10.8) G3: NA, NA Post hoc Tukey comparisons: G1<G2, p=.007 (Intrusion); p=.009 (Avoidance)	NA	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Bryant, 2003[3]	**CAPS-2, Frequency and Intensity subscales** Mean (SD) @ Post-treatment (within 1 week) G1: 13.50 (10.24), 12.00 (9.71) G2: 23.83 (15.30), 21.33 (12.49) p=.002 (Frequency); p=.003 (Intensity) @ 6 month Follow-up G1: 16.83 (13.04), 14.62 (9.12) G2: 25.25 (16.21), 24.50 (13.13) p=.03 (Frequency); p=.02 (Intensity)	**IES-Intrusion and Avoidance subscales** mean (SD) @ Post-treatment (within 1 week) G1: 10.17 (10.96), 4.08 (4.60) G2: 19.00 (8.25), 16.75 (9.97) p=.006; p=.001 @ 6 month Follow-up G1: 11.25 (9.81), 7.33 (7.22) G2: 20.17 (9.70), 15.67 (10.49) p=.02 (Intrusion); p=.005 (Avoidance)	**CAPS-2** Met criteria for PTSD, N (%) @ Post-treatment (within 1 week) G1: 1 (8%) G2: 7 (58%) p <.05 Effect size=1.16 @ 6 month Follow-up G1: 2 (17%) G2: 7 (58%) p <.05 Effect size=0.87	
Bryant, 1998[4]	NA	**IES-Intrusion and Avoidance subscales** mean (SD) @ Baseline G1: 24.17 (7.45), 29.33 (12.23) G2: 25.08 (5.56), 28.67 (7.08) @ Post-treatment (mean of 41.5 days) G1: 7.33 (7.69), 8.17 (8.54) G2: 15.83 (5.76), 24.17 (8.42) @ 6 month Follow-up G1: 8.58 (8.70), 7.08 (9.20) G2: 17.92 (8.98), 19.33 (9.48)	**CIDI-PTSD** N (%) of participants with PTSD @ Post-treatment (mean of 41.5 days) G1: 1 (8%) G2: 10 (83%) p <.01 @ 6 month Follow-up G1: 2 (17%) G2: 8 (67%)	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Bryant, 2005[5]	**CAPS-2 Intensity and Frequency subscales** NOTE: All CAPS-2 outcomes are from completers analysis because the scale was only administered at posttreatment and follow-up timepoints CAPS-2 Intensity, mean (SD) @ Posttreatment G1: 10.88 (8.27) G2: 10.83 (10.16) G3: 21.36 (11.28) Between-groups p <.001 G1<G3, p <.002 G2<G3, p <.005 @ 6-month Follow-up G1: 13.08 (11.08) G2: 14.09 (11.52) G3: 21.18 (11.85) Between-groups p <.05 G1<G3, p <.05 G2<G3, p <.05	**IES-Intrusion and Avoidance subscales** ITT results Mean (SD) @ Baseline G1: 27.12 (7.46), 21.58 (9.66) G2: 24.73 (8.06), 24.43 (9.49) G3: 24.58 (8.21), 19.92 (9.79) Between-groups p=NS (Intrusion); p=NS (Avoidance) @ Posttreatment G1: 16.58 (12.50), 11.06 (12.23) G2: 11.30 (9.98), 15.03 (13.36) G3: 19.83 (9.71), 18.54 (11.06) Between-groups p <.005; p=NS @ 6-month Follow-up G1: 16.97 (11.80), 14.30 (12.80) G2: 13.57 (9.52), 16.30 (12.68) G3: 20.21 (9.96), 18.04 (11.30) Between-groups p <.005 (Intrusion); p <.05 (Avoidance) Post hoc Tukey comparisons: G2<G3, p <.05; NR	**CAPS-2** ITT results (% with PTSD) @ Posttreatment G1: 36% G2: 30% G3: 50% Between-groups p=NS @ 6-month Follow-up G1: 42% G2: 40% G3: 58% Between-groups p=NS	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Bryant, 2005[5] (continued)	CAPS-2 Frequency, mean (SD) @ Posttreatment G1: 12.08 (9.41) G2: 12.35 (11.86) G3: 23.59 (13.29) Between-groups p <.001 G1<G3, p <.005 G2<G3, p <.01 @ 6-month Follow-up G1: 15.42 (13.61) G2: 14.83 (13.22) G3: 23.23 (14.64) Between-groups p= <.05 G1<G3, p=NS G2<G3, p <.05	Completers analysis results **IES-Intrusion and Avoidance subscales** Mean (SD) @ Baseline G1: 27.12 (7.46), 21.58 (9.66) G2: 24.73 (8.06), 24.43 (9.49) G3: 24.58 (8.21), 19.92 (9.79) Between-groups p=NS; p=NS @ Posttreatment G1: 16.58 (12.50), 11.06 (12.23) G2: 11.30 (9.98), 15.03 (13.36) G3: 19.83 (9.71), 18.54 (11.06) Between-groups p<.001, <.001 Post hoc Tukey comparisons: G1<G3, p <.05; p <.001 G2<G3, p <.001; p <.05 @ 6-month Follow-up G1: 16.97 (11.80), 14.30 (12.80) G2: 13.57 (9.52), 16.30 (12.68) G3: 20.21 (9.96), 18.04 (11.30) Between-groups p <.05, <.05 Post hoc Tukey comparisons: G1<G3, p <.05; p <.05 G2<G3, p <.05; p <.05	Completers analysis results @ Posttreatment (% with PTSD) G1: 13% G2: 9% G3: 46% Between-groups p values: G1<G3, p<.05 G2<G3, p<.005 @ 6-month Follow-up G1: 21% G2: 22% G3: 59% Between-groups p values: G1<G3, p<.01 G2<G3, p<.01	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Bryant, 1999[20]	**CAPS-2, Frequency and Intensity subscales** Mean (SD) @ Post-treatment G1: 13.69 (10.93), 12.00 (10.31) G2: 11.31 (10.73), 9.92 (9.00) G3: 22.60 (11.26), 20.53 (10.72) p=NR @ 6 month follow-up (NOTE: all follow-up outcomes used a smaller N of 41, not 45) G1: 14.62 (13.72), 15.00 (13.68) G2: 12.62 (13.63), 12.23 (11.77) G3: 26.47 (8.40), 29.00 (9.91) p=NR Group main effect: p <.05 (Frequency), p <.001 (Intensity) Specific group differences (Frequency) G3>G2, p <.01 G3>G1, p <.01 Specific group differences (Intensity) G3>G2, p <.001 G3>G1, p <.01	**IES, Intrusion and Avoidance subscales** Mean (SD) @ Pretreatment G1: 28.46 (5.59), 26.46 (6.54) G2: 27.62 (6.08), 26.46 (9.02) G3: 26.47 (4.69), 22.73 (5.57) p=NR @ Post-treatment G1: 13.15 (15.81), 10.31 (10.54) G2: 8.54 (8.64), 7.92 (8.20) G3: 22.80 (9.17), 21.33 (6.23) p=NR @ 6 month follow-up (NOTE: all follow-up outcomes used a smaller N of 41, not 45) G1: 10.31 (10.00), 8.54 (10.20) G2: 11.08 (8.86), 8.38 (10.32) G3: 15.67 (6.34), 20.13 (4.66) p=NR Group-by-time: p <.001 (Intrusion), p <.05 (Avoidance) Specific group-by-time differences (Intrusion) G3>G2 at T2, p <.001 Specific group-by-time differences (Avoidance) G3>G2 at T3, p <.001 G3>G1 at T3, p <.01	**CAPS-2** Met criteria for PTSD, N (%) @ Post-treatment G1: 3 (20%) G2: 2 (14%) G3: 9 (56%) p <.05 Specific between-group differences G3>G2, p=.02 G3>G1, p <.05 @ 6 month follow-up (NOTE: all follow-up outcomes used a smaller N of 41, not 45) G1: 3 (23%) G2: 2 (15%) G3: 10 (67%) p <0.01 Specific between-group differences G3>G2, p <.01 G3>G1, p <.05	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Campfield, 2001[6]	NA	**PDS** Number of symptoms (SD); symptom severity, mean (SD) @ Baseline (debriefing session) G1: 13.78 (1.82); 37.81 (7.71) G2: 15.29 (2.79); 41.39 (11.68) p <.01 (Number); p >.05 (Symptom severity) @ 2 days post-debriefing G1: 12.53 (2.38), 22.39 (9.26) G2: 15.00 (2.82), 37.51 (10.87) p <.001 (Number); p <.001 (Symptom severity) @ 4 days post-debriefing G1: 9.69 (3.64); 14.81 (9.11) G2: 14.78 (3.08); 35.76 (10.92) p <.001 (Number); p <.001 (Symptom severity) @ 2 weeks post-robbery G1: 5.56 (3.48), 6.94 (8.14) G2: 14.34 (3.58), 33.10 (11.59) p <.001 (Number); p <.001 (Symptom severity)	NA	PDS completed by participants after debriefing session in presense of 1st author; PDS administered via telephone for 2 and 4 days post-debriefing and 2 weeks post-robbery
Gamble, 2005[7]	NA	NA	**MINI-PTSD** N achieving PTSD diagnosis @ 4-6 weeks postpartum (N=102) G1: 17 G2: 16 RR (95% CI)=1.15 (0.66 to 2.02); p=.392 @ 3 months (N=103) G1: 3 G2: 9 RR (95% CI)=0.35 (0.10 to 1.23); p=.075	**MINI-PTSD** Trauma symptoms, Mean, SD) @ 4-6 weeks postpartum (N=102) G1: 4.81 (3.65) G2: 5.45 (3.01) Mean difference (95% CI): 0.67 (-0.68 to 1.957) p=NS @ 3 months (N=103) G1: 2.54 (2.44) G2: 3.83 (3.59) Mean difference (95% CI): -1.29 (-2.5 to -0.08)

				p=.035

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Melnyk, 2004[8]	NA	**Maternal PTSD Symptoms Post-hospitalization Stress Index - Parent** Mean (SD) @ 1 month G1: 7.3 (4.2) G2: 7.1 (4.3) @ 3 months post-discharge G1: 6.4 (4.3) G2: 7.4 (4.9) @ 6 months post-discharge G1: 5.6 (4.0) G2: 7.4 (5.7) @ 12 months post-discharge G1: 5.8 (3.8) G2: 7.8 (5.0) Different at 12 months, p <.05, Effect size=0.49	NA	None
Mulligan, 2012[9]	NA	**PCL-C score** Full sample median (IQR) @ Baseline G1: 21 (18-26) G2: 20 (17-26) Between-groups p=NS @ 6 months G1: NR G2: NR Between-groups p=NS Mixed-effects model results: coefficient (SE) of relationship between G1 assignment and PCL-C total score @ 6 months = -0.00 (0.02)	NR	None

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
O'Donnell, 2012[10]	**CAPS-2** Total score, mean (SD) @ 6 months G1: 31.95 (21.04) G2: 52.45 (33.14) Between-groups p <.05 @ 12 months G1: 25.26 (21.81) G2: 52.50 (26.93) Between-groups p <.05 12-month Hedges ˆg effect size (95% CI): 1.11 (0.34 to 1.88)	NA	**CAPS** N (%) achieving PTSD diagnosis @ 6 months (N=42) G1: 2 (9%) G2: 11 (55%) Between-groups p <.05 @ 12 months (N=31) G1: 4 (21%) G2: 7 (58%) Between-groups p <.05	
Rose, 1999[11]	NA	**IES** Mean (SD) @ 6 months G1: 19.7 (19.9) G2: 16.7 (18.6) G3: 23.3 (20.2) p >.10 **PSS-SR** Mean (SD) @ 6 months G1: 13.8 (13.3) G2: 10.9 (11.1) G3: 13.0 (12.4) p >.10	**PSS-SR** PTSD, N (%) @ 6 months G1: 12 (23%) G2: 5 (23%) G3: 11 (26%) p >.10	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Rothbaum, 2012[12]	**PSS-I score** Mean (SE) (95% CI): Total sample No baseline data collected @ 4 weeks ITT G1: 19.09 (1.83) (15.51 to 22.68) G2: 24.54 (1.70) (21.22 to 27.87) Effect size: 0.38 Between-groups p <.05 Main effect of group: p=.02 PSS-I score, mean (SE): rape victims (N=47) @ 4 weeks ITT G1: 20.10 (2.38) G2: 30.45 (2.73) Effect size: 0.70 Between-groups p <.01 PSS-I score, mean (SE): transportation accident victims (N=46) @ 4 weeks ITT G1: 17.95 (2.66) G2: 24.14 (1.95) Effect size: 0.49 Between-groups p=.06 PSS-I score, mean (SE): physical assault victims (n=37) @ 4 weeks ITT G1: NR G2: NR Effect size: 0.14 Between-groups p=.52 PSS-I score, mean (SE): other (N=7) Sample size not sufficient to allow for comparisons	**PDS score (for prior traumatic events)** Mean (SE) (95% CI) – ITT results @ Baseline G1: 18.90 (1.80) (15.35 to 22.39) G2: 19.46 (1.78) (15.97 to 22.95) Between-groups p=NR @ 4 weeks G1: 18.90 (2.34) (14.30 to 23.50) G2: 23.76 (2.29) (19.27 to 28.24) Effect size: 0.11 Between-groups p=NR Main effect of group: p=.11	**PSS-I** % patients meeting PTSD criteria: Total sample @ 4 weeks ITT G1: 46% G2: 51% Between-groups p=.60 NNT=20	None

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Ryding, 2004[13]	NA	**IES score** Median (IQR) @ 6 months G1: 12.0 (6.0 to 23.0) G2: 15.5 (5.5 to 27.5) p=.54	NA	**W-DEQ score** (measures fear of childbirth) Median (IQR) @ 6 months G1: 51.0 (36.0 to 60.0) G2: 49.5 (38.7 to 60.5) p=.8160
Shalev, 2011[14]	**CAPS** Mean (SD) @ Baseline Total score G1: 73.59 (21.34) G2: 71.78 (15.18) G3: 79.83 (15.60) G4: 74.91 (14.69) G5: 71.66 (15.22) G1 + G2 vs. G3 + G4 + G5: p=.31 (Note: Study may have analyzed between-group differences separately for each treatment group, in spite of how analyses of between-group differences are reported above and below.	**PSS-SR score** Mean (SD) @ Baseline G1: 30.88 (8.48) G2: 30.58 (8.34) G3: 36.55 (7.91) G4: 34.57 (6.55) G5: 31.13 (8.31) G1 + G2 vs. G3 + G4 + G5: p=.02	**CAPS** PTSD, N (%) @ Baseline G1: 63 (100) G2: 40 (100) G3: 23 (100) G4: 23 (100) G5: 93 (100) @ 5 month Follow-up G1: 12 (21.4) G2: 6 (18.2) G3: 13 (61.9) G4: 10 (55.6) G5: 46 (58.2) G1, G2<G3, G4, G5; p=.001 G3 vs. G4 vs. G5, p >.92	N's @ Baseline G1: 63 G2: 40 G3: 23 G4: 23 G5: 93 @ 5 month Follow-up G1: 56 G2: 33 G3: 21 G4: 18 G5: 79 @ 9 month Follow-up G1: 52 G2: 35 G3: 19 G4: 17 G5: 57 Note: @ baseline, sample met all the symptom criteria for PTSD.

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Shalev, 2011[14] (continued)	Reexperiencing G1: 21.21 (8.27) G2: 19.95 (6.54) G3: 21.22 (6.76) G4: 19.78 (7.75) G5: 19.59 (8.88) G1 + G2 vs. G3 + G4 + G5: p=.66 Avoidance G1: 29.90 (9.02) G2: 30.23 (6.68) G3: 33.87 (6.47) G4: 31.17 (6.65) G5: 29.30 (7.19) G1 + G2 vs. G3 + G4 + G5: p=.13 Hyperarousal G1: 22.48 (7.34) G2: 21.60 (6.08) G3: 24.74 (5.61) G4: 23.96 (6.03) G5: 22.76 (5.69) G1 + G2 vs. G3 + G4 + G5: p=.33 @ 5 month Follow-up CAPS score, mean (SD) Total score G1: 28.59 (25.02) G2: 29.48 (23.03) G3: 48.71 (29.63) G4: 47.11 (20.13) G5: 50.56 (27.51) G1, G2< G3, G4, G5: p=.001 Reexperiencing G1: 7.32 (7.44) G2: 6.85 (5.71) G3: 11.19 (8.55) G4: 11.56 (6.30) G5: 11.75 (8.26) G1, G2< G3, G4, G5: p=.002	@ 5 months G1: 11.02 (11.19) G2: 11.56 (10.47) G3: 22.52 (14.20) G4: 22.22 (11.86) G5: 22.14 (13.09) G1 + G2 vs. G3 + G4 + G5: p=.001 *mean between grp difference G1 vs. G2 (95% CI): −1.73 (−3.72 to 1.19]) *mean between grp difference G3 vs. G4 (95% CI): 2.29 (−0.57 to 10.27) *mean between grp difference G1 vs. G3 (95% CI): −7.86 (−14.11 to −1.62) *mean between grp difference G1 vs. G4 (95% CI): −10.16 (−17.13 to −3.19) *mean between grp difference G2 vs. G3 (95% CI): −9.60 (−16.30 to −2.90) *mean between grp difference G2 vs. G4 (95% CI): −11.89 (−19.27 to −4.52) @ 9 months G1: 10.35 (11.85) G2: 9.56 (10.60) G3: 21.63 (2.96) G4: 19.35 (12.53) G5: 13.11 (12.33) G1 + G2 vs. G3 + G4 + G5: p=.001	@ 9 months G1: 11 (21.2) G2: 8 (22.9) G3: 8 (42.1) G4: 8 (47.1) G5: 13 (22.8) p=.01** **Computed for a comparison of 36 participants from the SSRI and placebo subgroups and 144 participants from the PE (G1), CT (G2), and WL (G5) groups.	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Shalev, 2011[14] (continued)	Avoidance G1: 11.36 (11.27) G2: 12.12 (10.39) G3: 21.62 (12.92) G4: 18.56 (8.90) G5: 22.29 (12.75) G1, G2 < G3, G4, G5: p=.001 Hyperarousal G1: 9.91 (8.65) G2:10.52 (9.26) G3:15.90 (9.78) G4: 17.00 (8.57) G5: 16.52 (9.11) G1, G2 < G3, G4, G5: p=.001 @ 9 month Follow-up CAPS, mean (SD) Total score G1: 27.52 (26.91) G2: 27.89 (25.64) G3: 47.16 (26.71) G4: 45.71 (26.14) G5: 31.11 (25.07) Group-by-time, p <.001 G1, G2, G5< G3, G4: p=.01 G1<G5, p <.001 G2<G5, p <.003 G3>G5, p <.05 G4>G5, p <.003 G3=G4, p >.46 Omitting 5 month followup outcomes from model, mean difference (95% CI) G1 vs. G5, 0.83 (-6.44 to 4.79), p=NS G2 vs. G5, 1.55 (-4.79 to 7.89), p=NS G3 vs. G5, 8.93 (0.86 to 17.0), p=significant but NR			

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Shalev, 2011[14] (continued)	G4 vs. G5, 12.11 (4.29 to 19.9), p=significant but NR Reexperiencing G1: 6.67 (7.66) G2: 5.57 (5.63) G3: 9.68 (7.91) G4: 9.65 (8.49) G5: 7.39 (7.34) p=.20 Avoidance G1: 11.21 (11.93) G2: 12.97 (12.66) G3: 21.58 (11.42) G4: 18.18 (11.28) G5: 13.51 (10.80) G1, G2, G5 < G3, G4: p=.01 Hyperarousal G1: 9.63 (9.46) G2: 9.34 (9.60) G3: 15.89 (9.72) G4: 17.88 (9.88) G5: 10.21 (9.46) G1, G2, G5 < G3, G4: p=.004 Note: At 9 month follow-up, G5 has now become an active treatment group, having received 4 months of PE (equivalent to G1) *All mean between group differences were analyzed using ITT post hoc least significant difference analysis			

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Sijbrandij, 2006[15]	**SI-PTSD** PTSD severity scores, mean (SD) @ Baseline G1: 19.9 (12.2) G2: 19.9 (12.7) G3: 17.7 (11.0) p=NR @ 2 weeks G1: 18.1 (13.2) G2: 16.2 (10.7) G3: 15.9 (10.9) p=NR @ 6 weeks G1: 14.4 (13.8) G2: 11.9 (11.7) G3: 10.5 (9.1) p=NR @ 6 months G1: 10.2 (12.0) G2: 9.3 (9.4) G3: 9.6 (10.1) p=NR PTSD severity decreased in all 3 groups (p<.001), but NS between-groups difference for total symptom score: G1 (emotional) = G2 (educational) = G3 (control), p=.33 No sig between-groups differences on any subscales: Re-experiencing (p=.058), avoidance (p=.84), or hyperarousal (p=.20) Symptom reduction (95% CI) between 2 weeks and 6 months (adjusted for baseline): G1: 7.1 (4.7 to 9.5) G2: 6.4 (4.0 to 8.8) G3: 5.9 (3.6 to 8.2)	NA	**SI-PTSD** Overall @ 2 week Follow-up (N=10): 5.4% Overall @ 6 week Follow-up (N=9): 4.9% Overall @ 6 month Follow-up (N=8): 4.8%	

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Treggiari, 2009[16]	NA	**Normalized IES-R and PCL scores** Mean (SD) @ Discharge G1: 52 (33) G2: 57 (30) p=.39 @ 4 weeks after discharge G1: 46 (29) G2: 56 (29) 95% CI -20.9 to 2.0, p=.07 Note: Scores of IES-R and PCL were normalized by subtracting the mean and dividing by the SD to normalize to the same scale; scores were then ranked.	**PCL** % meeting symptom criteria for presumptive diagnosis of PTSD at 4 weeks after discharge G1: 10% G2: 9% p=.83	
Weis, 2006[17]	NA	**PTSS-10 score** Median (IQR) @ 6 months G1: 15.5 (14.8 to 21.8) G2: 25.5 (16.8 to 33.0) p=.03	**PTSS-10** Evidence of PTSD defined as stress symptom score >35 @ 6 months (%) G1: 21.4 G2: 7.1	Patients in groups did not differ signficantly with regard to number and type of traumatic memories, p ≤.33

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Wong, Under review[18]	NA	**PCL score** Completers analysis results Baseline G1: NR G2: NR Between-groups p=NS @ 1 month G1: NR G2: NR Between-groups p=.42 **Knowledge of PTSD Test** Self-recognition of PTSD symptoms – completers analysis results Data only collected at follow-up (below) @ 1 month G1: NR G2: NR Between-groups p=.05 Adjusted OR (G1 vs. G2) (controlling for PTSD symptoms) (95% CI): 4.27 (1.00 to 18.43)	**PCL** % patients with probable PTSD @ 1 month completers analysis G1: 46 G2: 51 Between-groups p=.83 OR (G1 vs. G2) (95% CI): 0.79 (0.23 to 2.67)	**Knowledge of PTSD Test** (measures knowledge about traumatic events, posttraumatic stress reactions, and treatment) Completers analysis results @ Baseline G1: NR G2: NR Between-groups p=NS @ Post-treatment (immediately afterward) G1: NR G2: NR β (95% CI): 0.56 (0.06 to 1.07) Between-groups p <.05 (G1 > G2) @ 1 month completers analysis G1: NR G2: NR β (95% CI): 0.24 (0.06 to 1.07) Between-groups p=NS

Evidence Table 4. PTSD incidence and symptom severity scale outcomes (continued)

Author, Year	Clinician Administered Scale for PTSD Symptom Reduction	Self-Administered Scale for PTSD Symptom Reduction	Incidence of PTSD	Comments/ Other Outcomes
Zatzick, In press[19]	**CAPS** CAPS score, mean (95% CI) No baseline data collected @ 1 month G1: 57.2 (52.3 to 62.2) G2: 59.0 (53.9 to 64.2) Effect size: 0.08 Between-groups p=NS No 3-month data collected @ 6 months G1: 42.9 (37.0 to 48.8) G2: 56.7 (50.7 to 62.7) Effect size: 0.53 Between-groups p <.01 No 9-month data collected @ 12 months G1: 38.6 (32.5 to 44.6) G2: 47.2 (41.2 to 53.3) Effect size: 0.32 Between-groups p <.05 Group-by-time interaction effects @ 12 months (G1 improvement compared to G2): p <.01 No significant interaction of TBI-by-group	**PCL** PCL-C score, mean (95% CI) Baseline G1: 51.2 (48.9 to 53.4) G2: 52.0 (49.5 to 54.5) Between-groups p=NS @ 1 month G1: 50.2 (47.4 to 52.9) G2: 51.1 (48.2 to 54.0) Effect size: 0.07 Between-groups p=NS @ 3 months G1: 45.9 (42.9 to 48.9) G2: 48.6 (45.5 to 51.8) Between-groups p=NS @ 6 months G1: 40.6 (37.3 to 43.9) G2: 49.9 (46.6 to 53.1) Effect size: 0.65 Between-groups p <.01 @ 9 months G1: 40.2 (36.8 to 43.5) G2: 45.5 (42.2 to 48.7) Between-groups p <.01 @ 12 months G1: 37.4 (34.0 to 40.7) G2: 42.5 (39.3 to 45.7) Effect size: 0.34 Between-groups p <.05 Group-by-time interaction effects @ 12 months (G1 improvement compared to G2): p <.001 No significant interaction of TBI-by-group	Adjusted main effect OR (95% CI) for change in PTSD diagnostic criteria @ 12 months (G1 compared to G2): 1.39 (0.77 to 2.51)	None

Abbreviations: CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; CI = confidence interval; CT = Cognitive therapy; ES = effect size; G = group; IES = Impact of Event Scale; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event-Intrusion subscale; IES-R = Impact of Event Scale-Revised; IQR = interquartile range; ITT = intent to treat analysis; IV = intravenous; mg = milligrams; min = minutes; N = number of participants; NA = not applicable; NNT = number needed to treat; NR = not reported; NS = not significant; OR = odds ratio; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; PDS = Posttraumatic Stress Diagnostic Scale;

PE = Prolonged exposure therapy; PSDS-SR = Posttraumatic Stress Diagnostic Scale-Self Report; PSS-I = PTSD Symptom Scale-Interview; PSS-SR = PTSD Symptom Scale-Self-Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; T = time; TBI = traumatic brain injury; W-DEQ = Wijma Delivery Expectancy/Experience Questionnaire; WL = Waitlist

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Beatty, 2010[1]	NA	DASS-21, Depression, Mean (SE) 3 months G1: 7.76 (0.83) G2: 7.03 (0.89) p=NS 6 months G1: 8.08 (1.08) G2: 6.41 (1.11) p=NS DASS-21, Anxiety, Mean (SE) 3 months G1: 7.48 (0.76) G2: 7.21 (0.81) p=NS 6 months G1: 7.97 (0.83) G2: 7.03 (0.85) p=NS Note: Baseline data only provided overall, which precluded mean change calculation DASS-21, Depression Overall: 6.49 DASS-21, Anxiety Overall: 5.62 Body Image, Mean (SE) 3 months G1: 59.98 (3.07) G2: 77.32 (3.28) p=.01 6 months G1: 62.87 (3.33) G2: 79.65 (3.40) p=.01	Quality of Life – Global, Mean (SE) 3 months G1: 66.52 (2.42) G2: 67.75 (2.58) p=NS 6 months G1: 69.02 (2.71) G2: 72.21 (2.77) p=NS	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Beatty, 2010[1] (continued)		Anxiousness preoccupation, Mean (SE) 3 months G1: 15.77 (0.65) G2: 17.58 (0.70) p=NS 6 months G1: 16.28 (0.65) G2: 16.01 (0.64) p=NS Helplessness/hopelessness, Mean (SE) 3 months G1: 10.07 (0.50) G2: 12.0 (0.54) p=.03 6 months G1: 10.26 (0.45) G2: 10.44 (0.46) p=NS Cognitive Avoidance, Mean (SE) 3 months G1: 8.38 (0.37) G2: 10.04 (0.40) p=.03 6 months G1: 9.79 (0.43) G2: 10.17 (0.44) p=NS				

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Bryant, 1999[20]	NA	STAI-State, mean (SD) @ pretreatment G1: 54.77 (10.28) G2: 51.69 (12.41) G3: 50.47 (7.39) p=NR @ post-treatment G1: 34.31 (16.95) G2: 35.92 (10.12) G3: 41.47 (12.91) p=NR @ 6 month follow-up G1: 35.00 (12.91) G2: 36.62 (12.69) G3: 44.73 (7.34) p=NR Group-by-time p <.05 Specific group-by-time differences G3 > G2 at T3, p<.05 G3 > G1 at T3, p<.02	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Bryant, 2008[2]	NA	Anxiety, BAI; Depression, BDI-2 (ITT sample) Mean (SD) : @ baseline (pretreatment) G1: 23.1 (12.6); 22.1 (11.0) G2: 27.5 (12.3); 24.2 (8.2) G3:22.2 (11.2); 23.8 (12.0) @ 6 weeks (posttreatment) G1: 13.4 (15.3); 12.1 (11.8) G2: 23.4 (14.2); 18.9 (13.3) G3:19.6 (13.7); 21.9 (13.8) BDI: G1<G3, p=.003 G2 vs. G3, p=NS BAI: G1<G3, p=.004 G1<G2, p=.008 G2 vs G3, p=NS @ 6 month follow-up G1: 12.8 (16.1); 12.4 (13.1) G2: 23.3 (16.7); 20.4 (13.1) G3: NA; NA Intrusion: G1<G2, p=.02 Avoidance: G1<G2, p=.03	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Bryant, 2003[3]	NA	BAI, BDI, mean (SD) @ Pre-treatment G1: 25.58 (11.43), 20.42 (11.66) G2: 26.83 (13.90), 24.17 (11.96) @ Post-treatment (within 1 week) G1: 13.17 (12.65), 13.75 (12.10) G2: 21.58 (17.49), 18.75 (12.61) p=0.05 (BAI), p=.56 (BDI) @ 6 month follow-up G1: 13.92 (10.98), 21.83 (18.72) G2: 15.42 (13.87), 20.33 (14.18) p=.19 (BAI), p=.69 (BDI)	NA	NA	NA	NA
Bryant, 1998[4]	NA	Depression, BDI-2 Mean (SD) : @ Baseline G1: 16.58 (10.18) G2: 17.17 (8.12) @ Post-treatment (mean of 41.5 days) G1: 7.25 (8.84) G2: 13.67 (9.80) @ 6 months G1: 6.08 (6.27) G2: 13.50 (7.86) Anxiety, STAI-State Mean (SD) @ Baseline G1: 50.83 (14.57) G2: 54.08 (10.51) @ Post-treatment (mean of 41.5 days) G1: 31.58 (9.66) G2: 44.67 (12.84)	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Bryant, 1998[4] (continued)	NA	@ 6 month follow-up G1: 34.75 (7.78) G2: 43.17 (7.66) Anxiety, STAI-Trait Mean (SD) @ Baseline G1: 47.08 (17.21) G2: 49.08 (9.71) @ Post-treatment (mean of 41.5 days) G1: 34.67 (10.91) G2: 42.08 (11.40) @ 6 month follow-up G1: 38.00 (9.26) G2: 47.5 (12.41)	NA	NA	NA	NA
Bryant, 2005[5]	NA	Depression, BDI-2 @ Baseline, mean (SD): G1: 18.40 (8.39) G2: 19.97 (10.01) G3: 22.04 (11.77) p=NS @ Post-treatment (ITT): G1: 11.37 (7.34) G2: 13.24 (11.83) G3: 14.96 (10.92) p=NS Effect sizes, pre- to post-treatment (ITT): G1: 1.04 (1.02) G2: 0.92 (0.62) G3: 0.58 (0.56) p=NR	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Bryant, 2005[5] (continued)	NA	@ 6-month follow-up (ITT): G1: 13.57 (8.78) G2: 14.61 (12.31) G3: 16.29 (11.95) p=NS Effect sizes, post-treatment to follow-up (ITT): G1: 1.90 (0.87) G2: 0.79 (0.53) G3: 0.12 (0.10) p=NR BAI, mean (SD) @ Baseline: G1: 27.27 (11.47) G2: 24.39 (11.23) G3: 28.67 (13.45) p=NS @ Post-treatment (ITT): G1: 15.47 (12.87) G2: 14.91 (13.31) G3: 20.25 (14.26) p=NS Effect sizes, pre- to post-treatment (ITT): G1: 2.21 (1.07) G2: 1.12 (0.75) G3: 0.60 (0.56) p=NR @ 6-month follow-up (ITT): G1: 14.04 (12.67) G2: 12.21 (11.91) G3: 21.00 (15.62) p=NS	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Bryant, 2005[5] (continued)		Effect sizes, post-treatment to follow-up (ITT): G1: 1.90 (0.87) G2: 0.79 (0.53) G3: 0.12 (0.10) p=NR				
Campfield, 2001[6]	NA	NA	NA	NA	NA	NA
Gamble, 2005[7]	NA	Depression, Edinburgh Postnatal Depression Scale (EPDS) > 12 (N, %)[a] @ 4-6 weeks postpartum (N=102) G1: 16 (32%) G2: 18 (34%) RR (95% CI): 0.96 (0.56 to 1.67) p=NS @ 3 months (N=103) G1: 4 (8%) G2: 17 (32%) RR (95% CI): 0.25 (0.09 to 0.69) p=.002 Depression, Depression Anxiety and Stress Scale-21 (DASS-21) > 13 (N, %)[a] @ 3 months (N=102) G1: 3 (6%) G2: 14 (26%) RR (95% CI): 0.23 (0.07 to 0.76) p=.005 Anxiety, DASS-21 > 9 (N, %) [a] @ 3 months (N=103) G1: 1 (2%) G2: 6 (11%) RR (95% CI): 0.18 (0.02 to 1.45) p=NS	NA	NA	NA	Self-report questionnaire: Usefulness of intervention in reconciling birth trauma High ratings (8-10 out of 10), N (%) G1: 43 (86%) G2: NA Note: No women rated intervention lower than 7 out of 10

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Melnyk, 2004[8]	NA	Depression subscale, Profile of Mood States, mean (SD) @ Time 1 (Baseline) G1: 6.0 (4.3) G2: 5.7 (4.1) p=NR @ Time 2 G1: 4.5 (4.5) G2: 3.8 (4.0) p=NR @ Time 3 G1: 3.7 (4.4) G2: 3.8 (4.2) p=NR @ Time 4 G1: 3.3 (4.2) G2: 3.2 (4.4) p=NR @ Time 6 (1 month post-discharge) G1: 2.6 (3.3) G2: 4.1 (4.3) p<0.05 at this time point @ Time 7 (3 months post-discharge) G1: 3.3 (4.4) G2: 4.2 (4.6) p=NR	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Melnyk, 2004[8] (continued)	NA	@ Time 8 (6 months post-discharge) G1: 2.0 (3.3) G2: 3.9 (5.2) p <.05 @ Time 9 (12 months post-discharge) G1: 2.5 (4.0) G2: 3.6 (4.0) Effect at time 9, p<0.01, p<0.05 with mulitple imputation analysis STAI, mean (SD): @ Time 1 (baseline) G1: 52.8 (13.0) G2: 52.8 (12.6) p=NR @ Time 2 G1: 45.6 (13.4) G2: 45.0 (11.8) p=NR @ Time 3 G1: 42.4 (12.8) G2: 42.4 (12.9) p=NR @ Time 4 G1: 40.6 (12.6) G2: 41.0 (13.6) p=NR	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Melnyk, 2004[8] (continued)	NA	@ Time 6 (1 month post-discharge) G1: 35.7 (12.2) G2: 39.8 (14.3) p=NR @ Time 7 (3 months post-discharge) G1: 38.4 (13.9) G2:40.7 (12.3) p=NR @ Time 8 (6 months post-discharge) G1: 36.0 (11.1) G2: 39.1 (13.8) p=NR @ Time 9 (12 months post-discharge) G1: 35.8 (12.8) G2: 40.9 (12.5) p=NR Within-group effect for G1 at time 9: 0.40, p<.01 (not with multiple imputation)	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Mulligan, 2012[9]	NA	Psychological distress – GHQ-12 possible mental disorder caseness, total sample N (%) Baseline (completers analysis) G1: 169 (15.4) G2: 198 (14.9) p=NS @ 6 months (completers analysis) Adjusted OR (95% CI) in G1 vs. G2: 0.84 (0.57 to 1.23) NOTE: ITT analyses also conducted for GHQ-12 outcomes with no differences in any outcomes Depression caseness (major or other depression) – PHQ @ 6 months only Adjusted OR (95% CI) in G1 vs. G2: 1.12 (0.71 to 1.77) AUDIT, total score @ 6 months only Mixed-effects model results: coefficient (95% CI) of relationship between G1 assignment and AUDIT score = -0.73 (-1.45 to -0.001) Binge drinking caseness @ 6 months only Adjusted OR (95% CI) in G1 vs. G2: 0.73 (0.58 to 0.92) Between-groups p <.01	Sleep, total score – self-report questionnaire @ 6 months only Adjusted incidence rate ratio (95% CI) in G1 vs. G2: 0.95 (0.90 to 1.01)	NA	NA	Note: All perceived utility items collected using self-report questionnaire N (%) responding "somewhat" or "very much" to question about personal satisfaction with briefing (completers analysis) Baseline G1: 886 (84.2) G2: 1072 (85.2) Between-groups p=.82 @ 6 months G1: 590 (75.1) G2: 591 (73.4) Between-groups p=.83 N (%) responding "somewhat" or "very much" to question about usefulness of briefing (completers analysis) Baseline G1: 791 (75.4) G2: 950 (75.8) Between-groups p=.76 @ 6 months G1: 540 (68.7) G2: 529 (65.7) Between-groups p=.35

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Mulligan, 2012[9] (continued)						N (%) responding "somewhat" or "very much" to question about briefing's relevance for personnel returning from deployment (completers analysis) Baseline G1: 876 (83.6) G2: 1042 (83.1) Between-groups p=.09 @ 6 months G1: 584 (74.4) G2: 584 (72.5) Between-groups p=.93 Ability of brief to help deal with coming home from operations @ 6 months only G1: 413 (52.9) G2: 381 (47.3) Between-groups p=.04 (Note: no longer significant after adjusting for variables that differed between groups at baseline and predictors of follow-up noncompletion)

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
O'Donnell, 2012[10]	NA	Depression - BDI, mean (SD) Pretreatment: G1: 30.13 (10.76) G2: 28.83 (11.18) @ 6 months (completers analysis): G1: 12.24 (11.02) G2: 31.20 (8.60) Between-groups p <.05 @ 12 months (completers analysis) G1: 13.95 (11.29) G2: 29.00 (8.37) Between-groups p <.05 12-month Hedges ^g effect size (95% CI): 1.45 (0.69 to 2.21)	NA	NA	NA	NA
Rose, 1999[11]	NA	BDI, mean (SD) @ 6 months G1: 12.1 (13.0) G2: 9.8 (9.2) G3: 13.9 (13.1) Between-groups p>.10	NA	NA	NA	NA
Ryding, 2004[13]	NA	EPDS score, median (IQR) @ 6 months G1: 6.0 (3.0 to 8.0) G2: 6.0 (3.5 to 11.0) p=.1256	NA	NA	NA	Self-report questionnaire: N (%) of women who received intervention reporting that it completely met their expectations: NR (71%)
Shalev, 2011[14]	NA	NA	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Sijbrandij, 2006[15]	NA	HADS (Anxiety): Anxiety Scores decreased in all 3 groups over time (p<.001), but NS difference between groups @ 2 weeks post-treatment: G1 = G2 = G3, p=.96 Symptom reduction (95% CI) between 2 weeks and 6 months (adjusted for baseline): G1: 2.4 (1.4 to 3.3) G2: 2.2 (1.2 to 3.2) G3: 2.1 (1.1 to 3.0) Other comorbid psychiatric conditions: HADS (Depression): Depression Scores decreased in all 3 groups over time (p<.001), but NS difference between groups @ 2 weeks post-treatment: G1 = G2 = G3, p=.23 Symptom reduction (95% CI) between 2 weeks and 6 months (adjusted for baseline): G1: 1.6 (0.6 to 2.6) G2: 1.5 (0.5 to 2.5) G3: 1.4 (0.4 to 2.4)	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Treggiari, 2009[16]	Incidence of any organ failure to day 7, N (%) @ ICU discharge G1: 45 (70) G2: 42 (65) Between-groups p=.49 ICU mortality, N (%) G1: 9 (14) G2: 9 (14) Between-groups p>.99 Hospital mortality, N (%) G1: 11 (17) G2: 12 (18) Between-groups p=.65	Anxiety and Depression subscores of Hospital Anxiety and Depression scale, respectively Mean (SD): @ discharge G1: 6.4 (4.0); 5.3 (3.4) G2: 7.1 (4.6); 6.5 (4.7) Anxiety: p=.37; Depression: p=.13 @ 4 weeks after discharge G1: 5.3 (4.2), 3.4 (3.7) G2: 5.0 (4.2), 3.1 (3.7) 95% CI: (-1.3 to 2.0), (-1.2 to 1.7), respectively	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Weis, 2006[17]	No	NA	SF-36 HRQL (Note: All HRQL outcomes collected @ 6 month follow-up) General Health Perception, median (25^{th}-75^{th} percentiles) G1: 72 (65-75) G2: 60 (49-63) Between-groups p<.01 Mental health, median (25th-75th percentiles) G1: 80 (66-84) G2: 64 (51-69) Between-groups p=.01 Physical function, median (25th-75th percentiles) G1: 85 (49-90) G2: 38 (35-60) Between-groups p=.01 SF-36 HRQL Physical role function, median (25th-75th percentiles) G1: 25 (0-75) G2: 0 (0-50) Between-groups p=.19 Pain, median (25th-75th percentiles) G1: 100 (72-100) G2: 62 (36-88) Between-groups p=.01	No	No	No

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Weis, 2006[17] (continued)	NA	NA	Social function, median (25th-75th percentiles) G1: 88 (75-100) G2: 69 (50-81) Between-groups p=.06 Vitality, median (25th-75th percentiles) G1: 58 (44-76) G2: 40 (29-46) Between-groups p<.01 Emotional role function, median (25th-75th percentiles) G1: 67 (17-100) G2: 0 (0-67) Between-groups p<.10	NA	NA	NA
Wong, Under review[18]	NA	NA	NA	NA	NA	NA

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Zatzick, In press[19]	NA	Depression symptoms – PHQ-9, mean (95% CI) Baseline ITT G1: 13.4 (12.3 to 14.6) G2: 14.2 (13.0 to 15.5) Between-groups p=NS @ 1 month ITT G1: 12.5 (11.3 to 13.7) G2: 13.2 (11.9 to 14.5) Effect size: 0.12 Between-groups p=NS @ 3 months ITT G1: 11.7 (10.5 to 13.0) G2: 13.0 (11.5 to 14.5) Between-groups p=NS @ 6 months ITT G1: 8.7 (7.4 to 10.1) G2: 11.3 (9.9 to 12.8) Effect size: 0.43 Between-groups p >.01 @ 9 months ITT G1: 9.7 (8.3 to 11.2) G2: 11.4 (9.9 to 12.9) Between-groups p=NS @ 12 months ITT G1: 8.4 (7.1 to 9.7) G2: 10.1 (8.6 to 11.7) Effect size: 0.26 Between-groups p=NS Group-by-time interaction effects @ 12 months (G1 improvement compared to G2): p=.07	NA	Physical health and function – SF-36 Physical Component Summary Score (PCS), mean (95% CI) Baseline ITT G1: 49.1 (46.5 to 51.7) G2: 50.6 (47.8 to 53.4) Between-groups p=NS @ 1 month ITT G1: 34.6 (32.0 to 37.3) G2: 32.4 (29.9 to 34.9) Effect size: 0.32 Between-groups p <.05 @ 3 months ITT G1: 39.0 (36.3 to 41.7) G2: 34.8 (32.4 to 37.2) Between-groups p <.01 @ 6 months ITT G1: 42.4 (39.6 to 45.3) G2: 37.8 (35.2 to 40.4) Effect size: 0.56 Between-groups p <.01 @ 9 months ITT G1: 43.2 (40.2 to 46.1) G2: 39.8 (37.2 to 42.5) Between-groups p <.05 @ 12 months ITT G1: 43.7 (41.0 to 46.5) G2: 41.2 (38.5 to 43.9) Effect size: 0.26 Between-groups p=NS	NA	Note: All perceived utility items collected during assessment interviews Adjusted main effect of group on likelihood that patients reported being very satisfied with general health care (G1 compared to G2) OR (95% CI): 2.00 (1.01 to 3.96) Adjusted main effect of group on likelihood that patients reported being very satisfied with emotional health care services (G1 compared to G2) OR (95% CI): 2.93 (1.84 to 4.67)

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
Zatzick, In press[19] (continued)		No significant interaction of TBI-by-group AUDIT-C (Consumption Items) score Baseline ITT G1: 3.1 (2.5 to 3.8) G2: 3.9 (3.2 to 4.6) Between-groups p=NS @ 1 month ITT G1: 1.4 (1.0 to 1.8) G2: 1.9 (1.2 to 2.5) Effect size: 0.19 Between-groups p=NS @ 3 months ITT G1: 1.9 (1.4 to 2.4) G2: 2.7 (2.0 to 3.4) Between-groups p <.05 @ 6 months ITT G1: 2.0 (1.4 to 2.6) G2: 2.8 (2.1 to 3.5) Effect size: 0.28 Between-groups p=NS @ 9 months ITT G1: 2.4 (1.8 to 3.0) G2: 2.6 (1.9 to 3.2) Between-groups p=NS @ 12 months ITT G1: 2.0 (1.5 to 2.6) G2: 2.4 (1.8 to 3.0) Effect size: 0.13 Between-groups p=NS		Group-by-time interaction effects @ 12 months (G1 improvement compared to G2): p <.01 No significant interaction of TBI-by-group		

Evidence Table 5. Comorbid conditions, quality of life, impairment, ability to return to work, and perceived utility (continued)

Author, Year	Comorbid Medical Condition Prevention/ Reduction	Comorbid Psychiatric Condition	Quality of Life	Disability/ Functional Impairment	Return to Work/ Active Duty OR Ability to Work	Perceived Utility
		Group-by-time interaction effects @ 12 months (G1 improvement compared to G2): p=.08 No significant interaction of TBI-by-group				

[a] Gamble, 2005 secondary outcome percentage data not directly provided by the study authors. Data provided here are calculated by authors of this report.

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test; AUDIT-C = AUDIT – Consumption Items; BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; Btwn = between; CI = confidence interval; DASS-21 = Depression and Anxiety Stress Scales-21; EPDS = Edinburgh Postnatal Depression Scale; G = group; GHQ = 12-item General Health Questionnaire; HADS = Hospital Anxiety and Depression Rating Scale; HRQL = health-related quality of life; ICU = intensive care unit; IQR = interquartile range; ITT = intent to treat analysis; N = number of participants; NA = not applicable; NR = not reported; NS = not significant; OR = odds ratio; PCS = Physical Component Score; PHQ-9 = Patient Health Questionnaire, 9-item version; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; SE = standard error; SF-36 = Medical Outcomes Study Health Survey – Short Form 36; TBI = traumatic brain injury

Evidence Table 6. Harms and adverse events of included trials

Author, Year	Overall Adverse Events	Withdrawals Due to Adverse Events	Mortality	Suicidality	Homicidality	Other Adverse Effects (i.e., Disturbed Sleep, Agitation, Sedation, Weight Gain, Others)
Beatty, 2010[1]	No	No	No	No	No	None
Bryant, 1998[4]	No	No	No	No	No	None
Bryant, 2003[3]	No	No	No	No	No	None
Bryant, 2008[2]	Yes	Yes	No	No	No	Distress See CAPS-2 score during the active treatment period (weeks 1-5)
Campfield, 2001[6]	No	No	No	No	No	None
Gamble, 2005[7]	No	No	No	No	No	None
Grainger, 1997[21]	No	No	No	No	No	None
Melnyk, 2004[8]	No	No	No	No	No	None
Mulligan, 2012[9]	No	No	Yes	No	No	G1 experienced 1 death following Battlemind intervention, although its cause is NR.
O'Donnell, 2012[10]	No	No	No	No	No	None
Rose, 1999[11]	No	No	No	No	No	None
Rothbaum, 2012[12]	No study-related adverse events reported	No patients withdrew as a result of their participation	No	No	No	None
Ryding, 2004[13]	No	No	No	No	No	None

Evidence Table 6. Harms and adverse events of included trials (continued)

Author, Year	Overall Adverse Events	Withdrawals Due to Adverse Events	Mortality	Suicidality	Homicidality	Other Adverse Effects (i.e., Disturbed Sleep, Agitation, Sedation, Weight Gain, Others)
Shalev, 2011[14]	No	No	No	No	No	None
Sijbrandij, 2006[15]	Yes	No	No	No	No	In participants with early hyperarousal, emotional debriefing led to higher PTSD scores than the control group at 6 weeks (p=0.005).
Treggiari, 2009[16]	No	No	Yes	No	No	Organ failure; death
Weis, 2006[17]	No	No	No	No	No	None
Wong, Under review[18]	No	No	No	No	No	Authors report that study provides no evidence that psychoeducation presents risk of harms in terms of PTSD symptoms or incidence for traumatic injury survivors, but no data about general or specific harms reported.
Zatzick, In press[19]	No	No	Yes	No	No	G1 experienced 5 deaths over the 12-month study period, compared to 6 deaths in G2. However, the authors did not conduct or report analyses showing how these mortality rates compare, and they did not report any harms related to the intervention.

Abbreviations: CAPS-2 = Clinician Administered PTSD Scale-2; G = group; NR = not reported; PTSD = posttraumatic stress disorder

Evidence Table 7. External applicability of included trials

Author, Year	Study Population	Intervention	Comparator	Outcomes
Beatty, 2010[1]	Yes Limited to Breast Cancer populations	Yes	Yes	Yes
Bryant, 2008[2]	Yes	Yes	Yes	Yes
Bryant, 2003[3]	Yes	Yes	Yes	Yes
Bryant, 1998[4]	Unclear Demographics of study sample not reported in great detail	Yes	Yes	Yes
Bryant, 2005[5]	Yes	No CBT and SC are widely applicable, but CBT-hypnosis is probably too specialized for widespread use.	Yes	Yes
Campfield, 2001[6]	Yes	Yes	Yes	No Outcomes only measured at 2 weeks
Gamble, 2005[7]	Yes	Yes	Yes	Yes
Melnyk, 2004[8]	No Only mothers	Yes	Yes	Yes
Mulligan, 2012[9]	Yes Limited to UK troops returning from deployment and not applicable to Royal Air Force	Yes Originally developed and used by the US Army	Yes	Yes
O'Donnell, 2012[10]	Unclear Ethnicity data NR, so determining how similar the sample is to the population of interest is not clear.	Unclear	Yes	Yes
Rose, 1999[11]	Yes	Yes	Yes	Yes
Rothbaum, 2012[12]	Yes	Yes	Yes	Yes

Evidence Table 7. External applicability of included trials (continued)

Author, Year	Study Population	Intervention	Comparator	Outcomes
Ryding, 2004[13]	No Limited to women who received C-section	Yes	Yes	Yes
Shalev, 2011[14]	Yes	Yes	Yes	Yes
Sijbrandij, 2006[15]	Yes NA	Yes	Yes NA	Yes NA
Treggiari, 2009[16]	No specific to ICU patients	Yes	Yes	No Outcomes at 4 weeks only measured
Weis, 2006[17]	No Limited to cardiac surgery patients	Yes	Yes	Yes
Wong, Under review[18]	Yes	Yes	Yes	No Outcomes only collected as much as 1 month post-intervention, which does not provide information about chronic PTSD.
Zatzick, In press[19]	Yes	Yes	Yes	Yes

Abbreviations: C-section = cesarean section; CBT = Cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; G = group; ICU = intensive care unit; NA = not applicable; NR = not reported; PTSD = posttraumatic stress disorder; SC = Supportive counseling; UK = United Kingdom; US = United States

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Appendix F. Risk-of-Bias Tables

Table F1. Risk of bias observational studies

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Carlier, 1998[22] **Prospective study design?** No	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** 100%	**Attempt to mask outcome assessors?** Yes **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** Yes	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NA **Any participants who started the trial excluded from analysis?** No	High Risk of recall bias because no data available until 8 months after trauma. High risk of selection bias and confounding from subjects' self-selection to treatment groups.
Eid, 2001[23] **Prospective study design?** Yes	**Groups recruited from same source population?** No **Both groups recruited over same time period?** Yes **% completed treatment** NR	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** Unclear **Confounding adequately accounted for either through study design or statistical analysis?** Unclear	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Unclear **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NA **Any participants who started the trial excluded from analysis?** NR	High Cohort study with a small sample size. No reported adjustment for confounders. Further risk of bias assessment impossible due to inadequate reporting of methods.

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Foa, 1995[24] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** 100%	**Attempt to mask outcome assessors?** Yes **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** Unclear **Any participants who started the trial excluded from analysis?** No	High Nonrandomized study with small sample size (N = 20). Attrition data NR. High risk of selection bias and confounding: participants matched on some variables but not all, and timing of outcomes differed by group.
Frappell-Cooke, 2010[25] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** 100%	**Attempt to mask outcome assessors?** NR **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** Unclear **Any participants who started the trial excluded from analysis?** No	High Nonrandomized study with high overall (24%) and differential (43%) attrition. Completers analysis only.

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Gelpin, 1996[26] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** Overall: NA G1: 69% G2: NA	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** Unclear **Any participants who started the trial excluded from analysis?** Unclear	High Unclear if only completers analysis used. Large risk of selection bias because administration of benzodiazepines based on clinician's evaluation of efficacy, side effects, distress level, and other characteristics like severity of trauma. Specific drug of choice (either alprazolam or clonazepam) administered in nonsystematic way. High risk of bias given likely effect of these issues on results because of small sample size (n=26).

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Grainger, 1997[21] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** NR	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** NA **Confounding adequately accounted for either through study design or statistical analysis?** Unclear	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Mixed **Method of Handling Dropouts** NA **Any participants who started the trial excluded from analysis?** Unclear	High Only 29% of participants receiving at least 1 session of EMDR included in analysis because only participants completing both baseline and posttreatment assessments analyzed. Inclusion criteria unclear (other than surviving Hurricane Andrew) and may have been established after treatment given to survivors. Unclear if only completers analysis used: only waitlist group completers reported. Unclear how late some participants might have first received treatment.

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Jotzo, 2005[27] **Prospective study design?** Yes	**Groups recruited from same source population?** No **Both groups recruited over same time period?** No **% completed treatment** NR	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** Unclear	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Unclear	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NR **Any participants who started the trial excluded from analysis?** Unclear	High No baseline PTSD data collected. Information about attrition, ITT, blinding, or confounding largely unavailable.
Krauseneck, 2010[28] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** Overall: 84% G1: NR G2: NR	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** Yes	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NR **Any participants who started the trial excluded from analysis?** No	High High risk of bias based primarily on unmeasured potential confounders: 1) Beta-blockers apparently administered postoperatively in Germany "according to a standard protocol"; 2) May be important clinical reasons for not giving beta-blockers to some patients (e.g., preoperative characteristics, such as history of asthma or COPD or postoperative course such as bradycardia, that could indicate illness severity after surgery;

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Krauseneck, 2010[28] (continued)						3) No discussion of how these potential confounders related to risk of PTSD symptoms.
Peres, 2011[29] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** NR	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** Unclear **Confounding adequately accounted for either through study design or statistical analysis?** Unclear	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** No **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NA **Any participants who started the trial excluded from analysis?** Unclear	High Not randomized, and attrition and number of subjects included in analysis NR. Impossible to determine similarity of original groups. Unclear how statistical analyses were conducted.

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Peris, 2011[30] **Prospective study design?** No	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** No **% completed treatment** NR	**Attempt to mask outcome assessors?** No **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NA **Any participants who started the trial excluded from analysis?** NR	High Nonrandomizated study with high overall (44%) and differential (16%) attrition. Study groups evaluated at two different time periods. Outcome assessment not blinded.
Richards, 2001[31] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Unclear **% completed treatment** NR	**Attempt to mask outcome assessors?** No **Differences between groups taken into account in statistical analysis?** No **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** Completers analysis **Any participants who started the trial excluded from analysis?** Unclear	High High overall attrition (50%). Unclear whether control group was concurrent.

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Rothbaum, 2008[32] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** No **% completed treatment** 100%	**Attempt to mask outcome assessors?** Unclear **Differences between groups taken into account in statistical analysis?** NR **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** Completers analysis **Any participants who started the trial excluded from analysis?** NR	High Nonrandomized study with small sample size (n=10). High overall attrition (20%). Completers analysis only. Possible statistically significant between-group differences at baseline (e.g., age, sex). No attempts to adjust for potential confounding from participants' trauma histories and whether previous traumas from adulthood or childhood. Participants not screened for ASD or PTSD at baseline when eligibility assessed.

Table F1. Risk of bias observational studies (continued)

Author, Year	Groups	Masked Statistical Analysis	Attrition	Miscellaneous	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Vaiva, 2003[33] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** Overall: 89% G1: 81% G2: 100%	**Attempt to mask outcome assessors?** Yes **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** Yes **Method of Handling Dropouts** NA **Any participants who started the trial excluded from analysis?** NR	High Attrition data NR and unclear how attrition handled in analysis. No baseline PTSD symptom data collected. Risk of selection bias due to participant self-selection into treatment groups, which is not addressed in analysis.
Vijayakumar, 2008[34] **Prospective study design?** Yes	**Groups recruited from same source population?** Yes **Both groups recruited over same time period?** Yes **% completed treatment** NR	**Attempt to mask outcome assessors?** No **Differences between groups taken into account in statistical analysis?** Yes **Confounding adequately accounted for either through study design or statistical analysis?** No	**Overall attrition ≥20%?** NR **Differential attrition ≥15%?** NR	**I/E criteria equally applied in both groups?** Yes **Time of follow-up equal in both groups?** Yes	**Outcome measures equal, valid and reliable?** No **Method of Handling Dropouts** Other **Any participants who started the trial excluded from analysis?** Unclear	High Attrition rates and method of handling dropouts NR. PTSD measure piloted for this study, but no validity data provided. Only one statistically significant baseline difference (illiteracy) taken into account in statistical analysis. Outcome assessors not blinded.

Abbreviations: COPD = chronic obstructive pulmonary disease; EMDR = Eye movement desensitization and reprocessing therapy; G = group; I/E = inclusion/exclusion; N = number of participants; NR = not reported; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table F2. Risk of bias RCTs

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Acierno, 2004[35]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Unclear **% completed treatment** Overall: 71% G1: NR G2: NR	**Outcome assessors masked?** No **Care providers masked?** No **Patients masked?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Unclear	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High No baseline PTSD ratings. High overall attrition (29%). Completers analysis only.
Adler, 2008[36]	**Randomization adequate?** Unclear **Allocation concealment adequate?** No	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** No **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High Randomization method not described, so impossible to determine how it affects risk of bias. High overall attrition (71%). Statistical approach to control for effect of attrition not sufficient to account for risk of bias due to attrition. No allocation concealment.
Adler, 2009[37]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** Overall: 46.1% G1: 46.2% G2: 48.1% G3: 44.3% G4: 46.0%	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** Multiple imputation	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	High Study staff masked at followup but not baseline. High overall attrition (>50%). ITT not sufficient to account for risk of bias due to attrition.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Beatty, 2010[1]	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes	**Groups similar at baseline?** Yes **% completed treatment** 100%	**Outcome assessors masked?** No **Care providers masked?** Unclear **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** Other	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	Medium Outcome assessors not masked, as outcomes were self-assessed.
Brom, 1993[38]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** NR	**Outcome assessors masked?** Unclear **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Unclear **Method of handling dropouts in ITT** Unclear	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	High Randomization process not described, so impossible to determine how it affects risk of bias. High overall attrition (20%), and unclear how attrition handled. Statistically significant group differences at baseline. Unclear if outcome assessors masked.
Bryant, 1998[4]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** Unclear	**Overall attrition ≥20%?** Unclear **Differential attrition ≥15%?** Unclear	**ITT used?** Unclear **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	Medium Some treatment adherence monitoring by the lead author (reviewed case notes and participant records). Sessions not audiotaped.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Bryant, 1999[20]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** Overall: 75.5% G1: NR G2: NR	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Unclear	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High High overall attrition (23%). Completers analysis only.
Bryant, 2003[3]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT used?** NA **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Medium No data reported on number of sessions completed per group. All participants retained through 6-month follow-up.
Bryant, 2003[39]	**Randomization adequate?** Yes **Allocation concealment adequate?** No	**Groups similar at baseline?** Unclear **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** LOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	High High overall attrition (49%) from end of parent studies (see Bryant et al., 1998 and Bryant et al., 1999).[4, 20] ITT not sufficient to account for high risk of bias due to attrition.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Bryant, 2005[5] Bryant, 2006[40]	**Randomization adequate?** Yes **Allocation concealment adequate?** No	**Groups similar at baseline?** Unclear **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** Yes **Method of handling dropouts in ITT** LOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Medium Bryant, 2005: Differential attrition 15%, 4%, and 19% for G1-G3, G1-G2, and G2-G3 differences, respectively. High overall attrition (21%). Bryant, 2006 (follow-up study to Bryant, 2005, above): High overall attrition (39%) from end of parent study. ITT not sufficient to account for high risk of bias due to attrition.
Bryant, 2008[2]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** Overall: 77% G1: 83% G2: 77% G3: 70%	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** LOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Low High overall attrition (30%), but ITT accounted for risk of bias due to attrition. Note on treatment fidelity: quality rating of 45 randomly seclected audiotaped sessions (17%) was 5.8 out of a 1-7 scale (1=unacceptable; 7=very good).

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Bugg, 2009[41]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Yes	**Groups similar at baseline?** No **% completed treatment** Overall: NR G1: 45.8% G2: NA	**Outcome assessors masked?** Unclear **Care providers masked?** NA **Patients masked?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** LOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NA	High High overall attrition (51% including postrandomization exclusions). Relatively large proportion not completing all three intervention sessions (31%). Statistically significant differences between groups by sex.
Campfield, 2001[6]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** NR	**Outcome assessors masked?** Unclear **Care providers masked?** Unclear **Patients masked?** Unclear	**Overall attrition ≥20%?** Unclear **Differential attrition ≥15%?** Unclear	**ITT used?** NR **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	Medium Unsure if attrition occurred or if ITT was conducted. Nature of the robbery and area of employment substantially different across groups, raising the possibility that there were other important differences across groups.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Crespo, 2010[42]	**Randomization adequate?** No **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** Overall: 74.6% G1: 71.4% G2: 76%	**Outcome assessors masked?** Unclear **Care providers masked?** NR **Patients masked?** NR	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High Randomization process at high risk for bias. High overall attrition (32%). Statistically significant baseline differences in education level, depression symptom levels, and reason for seeking treatment (exposure group's presenting reason more often violence than communication skills group).
Deahl, 2000[43]	**Randomization adequate?** No **Allocation concealment adequate?** NR	**Groups similar at baseline?** Yes, except for experience of extreme distress **% completed treatment** 100%	**Outcome assessors masked?** Yes **Care providers masked?** NR **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Unclear	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	High Not true randomization. High overall attrition (48%). Baseline data collected from only 64% of the whole sample before intervention. Unclear whether study used the same truly random samples for the postbaseline outcomes as at baseline. Data not available for all participants at all times but no reasons for missing data given.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Foa, 2006[44]	**Randomization adequate?** No **Allocation concealment adequate?** NR	**Groups similar at baseline?** No, but controlled for **% completed treatment** 73%	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** Yes **Method of handling dropouts in ITT** LOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	High High overall (27%) and differential attrition (SC vs. assessment-only: 16%). ITT not sufficient to account for risk of bias due to attrition.
Freyth, 2010[45]	**Randomization adequate?** No **Allocation concealment adequate?** NR	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** NR	**Overall attrition ≥20%?** Unclear **Differential attrition ≥15%?** Unclear	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	High Inadequate randomization. Attrition reported only for 4-year followup time point, and unclear at 3-month followup time point (last data collection point for all main outcomes). Unclear if all participants retained at posttreatment.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Gamble, 2005[7]	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes	**Groups similar at baseline?** Yes **% completed treatment** 100%	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Medium Many measures taken to reduce bias and only single case of attrition at 4-6 week timepoint, but potential confounding because no pre-screening for previous PTSD or other psychiatric disorders. Considerable sample size (N=103) and PTSD instrument modified to focus on childbirth as traumatic event.
Gidron, 2001[46]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** Yes	**Overall attrition ≥20%?** Unclear **Differential attrition ≥15%?** Unclear	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High No baseline PTSD measure. Method of randomization unclear. Attrition data not reported. In addition, no statistical correction for multiple comparisons. High risk of bias due to likely effects of these issues on results because of small sample size (n =17).

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Hobbs, 1996[47]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** 100%	**Outcome assessors masked?** NA **Care providers masked?** NA **Patients masked?** NR	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** Yes	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High High differential attrition (16%). Completers analysis only.
Holmes, 2007[48]	**Randomization adequate?** No **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Unclear **% completed treatment** Overall: NA G1: 53% G2: NA	**Outcome assessors masked?** Yes **Care providers masked?** NA **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** NR **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	High High overall (36%) and differential attrition (25%). No ITT reported.
Kenardy, 2008[49]	**Randomization adequate?** No **Allocation concealment adequate?** No	**Groups similar at baseline?** Unclear **% completed treatment** Overall: 63% G1: NR G2: NR	**Outcome assessors masked?** Unclear **Care providers masked?** Unclear **Patients masked?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** LOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High Inadequate randomization. Very high overall attrition (36%). ITT not sufficient to account for risk of bias from attrition.
Melnyk, 2004[8]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Unclear **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** Yes **Method of handling dropouts in ITT** Multiple imputation	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	Medium High overall (58%) and differential (16%) attrition, but ITT found that attrition did not change the results of the data pertaining to PTSD symptom severity.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Mulligan, 2012[9]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** No **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** Other (unspecified)	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	Medium 34% overall attrition and assessment not blinded, although no differences between completers and noncompleters found when ITT used.
O'Donnell, 2012[10]	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes	**Groups similar at baseline?** No **% completed treatment** G1: 75% G2: NA (Note: 57% received treatment for their mental health problems)	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** Unclear	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** Other (unspecified)	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Medium High overall attrition (26%) and unclear if patients blinded to treatment assignment. Multiple factors, including differential attrition <15%, use of adequate randomization, allocation concealment, and high treatment fidelity reduced risk of bias.
Pitman, 2002[50]	**Randomization adequate?** NR **Allocation concealment adequate?** NR	**Groups similar at baseline?** Yes **% completed treatment** 100%	**Outcome assessors masked?** NR **Care providers masked?** Yes **Patients masked?** Yes	**Overall attrition ≥20%?** Yes **Differential atttrition ≥15%?** Yes	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NA	High Small study sample with high overall (41%) and differential (15%) atttrion. Completers analysis only.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Resnick, 1999[51]	**Randomization adequate?** No **Allocation concealment adequate?** NR	**Groups similar at baseline?** Yes **% completed treatment** Overall: NA G1: 87% G2: NA	**Outcome assessors masked?** No **Care providers masked?** NA **Patients masked?** NR	**Overall attrition ≥20%?** Unclear **Differential attrition ≥15%?** Unclear	**ITT analyses used?** NR **Method of handling dropouts in ITT analysis** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NA	High Inadequate randomization. Outcome assessment not blinded. Difficult to assess differential attrition because the number of participants in each arm completing assesments varied by assessment and time point. Noncomparability of assessment schedules for one of the conditions.
Rose, 1999[11]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** Overall: 87% G1: NR G2: NR G3: NR	**Outcome assessors masked?** Unclear **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** Unclear	**ITT analyses used?** Yes **Method of handling dropouts in ITT analysis** BOCF	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	Medium ITT used as post-hoc rather than primary analysis, using baseline values for missing values which did not change results overall. Attrition <20% for 6 month follow-up, but >20% for 11 month follow-up). Large differences in sex and age after 16 across groups.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Rothbaum, 2012[12]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** Overall: NA G1: 26% G2: NA	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT analyses used?** Yes **Method of handling dropouts in ITT analysis** Multiple imputation	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Medium Multiple imputation used to account for missing values in total sample randomized. Note: high risk of bias for 12-week follow-up outcomes because of high overall attrition at that timepoint (>30%).
Ryding, 2004[13]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** Overall: 90.5%[a] G1: 92% G2: 89%	**Outcome assessors masked?** Unclear **Care providers masked?** Unclear **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT analyses used?** No **Method of handling dropouts in ITT analysis** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	Medium Attrition based on number of participants who completed the questionaire (not completion of group counseling sessions). Lack of baseline data collected soon or immediately post-trauma, which could obscure actual differences in change from baseline to 6 months.
Schelling, 2004[52]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** NR **Care providers masked?** No **Patients masked?** Yes	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT analyses used?** No **Method of handling dropouts in ITT analysis** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NA	High High overall (47%) and differential (15%) attrition, including post-randomization exclusions. Completers analysis only.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Schelling, 2001[53]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** Yes **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT analyses used?** No **Method of handling dropouts in ITT analysis** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NA	High High overall attrition (50%). Unclear if participants blinded in intital study.
Shalev, 2011[14]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** Attended all treatment sessions (G5 data not included here - see Comments) Overall: 63.9%[a] G1: 55.6% G2: 60.0% G3: 79.9% G4: 43.5% Partial completers (≥3 sessions and compliance with homework or medication) Overall: G1: 17.5% G2: 25.0% G3: 17.4% G4: 39.1%	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Medium Because this trial utilized equipoise-stratified samples, both nonstratified comparisons across groups and also group comparisons within strata reported. Data from stratified group not abstracted because group preference not of interest to this report and there is also some redundant reporting. Non-stratified completers analysis accounts for all groups. Note: G5 (delayed PE first provided after 5-month followup) was considered ineligible because of its timing and its outcomes and information are therefore not reported in the CER or here.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Shalev, 2011[14] (continued)							Participants in G3 & G4 arms masked to their condition. Groups overall similar at baseline although there were more female participants in the CT group than in the other groups (p<0.03), and there were higher PSS-SR scores in the SSRI group than in the other groups (p<0.02).
Sijbrandij, 2006[15]	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes	**Groups similar at baseline?** No **% completed treatment** Overall: 95% G1: 96% G2: 89% G3: 100%	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** NR	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** Yes	Low
Stein, 2007[54]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** Yes **Patients masked?** Yes	**Overall attrition ≥20%?** Unclear **Differential attrition ≥15%?** Unclear	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Mixed **Adequate treatment fidelity (therapist adherence) reported?** No	High ITT likely not conducted. No reporting of important baseline characteristics by treatment group or between-group comparisons. PCL-C outcomes not reported except in line graph.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Tecic, 2011[55]	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** NR **Care providers masked?** Yes **Patients masked?** Yes	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	High High overall (44%) and differential (22%) attrition. Unclear whether ITT used.
Treggiari, 2009[16]	**Randomization adequate?** Yes **Allocation concealment adequate?** Yes	**Groups similar at baseline?** Yes **% completed treatment** Overall: 75% G1: 76% G2: 74%	**Outcome assessors masked?** Yes **Care providers masked?** No **Patients masked?** Yes	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT analysis** Other (unspecified)	**Outcome measures equal, valid and reliable?** Mixed **Adequate treatment fidelity (therapist adherence) reported?** No	Medium Not sure how dropouts in ITT handled, not all that were randomized were included in analysis due to protocol violation (N=1) and withdrawal of consent (N=7).
Weis, 2006[17]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** No **% completed treatment** Overall: 78% G1: 74% G2: 82%	**Outcome assessors masked?** Unclear **Care providers masked?** Yes **Patients masked?** Yes	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** No	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	Medium Substantial difference in TISS score and duration of ICU stay at baseline between groups.

Table F2. Risk of bias RCTs (continued)

Author, Year	Randomization	Groups	Masked	Attrition	ITT	Outcomes	Risk of Bias Notes Explaining Risk of Bias
Wong, Under review[18]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** Overall: 80%[a] G1: 81% G2: 79%	**Outcome assessors masked?** Unclear **Care providers masked?** Unclear **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NA	Medium No ITT used, only completers analysis used. Note: outcome measure was self-report measure PCL, so outcome assessor not blinded to intervention; fidelity is not applicable in this case of a one time education video intervention.
Zatzick, In press[19]	**Randomization adequate?** Yes **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** Overall: 80.7%[a] G1: 83.6% G2: 77.7%	**Outcome assessors masked?** No **Care providers masked?** No **Patients masked?** No	**Overall attrition ≥20%?** No **Differential attrition ≥15%?** No	**ITT used?** Yes **Method of handling dropouts in ITT** Other (unspecified)	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** NR	Low
Zohar, 2011[56]	**Randomization adequate?** Unclear **Allocation concealment adequate?** Unclear	**Groups similar at baseline?** Yes **% completed treatment** NR	**Outcome assessors masked?** Yes **Care providers masked?** Unclear **Patients masked?** Yes	**Overall attrition ≥20%?** Yes **Differential attrition ≥15%?** Yes	**ITT used?** No **Method of handling dropouts in ITT** NA	**Outcome measures equal, valid and reliable?** Yes **Adequate treatment fidelity (therapist adherence) reported?** No	High High overall (32%) and differential (20%) attrition. Only p values for between-group CAPS score differences reported. Outcomes displayed in bar graphs, but mean scores and measures of variance not reported.

[a] Data calculated by authors of this report

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; BOCF = baseline observation carried forward; CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; CER = comparative effectiveness review; CI = confidence interval; CT = Cognitive therapy; G = group; ICU = intensive care unit; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event-Intrusion subscale; ITT = intent to treat analysis; LOCF = last observation carried forward; N = number of participants; NA = not applicable; NR = not reported; NS = not significant; PCL = PTSD Checklist; PCL-C = PTSD Checklist-Civilian Version; PE = prolonged

exposure therapy; PSS-SR = PTSD Symptom Scale-Self Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SSRI = selective serotonin reuptake inhibitor; TISS = Therapeutic Intervention Scoring System; WL = Waitlist

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Appendix G. Psychological, Pharmacological, and Emerging Interventions: Strength-of-Evidence Grades

Key Question 1.

Table G1. Cognitive behavioral therapy compared with an inactive comparator (usual care)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 6 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, CAPS, 9% vs. 55%, p<0.05	Insufficient
Incidence of PTSD at 12 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, CAPS, 21% vs. 58%, p<0.05	Insufficient
PTSD symptom severity at 6 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, CAPS total, 31.95 vs. 52.45, p<0.05	Insufficient
PTSD symptom severity at 12 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, CAPS total, 25.26 vs. 52.50, p<0.05; Cohen's d (95% CI) = 1.11 (0.34 to 1.88)	Insufficient
Incidence of major depression at 6 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, MINI MDE, 18% vs. 45%, p=NS	Insufficient
Incidence of major depression at 12 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, MINI MDE, 11% vs. 50%, p<0.05	Insufficient
Incidence of an anxiety disorder at 6 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, MINI, 18% vs. 30%, p=NS	Insufficient
Incidence of an anxiety disorder at 12 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, MINI, 11% vs. 7%, p=NS	Insufficient
Depression symptom severity at 6 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, BDI, 12.24 vs. 31.20, p<0.05	Insufficient
Depression symptom severity at 12 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, BDI, 13.95 vs. 29.00, p<0.05, Cohen's d = 1.45 (0.69 to 2.21)	Insufficient
Anxiety symptom severity at 6 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, HADS-A, 6.38 vs. 11.87, p<0.05	Insufficient
Anxiety symptom severity at 12 months: 1; 46; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. UC, HADS-A, 7.84 vs. 11.00, p<0.05, Cohen's d (95% CI) = 0.76 (0.06 to 1.46)	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient

Table G1. Cognitive behavioral therapy compared with an inactive comparator (usual care) (continued)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Downgraded due to lack of blinding

[b] Small sample size (< 300 observations)

Abbreviations: BDI = Beck Depression Inventory; CAPS = Clinician Administered PTSD Scale; CBT = Cognitive behavioral therapy; CI = confidence interval; HADS-A = Hospital Anxiety and Depression Scale-Anxiety subscale; MDE = Major Depressive Episode; MINI = Mini International Neuropsychiatric Interview; NA = not applicable; NS = not significant; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; UC = Usual care

Table G2. Cognitive therapy compared with an inactive comparator (waitlist)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[b]	CT vs. WL, CAPS-2, 63% vs. 77%, p=NR	Insufficient
Incidence of PTSD at 5 months: 1; 112; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CT vs. WL, CAPS, 20.0% vs. 58.7%, p=0.002	Insufficient
PTSD symptom severity at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[b]	CT vs. WL, CAPS-2 total, 43.0 vs. 55.9, p=NR; IES-I, 17.7 vs. 22.1, p=NR; IES-A, 17.1 vs. 22.6, p=NR	Insufficient
PTSD symptom severity at 5 months: 1; 112; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CT vs. WL, CAPS total, 29.5 vs. 50.6, p=NR; CAPS re-experiencing, 6.9 vs. 11.8, p=NR; CAPS avoidance, 12.1 vs. 22.3, p=NR; CAPS hyperarousal, 10.5 vs. 16.5, p=NR; PSS-SR total, 11.6 vs. 22.1, p=NR	Insufficient
Depression symptom severity at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[b]	CT vs. WL, BDI-2, 18.9 vs. 21.9; p=NS	Insufficient
Anxiety symptom severity at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[b]	CT vs. WL, BAI, 23.4 vs. 19.6, p=NS	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] No ITT; completer analysis of 133 randomized participants

[b] Small sample size (< 300 observations)

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; CI = confidence interval; CT = Cognitive therapy; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event-Intrusion subscale; ITT = intent to treat analysis; NA = not applicable; NR = not reported; NS = not significant; PSS-SR = PTSD Symptom Scale-Self Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; WL = Waitlist

Table G3. Debriefing compared with inactive control condition

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 2 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, SI-PTSD, data=NR[b], p=NR	Insufficient
Incidence of PTSD at 6 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, SI-PTSD, data=NR[b], p=NR	Insufficient
Incidence of PTSD at 6 months: 2; 341; RCT	1 Low; 1 Medium[c, d]	Consistent	Direct	Imprecise[e]	Debriefing vs. control, SI-PTSD, PSS-SR, data=NR[b], p=NR Debriefing vs. Assessment only, 23% vs. 26%, p=NS	Low
PTSD symptom severity at 2 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, SI-PTSD, Emotional debriefing (18.1), Educational debriefing (16.2), Control (15.9), p=NR[f]	Insufficient
PTSD symptom severity at 6 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, SI-PTSD, Emotional debriefing (14.4), Educational debriefing (11.9), Control (10.5), p=NR[f]	Insufficient
PTSD symptom severity at 6 months: 2; 341; RCT	1 Low; 1 Medium[c, d]	Consistent	Direct	Imprecise[g]	Debriefing vs. control, SI-PTSD, Emotional debriefing (10.2), Educational debriefing (9.3), Control (9.6), p=NR[f] Debriefing vs. Assessment only, PSS-SR: 13.8 vs. 13.0, p=NR; IES: 19.7 vs. 23.3, p=NR	Low
Depression symptom severity at 2 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, HADS-D, Emotional debriefing (5.7), Educational debriefing (4.7), Control (4.5), p=NR[f]	Insufficient
Depression symptom severity at 6 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, HADS-D, Emotional debriefing (4.3), Educational debriefing (3.3), Control (3.7), p=NR[f]	Insufficient
Depression symptom severity at 6 months: 2; 341; RCT	1 Low; 1 Medium[c, d]	Consistent	Direct	Imprecise[g]	Debriefing vs. control, HADS-D, Emotional debriefing (3.8), Educational debriefing (3.2), Control (3.2), p=NR[f] Debriefing vs. Assessment only, BDI, 12.1 vs. 13.9, p=NS	Low
Anxiety symptom severity at 2 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, HADS-A, Emotional debriefing (7.6), Educational debriefing (6.6), Control (6.4), p=NR[f]	Insufficient
Anxiety symptom severity at 6 weeks: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, HADS-A, Emotional debriefing (5.6), Educational debriefing (5.1), Control (4.7), p=NR[f]	Insufficient
Anxiety symptom severity at 6 months: 1; 236; RCT	Low	Unknown, single study	Direct	Imprecise[a]	Debriefing vs. control, HADS-A, Emotional debriefing (5.0), Educational debriefing (4.4), Control (4.6), p=NR[f]	Insufficient

Table G3. Debriefing compared with inactive control condition (continued)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility at 6 months: 1; 105; RCT	Medium[c, h]	Unknown, single study	Indirect	Imprecise[a]	Debriefing vs. Assessment only, data=NR, p=NS	Low

[a] Small sample size (< 300 observations)

[b] Text states "no significant differences between the three intervention groups"; however, the data are reported only for the sample as a whole (week 2 = 5.4%, week 6 = 4.9%; 6 month = 4.8%) rather than by treatment group

[c] Groups differed on some baseline measures; completer analysis for follow-up assessments

[d] Due to very high overall attrition (i.e., greater than 40% at 11-month followup) in one of these studies, we considered all of its outcomes collected at that timepoint as having a high risk of bias and therefore do not report them

[e] One study stated that incidence was not different between treatment groups; however, no data were reported to support this statement

[f] Mixed-model analysis performed on entire sample indicated no group differences; however, no pairwise post-hoc comparisons were reported

[g] Different instruments used to assess symptoms

[h] Due to very high overall attrition (i.e., greater than 40% at 11-month followup) in this study, we considered all of its outcomes collected at that timepoint as having a high risk of bias and therefore do not report them

Abbreviations: BDI = Beck Depression Inventory; CAPS = Clinician Administered PTSD Scale; CI = confidence interval; HADS-A = Hospital Anxiety and Depression Scale-Anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale-Depression subscale; IES = Impact of Event Scale; NA = not applicable; NR = not reported; NS = not significant; PSS-SR = Post-traumatic Symptom Scale - Self-Report; PTSD = posttraumatic stress disorder; RCT = Randomized control trial; SI-PTSD = Structured Interview for PTSD; UC = Usual care

Table G4. Prolonged exposure compared with inactive control condition

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 4 weeks: 1; 137; RCT	Medium	Unknown, single study	Direct	Imprecise[b]	PE vs. Assessment only, PSS-I, 41% vs. 51%, p=0.60	Insufficient
Incidence of PTSD at end of treatment: 1; 60; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	PE vs. WL, CAPS-2, 33% vs. 77%, p<0.001	Insufficient
Incidence of PTSD at 5 months: 1; 128; RCT	Medium[c]	Unknown, single study	Direct	Imprecise[b]	PE vs. WL, CAPS, 21.6% vs. 57.1%, p<0.003[d]	Insufficient
PTSD symptom severity at end of treatment: 1; 60; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	PE vs. WL, CAPS-2 total, 31.5 vs. 55.9, p<0.001; IES-I, 12.4 vs. 22.1, p<0.002; IES-A, 11.7 vs. 22.6, p<0.001	Insufficient
PTSD symptom severity at 5 months: 1; 135; RCT		Unknown, single study	Direct	Imprecise[b]	PE vs. WL, CAPS total, 28.6 vs. 50.6, p=NR; CAPS re-experiencing, 7.3 vs. 11.8, p=NR; CAPS avoidance, 11.4 vs. 22.3, p=NR; CAPS hyperarousal, 9.9 vs. 16.5, p=NR; PSS-SR total, 11.0 vs. 22.1, p=NR	Insufficient
Incidence of depression at 4 weeks: 1; 137	Medium	Unknown, single study	Direct	Imprecise[b]	PE vs. Assessment only, BDI-2 > 13, 49% vs. 68%, p=0.08	Insufficient
Depression symptom severity at 4 weeks: 1; 137	Medium	Unknown, single study	Direct	Imprecise[b]	PE vs. Assessment only, BDI-2, 15.4 vs. 21.4, p<0.05	Insufficient
Depression symptom severity at end of treatment: 1; 60; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	PE vs. WL, BDI-2, 12.1 vs. 21.9, p=0.03	Insufficient
Anxiety symptom severity at end of treatment: 1; 60; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	PE vs. WL, BAI, 13.4 vs. 19.6, p=0.03	Insufficient
Incidence of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient

Table G4. Prolonged exposure compared with inactive control condition (continued)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Attrition was high for the study overall (> 20%) and differed across groups by > 15%

[b] Small sample size (< 300 observations)

[c] No ITT; completer analysis of 156 randomized participants; high attrition; differential attrition across groups

[d] Stratified pairwise comparison

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; CAPS/CAPS-2 = Clinician Administered PTSD Scale/Clinician Administered PTSD Scale-2; CI = confidence interval; CR = Cognitive restructuring; CT = Cognitive therapy; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event-Intrusion subscale; ITT = intent to treat analysis; NA = not applicable; NR = not reported; NS = not significant; PE = Prolonged exposure therapy; PSS-I = PTSD Symptom Scale-Interview; PSS-SR = PTSD Symptom Scale-Self-Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; WL = Waitlist

Table G5. Psychoeducation compared with inactive control condition

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 1 month: 1; 79; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. control, PCL, 46% vs. 51%	Insufficient
Incidence of PTSD at 6 months: 1; 103; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. Assessment only, PSS-SR, 11% vs. 26%, p=NR	Insufficient
PTSD symptom severity at 6 months: 1; 103; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. Assessment only, PSS-SR, 10.9 vs. 13.0, p=NR; IES, 16.7 vs. 23.3, p=NR	Insufficient
Depression symptom severity at 6 months: 1; 103; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. Assessment only, BDI, 9.8 vs. 13.9, p=NR	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Groups differed on some baseline measures; completer analysis for follow-up assessments

[b] Due to very high overall attrition (i.e., greater than 40% at 11-month followup) in this study, we considered all outcomes collected at that timepoint as having a high risk of bias and therefore do not report them

[c] Small sample size

Abbreviations: BDI = Beck Depression Inventory; CI = confidence interval; IES = Impact of Event Scale; NA = not applicable; NR = not reported; NS = Not significant; PCL = = PTSD Checklist; PSS-SR = Post-traumatic Stress Disorder Symptom Scale-Self-Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G6. Self Help Booklet compared with an inactive comparator (Information Booklet)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity at 3 month follow-up: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, PSDS-SR, 5.43 vs. 9.46; PSDS-SR change, Cohen's d = -0.59 vs. -0.16, p<0.05	Insufficient
PTSD symptom severity at 6 month follow-up: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, PSDS-SR, 6.78 vs. 8.98; PSDS-SR change, Cohen's d = -0.47 vs. -0.13, p=NR	Insufficient
Depression symptom severity at 3 months: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, DASS-Depression, 7.8 vs. 7.0, p=NR	Insufficient
Depression symptom severity at 6 months: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, DASS-Depression, 8.1 vs. 6.4, p=NR	Insufficient
Anxiety symptom severity at 3 months: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, DASS-Anxiety, 7.5 vs. 7.2, p=NR	Insufficient
Anxiety symptom severity at 6 months: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, DASS-Anxiety, 8.0 vs. 7.0, p=NR	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NB	NA	Insufficient
Quality of Life at 3 months: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, Global QOL, 66.6 vs. 67.8, p=NR	Insufficient
Quality of Life at 6 months: 1; 49; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SHB vs. Information only control, Global QOL, 69.0 vs. 72.2, p=NR	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unblinded

[b] Small sample size (< 300 observations)

Abbreviations: CI = confidence interval; DASS = Depression Anxiety and Stress Scale-21; Info = Information booklet; NA = not applicable; NR = not reported; PSDS-SR = Posttraumatic Stress Diagnostic Scale-Self Report; PTSD = posttraumatic stress disorder; QOL = Quality of life (European Organisation for Research and Treatment of Cancer quality of life core questionnaire); RCT = randomized controlled trial; SHB = Self-help booklet

Table G7. Stepped collaborative care intervention compared with usual care

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 12 months: 1; 207; RCT	Low	Unknown, single study	Direct	Imprecise[a]	CC vs. UC, CAPS, OR (95% CI) = 1.39 (0.77 to 2.51), p<0.05	Insufficient
PTSD symptom severity at 1 month; 1; 207; RCT	Low	Unknown, single study	Direct	Imprecise[a]	CC vs. UC, PCL-C total, 50.2 vs. 51.1, p=NS	Insufficient
PTSD symptom severity at 3 months; 1; 207; RCT	Low	Unknown, single study	Direct	Imprecise[a]	CC vs. UC, PCL-C total, 45.9 vs. 48.6, p=NS	Insufficient
PTSD symptom severity at 6 months: 1; 207; RCT	Low	Unknown, single study	Direct	Precise	CC vs. UC, CAPS total, 42.9 vs. 56.7, p<0.01 CC vs. UC, PCL-C total, 40.6 vs. 49.9, p<0.01	Low
PTSD symptom severity at 9 months: 1; 207; RCT	Low	Unknown, single study	Direct	Precise	CC vs. UC, PCL-C total, 40.2 vs. 45.5, p<0.01;	Low
PTSD symptom severity at 12 months: 1; 207; RCT	Low	Unknown, single study	Direct	Precise	CC vs. UC, CAPS total, 38.6 vs. 47.2, p<0.05 CC vs. UC, CAPS group-by-time interaction, greater decrease in PTSD severity in CC (p<0.01) CC vs. UC, PCL-C total, 37.4 vs. 42.5, p<0.05 CC vs. UC, PCL-C group-by-time interaction, greater decrease in PTSD severity in CC (p<0.001)	Low
Severity of major depression at 12 months: 1; 207; RCT	Low	Unknown, single study	Direct	Imprecise[a]	CC vs. UC, PHQ-9, 8.4 vs. 10.1, p=NS	Insufficient
Alcohol use at 12 months: 1; 207; RCT	Low	Unknown, single study	Direct	Imprecise[a]	CC vs. UC, AUDIT, 2.0 vs. 2.4, p=NS	Insufficient
Functional impairment at 12 months: 1; 207; RCT	Low	Unknown, single study	Direct	Imprecise[a]	CC vs. UC, SF-36, 43.7 vs. 41.2, p=NS	Insufficient

[a] Not statistically significant

Abbreviations: AUDIT = Alcohol Use Disorders Identification Test; CAPS = Clinician Administered PTSD Scale; CC = collaborative care; NA = not applicable; NS = not significant; OR = odds ratio; PCL-C = PTSD Checklist-Civilian Version; PHQ-9 = Patient Health Questionnaire-9 item version; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SF-36 = 36-item Medical Outcomes Study Short Form; UC = usual care

Table G8. Supportive counseling compared with inactive control condition

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 4-6 weeks: 1; 103; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, MINI-PTSD, 34% vs. 30%, p=NS, RR (95% CI) = 1.15 (0.66 to 2.02)	Insufficient
Incidence of PTSD at 3 months: 1; 103; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, MINI-PTSD, 6% vs. 17%, p=NS, RR (95% CI) = 0.35 (0.10 to 1.23)	Insufficient
PTSD symptom severity at 1 month: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, PHSI-P, 7.2 vs. 7.3, p=NR	Insufficient
PTSD symptom severity at 3 months: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, PHSI-P, 6.4 vs. 7.5, p=NR	Insufficient
PTSD symptom severity at 6 months: 2; 336; RCT	Medium[a] Medium[a]	Consistent	Direct	Imprecise[d]	SC vs. control, PHSI-P, 5.8 vs. 7.2, p=NS; IES, 12.0 vs. 15.5, p=NS	Insufficient
PTSD symptom severity at 12 months: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, PHSI-P, 5.9 vs. 7.9, p<0.05	Insufficient
Depression symptom severity at 4-6 weeks: 1; 103; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, EPDS > 12, 32% vs. 34%, p=NR	Insufficient
Depression symptom severity at 1 month: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, POMS depression subscale, 2.6 vs. 4.1, p<0.05	Insufficient
Depression symptom severity at 3 months: 2; 277; RCT	Medium[a] Medium[a, c]	Inconsistent	Direct	Imprecise[b, d]	SC vs. control, DASS-Depression >13, 6% vs. 26%, RR (95% CI) = 0.23 (0.07 to 0.76); EPDS > 12, 8% vs. 32%, p=0.002, RR (95% CI) = 0.25 (0.09 to 0.69); POMS depression subscale, 3.3 vs. 4.2, p=NS	Low
Depression symptom severity at 6 months: 2; 277; RCT	Medium[a] Medium[a, c]	Inconsistent	Direct	Imprecise[b, d]	SC vs. control, POMS depression subscale, 2.0 vs. 3.9, p<0.05; EPDS, 6.0 vs. 6.0, p=NS	Low
Depression symptom severity at 12 months: 1; 174; RCT	Medium[a, c]	Unknown, singe study	Direct	Imprecise[b]	SC vs. control, POMS depression subscale: 2.5 vs. 3.6, p=NS	Insufficient
Anxiety symptom severity at 1 month: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, STAI, 35.7 vs. 39.8, p=NS	Insufficient
Anxiety symptom severity at 3 months: 2; 277; RCT	Medium[a] Medium[a, c]	Consistent	Direct	Imprecise[b, d]	SC vs. control, DASS-Anxiety > 9, 2% vs. 11%, p=NR, RR (95% CI) = 0.18 (0.02 to 1.45); STAI, 38.4 vs. 40.7, p=NS	Low
Anxiety symptom severity at 6 months: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, STAI, 36.0 vs. 39.1, p=NS	Low

Anxiety symptom severity at 12 months: 1; 174; RCT	Medium[a, c]	Unknown, single study	Direct	Imprecise[b]	SC vs. control, STAI, 35.8 vs. 40.9, p<0.01	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient

Table G8. Supportive counseling compared with inactive control condition (continued)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility at 3 months: 1; 50	Medium[a]	Unknown, single study	Direct	Imprecise[b]	86% rated the perceived utility of SC as 8 or higher on a 10-point scale	Insufficient
Perceived utility at 6 months: 1; 58; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	71% reported SC completely met their expectation, and 60% reported SC fulfilled the main purpose	Insufficient

[a] Completer analysis only

[b] Small sample size (< 300 observations)

[c] High (> 20%) attrition overall; high (> 15%) differential attrition between groups

Abbreviations: CI = confidence interval; DASS = Depression Anxiety and Stress Scale-21; EPDS = Edinburgh Postnatal Depression Scale; IES = Impact of Event Scale; MINI-PTSD = Mini-International Neuropsychiatric Interview-Post-Traumatic Stress Disorder; NA = not applicable; NR = not reported; NS = not significant; PHSI-P = Post-Hospital Stress Index for Parents; POMS = Profile of Mood States; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; RR = relative risk; SC = Supportive counseling; STAI = State-Trait Anxiety Inventory

Table G9. Hydrocortisone compared with placebo

Outcome: Number of Studies, Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 1; 28; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Hydrocortisone vs. placebo, PTSS-10, 7.1% vs. 21.4%, p=NR	Insufficient
PTSD symptom severity at 6 months[a]: 1; 28; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Hydrocortisone vs. placebo, PTSS-10 median rank, 15.5 vs. 25.5, p=0.03	Insufficient
Incidence and severity of psychological symptoms at 6 months: 1; 28; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Hydrocortisone vs. placebo, Unnamed structured and validated questionnaire, no significant difference between groups in number and type of traumatic memories, p≤0.33	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life at 6 months: 1; 28; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Hydrocortisone vs. placebo, SF-36 physical function, 85 vs. 38, p=0.01; Pain, 25 vs. 0, p=0.01; general health perception, 72 vs. 60, p<0.01; vitality, 58 vs. 40, p<0.01; mental health, 80 vs. 64, p=0.01	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Groups different at baseline on some measures; high (> 20%) overall attrition

[b] Small sample size (< 300 observations)

Abbreviations: CI = confidence interval; NA = not applicable; NR = not reported; PTSD = posttraumatic stress disorder; PTSS-10 = Posttraumatic Stress Symptom 10 Question Inventory; RCT = randomized controlled trial; SF-36 = Medical Outcomes Study Health Survey – Short Form-36

Table G10. SSRI (Escitalopram) compared with inactive control condition

Outcome: Number of Studies, Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 5 months: 1; 39; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Escitalopram vs. placebo, CAPS, 55.6% vs. 61.9%, OR (95% CI) = 0.77 (0.21 to 2.77), p=NS[c] Escitalopram vs. WL, CAPS, 61.9% vs. 58.2%, p=NS	Insufficient
Incidence of PTSD 9 months: 1; 36; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Escitalopram vs. placebo, CAPS, 42.1% vs. 47.1%, p=NR	Insufficient
PTSD symptom severity at 5 months: 1; 39; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Escitalopram vs. placebo, CAPS total, 48.7 vs. 47.1, p=NR Escitalopram vs. WL, CAPS total, 48.7 vs. 50.6, p=NR	Insufficient
PTSD symptom severity at 9 months: 1; 36; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	Escitalopram vs. placebo, CAPS total, 47.1 vs. 45.7, p=NR	Insufficient
Incidence and severity of psychological symptoms: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] High (> 20%) overall attrition; completer analysis only of 46 randomized

[b] Small sample size (< 300 observations)

[c] Stratified pairwise comparison

Abbreviations: CAPS = Clinician Administered PTSD Scale; CI = confidence interval; CT = Cognitive therapy; NA = not applicable; NR = not reported; NS = not significant; OR = odds ratio; PSS-SR = PTSD Symptom Scale-Self Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SSRI = Selective serotonin reuptake inhibitor; WL = waitlist

Table G11. Battlemind training compared with a standard post-deployment brief

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
PTSD symptom severity at 4-6 months: 1; 2,443; RCT	Medium	Unknown, single study	Direct	Imprecise	Battlemind training not different than standard care, PCL-C, coefficient (SE) = -0.00 (0.02), p=NR	Insufficient
Incidence of major or other depression at 4-6 months: 1; 2,443; RCT	Medium	Unknown, single study	Direct	Imprecise	Battlemind training not different than standard care, PHQ-9, Adjusted OR (95% CI) = 1.12 (0.71 to 1.77), p=NR	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility at end of treatment: 1; 1,741; RCT	Medium	Unknown, single study	Direct	Imprecise	Battlemind training not different than standard care, 75.4% vs. 75.8%, p=0.76	Insufficient
Perceived utility at 4-6 months: 1; 1,069; RCT	Medium	Unknown, single study	Direct	Imprecise	Battlemind training not different than standard care, 68.7% vs. 65.7%, p=0.35	Insufficient

Abbreviations: CI = confidence interval; NA = not applicable; NR = not reported; OR = odds ratio; PCL-C = PTSD Checklist-Civilian Version; PHQ-9 = Patient Health Questionnaire-9 item version; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SE = standard error

Table G12. Cognitive behavioral therapy compared with cognitive behavioral therapy + hypnosis

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at end of treatment: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, CAPS-2, 36% vs. 30%, p=NR	Insufficient
Incidence of PTSD at 6 months: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, CAPS-2, 42% vs. 40%, p=NR	Insufficient
PTSD symptom severity at end of treatment: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, IES-I, 16.58 vs. 11.30, p<0.05; *G*[c] = 1.55 vs. 2.23	Insufficient
PTSD symptom severity at 6 months: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, IES-I, 16.97 vs. 13.57, p=NR; *G*[c] = 1.72 vs. 1.69	Insufficient
Depression symptom severity at end of treatment: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, BDI-2, 13.24 vs. 11.37, p=NR	Insufficient
Depression symptom severity at 6 months: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, BDI-2, 14.61 vs. 13.57, p=NR	Insufficient
Anxiety symptom severity at end of treatment: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, BAI, 14.91 vs. 15.47, p=NR	Insufficient
Anxiety symptom severity at 6 months: 1; 63; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT vs. CBT+Hypnosis, BAI, 15.67 vs. 17.07, p=NR	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] High (> 20%) overall attrition; high (> 15%) differential attrition between groups

[b] Small sample size

[c] Hodges *G* effect size

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; CAPS-2 = Clinician Administered PTSD Scale-2; CBT = Cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; CI = confidence interval; IES-I = Impact of Event-Intrusion subscale; NA = not applicable; NR = not reported; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G13. Cognitive behavioral therapy compared with supportive counseling

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at end of treatment: 3; 105; RCT	Medium[a]	Consistent	Direct	Imprecise[b]	CIDI-PTSD, CAPS, RR (95% CI) = 0.27 (0.05 to 1.29) favors CBT	Low
Incidence of PTSD at 6 months: 3; 105; RCT	Medium[a]	Consistent	Direct	Imprecise[c]	CIDI-PTSD, CAPS, RR (95% CI) = 0.46 (0.21 to 1.01) favors CBT	Low
PTSD symptom reduction at end of treatment: 3; 105; RCT	Medium[a]	Consistent	Direct	Precise[d]	IES-I, WMD -7.85 (-11.18 to -4.53) favors CBT	Moderate
PTSD symptom reduction at 6 months: 3; 105; RCT	Medium[a]	Consistent	Direct	Precise[e]	IES-I, WMD -8.19 (-11.79 to -4.58) favors CBT	Moderate
PTSD symptom reduction at end of treatment: 3; 105; RCT	Medium[a]	Consistent	Direct	Precise[f]	IES-A, WMD -14.04 (-19.37 to -8.71) favors CBT	Moderate
PTSD symptom reduction at 6 months: 3; 105; RCT	Medium[a]	Consistent	Direct	Precise[g]	IES-A, WMD -9.94 (-15.06 to -4.83) favors CBT	Moderate
Depression symptom reduction at end of treatment: 3; 105; RCT	Medium[a]	Inconsistent	Direct	Imprecise[h]	BDI-2, SMD -0.15 (-0.53 to 0.24)	Low
Depression symptom reduction at 6months: 3; 105; RCT	Medium[a]	Inconsistent	Direct	Imprecise[i]	BDI-2, SMD -0.21 (-0.70 to 0.27)	Low
Anxiety symptom reduction at end of treatment: 3; 105; RCT	Medium[a]	Consistent	Direct	Imprecise[j]	BAI, STAI, SMD -0.25 (-0.64 to 0.13)	Moderate
Anxiety symptom reduction at 6 months: 3; 105; RCT	Medium[a]	Consistent	Direct	Imprecise[k]	BAI, STAI, SMD -0.28 (-0.67 to 0.11)	Moderate
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Reasons for downgrading include lack of reporting on number of treatment sessions completed (1 study), high (> 20%) overall attrition rate (1 study), unclear randomization scheme (1 study)

[b] Although the direction of effects was consistent, the meta-analysis had considerable statistical heterogeneity (I^2=71.8%), reflecting the fact that two of the three medium risk of bias trials found large magnitudes of benefit but one medium risk of bias study found no difference between treatment groups. When we repeated the analysis including an

additional high risk of bias study that found a small benefit, the heterogeneity was reduced (I^2=58.78%). Even though the direction of effect was consistent across trials, we rated the findings as imprecise and thus graded the SOE as low rather than moderate.

[c] Although the direction of effects was consistent, the meta-analysis had considerable statistical heterogeneity (I^2=44.9%), reflecting the fact that two of the three medium risk of bias trials found large magnitudes of benefit but one medium risk of bias study found no difference between treatment groups. When we repeated the analysis including an additional high risk of bias study that found a small benefit, the heterogeneity was reduced (I^2=32.0%). Even though the direction of effect was consistent across trials, we rated the findings as imprecise and thus graded the SOE as low rather than moderate.

[d] The analysis found very low statistical heterogeneity (I^2=1.3%) and a subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a slightly larger benefit of CBT (WMD, -8.39; 95% CI, -11.45 to -5.34) with no statistical heterogeneity (I^2=0.0%), increasing our confidence in the finding of a moderate effect size and finding a consistent, precise result.

[e] The analysis found very low statistical heterogeneity (I^2=6.8%). A subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a slightly smaller benefit of CBT (WMD, -7.91; 95% CI, -10.85 to -4.98) with no statistical heterogeneity (I^2=0.0%), reinforcing our confidence in the finding of a moderate effect size and a consistent, precise result.

[f] Although the direction of the effect was consistent, the analysis found moderate statistical heterogeneity (I^2=53.8%). A subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a slightly larger benefit of CBT (WMD, -14.17; 95% CI, -17.82 to -10.51) with reduced statistical heterogeneity (I^2=31.9%), reinforcing our confidence in the finding of a large effect size and a consistent, precise result.

[g] Although the direction of the effect was consistent , the analysis found moderate statistical heterogeneity (I^2=44.0%). A subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a slightly larger benefit of CBT (WMD, -11.49; 95% CI, -16.09 to -6.90) albeit with greater statistical heterogeneity (I^2=52.7%), which did not substantively change our confidence in the finding of a large effect size and a consistent, precise result.

[h] The analysis found no statistical heterogeneity (I^2=0.0%) and the direction of effect was not consistent across trials ranging from a very low effect size in favor of SC to a moderate effect size in favor of CBT. A subsequent sensitivity analysis (n=136) including one high risk of bias study indicated lower statistical heterogeneity (I^2=0.0%) and a slightly larger but still insignificant benefit of CBT (SMD, -0.22; 95% CI, -0.56 to 0.12).

[i] The analysis found moderate statistical heterogeneity (I^2=30.0%) and the direction of effect was not consistent across trials. A subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a slightly larger but still insignificant benefit of CBT (SMD, -0.25; 95% CI, -0.62 to 0.12) with low statistical heterogeneity (I^2=10.1%).

[j] The analysis found no statistical heterogeneity (I^2=0.0%) and a subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a slightly larger but still insignificant benefit of CBT (SMD, -0.39; 95% CI, -0.74 to -0.04) with very low statistical heterogeneity (I^2=2.2%).

[k] The analysis found no statistical heterogeneity (I^2=0.0%) and a subsequent sensitivity analysis (n=136) including one high risk of bias study indicated a larger but still insignificant benefit of CBT (SMD, -0.59; 95% CI, -1.16 to -0.01) with very low statistical heterogeneity (I^2=2.2%).

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; CAPS = Clinician Administered PTSD Scale; CBT = Cognitive behavioral therapy; CI = confidence interval; CIDI-PTSD = Composite International Diagnostic Interview PTSD Module; CT = Cognitive therapy; IES-A = Impact of Event-Avoidance subscale; IES-I = Impact of Event-Intrusion subscale; n = number of participants; NA = not applicable; NS = Not significant; OR = Odds ratio; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; RR = risk ratio; SC = Supportive counseling; SMD = standardized mean difference; SOE = strength of evidence; STAI = State-Trait Anxiety Inventory; WMD = weighted mean difference

Table G14. Cognitive behavioral therapy + hypnosis compared with supportive counseling

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at end of treatment: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, CAPS-2, 30% vs. 50%, p=NR	Insufficient
Incidence of PTSD at 6 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, CAPS-2, 40% vs. 58%, p=NR	Insufficient
PTSD symptom severity at end of treatment: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, IES-I, 11.30 vs. 19.83, p<0.05	Insufficient
PTSD symptom severity at 6 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, IES-I, 13.57 vs. 20.21, p<0.05	Insufficient
Severity of depressive symptoms at end of treatment: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, BDI-2, 11.37 vs. 14.96, p=NR	Insufficient
Severity of depressive symptoms at 6 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, BDI-2, 13.57 vs. 16.29, p=NR	Insufficient
Severity of anxiety symptoms at end of treatment: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, BAI, 15.47 vs. 20.25, p=NR	Insufficient
Severity of anxiety symptoms at 6 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CBT+Hypnosis vs. SC, BAI, 17.07 vs. 21.13, p=NR	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	NA
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] High (> 20%) overall attrition; high (> 15%) differential attrition between groups; no data reported on # of sessions completed per group

[b] Small sample size (< 300 observations)

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; CAPS-2 = Clinician Administered PTSD Scale-2**;** CBT = Cognitive behavioral therapy; CBT+Hypnosis = CBT combined with hypnosis; CI = confidence interval; IES-I = Impact of Event Scale - Intrusion subscale; NA = not applicable; NR = not reported; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SC = Supportive counseling

Table G15. Cognitive therapy compared with prolonged exposure therapy

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS-2, 33% vs. 63%, p=0.002: OR (95% CI) = 2.52 (1.28 to 4.93)	Insufficient
Incidence of PTSD at 5 months: 1; 87; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS, 21.6 vs. 20.0: OR (85% CI) = 0.87 (0.29 to 2.62)], p=0.83[c]	Insufficient
Incidence of PTSD at 6 months: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS-2, 37% vs. 63%, p=0.007; OR (95% CI) = 2.10 (1.12 to 3.94); NNT=3.75	Insufficient
Incidence of PTSD at 9 months: 1; 87; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS, 21.2% vs. 22.9%, p=NR	Insufficient
PTSD symptom severity at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS-2 total, 31.5 vs. 43.0, p=NR, Cohen's d = 0.42 (-0.09 to 0.92); IES-I, 12.4 vs. 17.7, p=NR, Cohen's d = 0.44 (-0.07 to 0.95); IES-A, 11.7 vs. 17.1, p=NR, Cohen's d = 0.43 (-0.08 to 0.94)	Insufficient
PTSD symptom severity at 5 months: 1; 89; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS total, 28.59 vs. 29.48, p=NR; CAPS re-experiencing, 7.32 vs. 6.85, p=NR; CAPS avoidance, 11.36 vs. 12.12, p=NR; CAPS hyperarousal, 9.91 vs. 10.52, p=NR	Insufficient
PTSD symptom severity at 6 months: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS-2 total, 32.1 vs. 49.8, p=NR, Cohen's d = 0.60 (0.08 to 1.11); IES-I, 11.4 vs. 18.6, p=NR, Cohen's d = 0.63 (0.11 to 1.15); IES-A, 12.8 vs. 19.2, p=0.03, Cohen's d = 0.44 (-0.02 to 1.01)	Insufficient
PTSD symptom severity at 9 months: 1; 87; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, CAPS total: 27.52 vs. 27.89, p=NR; CAPS re-experiencing: 6.67 vs. 5.57, p=NR; CAPS avoidance: 11.21 vs. 12.97, p=NR; CAPS hyperarousal: 9.63 vs. 9.34, p=NR	Insufficient
Depression symptom severity at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, BDI-2, 12.1 vs. 18.9, p=NR, Cohen's d = 0.54 (0.01 to 1.05)	Insufficient
Depression symptom severity at 6 months: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, BDI-2, 12.4 vs. 20.4, p=NR, Cohen's d = 0.60 (0.09 to 1.12)	Insufficient

Anxiety symptom severity at end of treatment: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, BAI, 13.4 vs. 23.4, p=0.008, Cohen's d = 0.67 (0.15 to 1.19)	Insufficient
Anxiety symptom severity at 6 months: 1; 60; RCT	Low	Unknown, single study	Direct	Imprecise[a]	PE vs. CT, BAI, 12.8 vs. 23.3, p=NR, Cohen's d = 0.63 (0.11 to 1.15)	Insufficient

Table G15. Cognitive therapy compared with prolonged exposure therapy (continued)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Small sample size (< 300 observations)

[b] Completer analysis of 103 randomized participants

[c] Stratified pairwise group comparison

Abbreviations: BAI = Beck Anxiety Inventory; BDI-2 = Beck Depression Inventory-2; CAPS = Clinician Administered PTSD Scale; CAPS-2 = Clinician Administered PTSD Scale-2; CI = confidence interval; CT = Cognitive therapy; IES-A = Impact of Event Scale - Avoidance subscale; IES-I = Impact of Event Scale - Intrusion subscale; NA = not applicable; NNT = number needed to treat; NR = not reported; OR = odds ratio; PE = Prolonged exposure therapy; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G16. Debriefing compared with an active control condition (debriefing)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 2 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Data=NR, p=NR[b]	Insufficient
Incidence of PTSD at 6 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Data=NR, p=NR[b]	Insufficient
Incidence of PTSD at 6 months: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Data=NR, p=NR[b]	Insufficient
PTSD symptom severity at 2 weeks[c]: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, SI-PTSD, 18.1 vs. 16.2, p=NR[c]	Insufficient
PTSD symptom severity at 6 weeks[c]: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, SI-PTSD, 14.4 vs. 11.9, p=NR[c]	Insufficient
PTSD symptom severity at 6 months: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, SI-PTSD, 10.2 vs. 9.3, p=NR[c]	Insufficient
Depression symptom severity at 2 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, HADS-D, 5.7 vs. 4.7, p=NR[c]	Insufficient
Depression symptom severity at 6 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, HADS-D, 4.3 vs. 3.3, p=NR[c]	Insufficient
Depression symptom severity at 6 months: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, HADS-D, 3.8 vs. 3.2, p=NR[c]	Insufficient
Anxiety symptom severity at 2 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, HADS-A, 7.6 vs. 6.6, p=NR[c]	Insufficient
Anxiety symptom severity at 2 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, HADS-A, 5.6 vs. 5.1, p=NR[c]	Insufficient
Anxiety symptom severity at 2 weeks: 1; 155	Low	Unknown, single study	Direct	Imprecise[a]	Emotional debriefing vs. Educational debriefing, HADS-A, 5.0 vs. 4.4, p=NR[c]	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient

Table G16. Debriefing compared with an active control condition (debriefing) (continued)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Small sample size (< 300 observations)

[b] Data are reported for the entire sample (week 2 = 5.4%, week 6 = 4.9%; 6 month = 4.8%) rather than by treatment group; the text indicates 'no significant differences' between groups

[c] Mixed-model analysis performed on entire sample including a control treatment group indicated no group differences; however, no pairwise post-hoc comparisons were reported

Abbreviations: CI = confidence interval; HADS-A = Hospital Anxiety and Depression Scale–Anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale–Depression subscale; NA = not applicable; NR = not reported; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SI-PTSD = Structured Interview for PTSD

Table G17. Psychoeducation compared with an active control condition (Debriefing combined with psychoeducation)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 6 months: 1; 106; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. Debriefing combined with psychoeducation, PSS-SR, 11% vs. 23%, p=NS	Insufficient
PTSD symptom severity at 6 months: 1; 106; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. Debriefing combined with psychoeducation, PSS-SR, 10.9 vs. 13.8, p=NS; IES, 16.7 vs. 19.7, p=NS	Insufficient
Depression symptom severity at 6 months: 1; 106; RCT	Medium[a, b]	Unknown, single study	Direct	Imprecise[c]	Psychoeducation vs. Debriefing combined with psychoeducation, BDI, 9.8 vs. 12.1, p=NS	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Primary analysis not ITT; 11-month attrition > 20%

[b] Due to very high overall attrition (i.e., greater than 40% at 11-month followup) in this study, we considered all outcomes collected at that timepoint as having a high risk of bias and therefore do not report them

[c] Small sample size (< 300 observations)

Abbreviations: BDI = Beck Depression Inventory; CI = confidence interval; IES = Impact of Event Scale; ITT = intent to treat analysis; NA = not applicable; NR = not reported; NS = not significant; PSS-SR = PTSD Symptom Scale-Self-Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G18. Cognitive therapy compared with SSRI (Escitalopram)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 5 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CT vs. SSRI, CAPS, 18.2% vs. 61.9%, p=NR[c]	Insufficient
Incidence of PTSD 9 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CT vs. SSRI, CAPS, 22.8% vs. 42.1%, p=NR[c]	Insufficient
PTSD symptom severity at 5 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CT vs. SSRI, CAPS total, 29.5 vs. 48.7, p=NR[c]; PSS-SR, 11.6 vs. 22.5, p=NR[c]	Insufficient
PTSD symptom severity at 9 months: 1; 54; RCT	Medium[a]	Unknown, single study	Direct	Imprecise[b]	CT vs. SSRI, CAPS total, 27.9 vs. 47.2, p=NR[c]; PSS-SR, 9.6 vs. 21.6, p=NR[c]	Insufficient
Incidence and severity of psychological symptoms: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Completer analysis of 63 randomized rather than ITT; high (> 20%) overall attrition; high (> 15%) differential attrition between groups

[b] Small sample size (< 300 observations)

[c] Text indicates means are significantly different but no post-hoc p values are provided

Abbreviations: CAPS = Clinician Administered PTSD Scale; CI = confidence interval; CT = Cognitive therapy; ITT = intent to treat analysis; NA = not applicable; NR = not reported; PSS-SR = PTSD Symptom Scale-Self Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SSRI = Selective serotonin reuptake inhibitor

Table G19. Prolonged exposure compared with SSRI (Escitalopram)

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD at 5 months: 1; 77; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. SSRI, CAPS, 21.4% vs.61.9%, p=NR[c]	Insufficient
Incidence of PTSD at 9 months: 1; 71; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. SSRI, CAPS, 21.2% vs. 42.1%, p=NR[c]	Insufficient
PTSD symptom severity at 5 months: 1; 77; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. SSRI, CAPS total, 28.6 vs. 48.7, p=NR[c]; PSS-SR, 11.0 vs. 22.5, p=NR[c]	Insufficient
PTSD symptom severity at 9 months: 1; 71; RCT	Medium[b]	Unknown, single study	Direct	Imprecise[a]	PE vs. SSRI, CAPS total, 27.2 vs. 47.2, p=NR[c]; PSS-SR, 10.4 vs. 21.6, p=NR[c]	Insufficient
Incidence and severity of psychological symptoms: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence/severity of comorbid conditions: 0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Completer analysis of 86 randomized rather than ITT; high (> 20%) overall attrition; high (> 15%) differential attrition between groups

[b] Small sample size (< 300 observations)

[c] Text indicates means are significantly different but no post-hoc p values are provided

Abbreviations: CAPS = Clinician Administered PTSD Scale; CI = confidence interval; ITT = intent to treat analysis; NA = not applicable; NR = not reported; PE = Prolonged exposure therapy; PSS-SR = PTSD Symptom Scale-Self Report; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SSRI = Selective serotonin reuptake inhibitor

Key Question 2.

Table G20. Immediate critical incident stress debriefing compared with delayed critical incident stress debriefing

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias;	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity[a]: 1; 72; RCT	Medium[b]	NA[c]	Direct	Not reported[d]	PDS, 8.8 symptoms fewer in immediate CISD than delayed CISD group (95% CI, NR)	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Mean change from baseline to 2 weeks on the PDS.

[b] Unmasked RCT

[c] Downgraded as a single study

[d] Downgraded for unclear precision

Abbreviations: CI = confidence interval; CISD = Critical Incident Stress Debriefing; NA = not applicable; NR = not reported; PDS = Posttraumatic Stress Diagnostic Scale; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G21. Strength of evidence comparing light versus deep sedation

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0,0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity: 1; 135; RCT	Medium[a]	NA[b]	Direct	Not reported[c]	Similar effects (10% vs. 9% with PTSD symptoms)	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide) 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Downgraded as a single study

[c] Downgraded for unclear precision

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Key Question 3.

Table G22. Strength of evidence for subgroup effects of gender

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity: 2; 268; RCT	Medium[a]	Consistent[b]	Direct	Not reported[c]	Not reported[d]	Low[e]
Depression symptom severity: 1; 157; RCT	Medium[a]	Unknown[f]	Direct	Not reported[c]	Not reported[d]	Insufficient[g]
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Upgraded for consistency

[c] Downgraded for unclear precision

[d] Downgraded for unclear magnitude of effect

[e] Low SOE because magnitude and precision of effect not reported by either of the two studies.

[f] Downgraded as a single study

[g] Insufficient because findings reported by only one medium risk of bias trial and magnitude, direction and precision not reported.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SOE = strength of evidence

Table G23. Strength of evidence for subgroup effects of previous depression

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity: 1; 157; RCT	Medium[a]	Unknown[b]	Direct	Not reported[c]	Not reported[d]	Insufficient[e]
Depression symptom severity: 1; 157; RCT	Medium[a]	Unknown[b]	Direct	Not reported[c]	Not reported[d]	Insufficient[e]
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Downgraded as a single study

[c] Downgraded for unclear precision

[d] Downgraded for unclear magnitude of effect.

[e] Insufficient because findings reported by only one medium risk of bias trial and magnitude, direction and precision not reported.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G24. Strength of evidence for subgroup effects of history of child abuse

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity: 1; 157; RCT	Medium[a]	Unknown[b]	Direct	Not reported[c]	Not reported[d]	Insufficient[e]
Depression symptom severity: 1; 157; RCT	Medium[a]	Unknown[b]	Direct	Not reported[c]	Not reported[d]	Insufficient[e]
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Downgraded as a single study

[c] Downgraded for unclear precision

[d] Downgraded for unclear magnitude of effect.

[e] Insufficient because findings reported by only one medium risk of bias trial and magnitude, direction and precision not reported.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G25. Strength of evidence for subgroup effects of severity of baseline distress

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity: 2; 285; RCT	Medium[a]	Inconsistent[b]	Direct	Not reported[c]	Not reported[d]	Insufficient[e]
Depression symptom severity: 2; 285; RCT	Medium[a]	NA	NA	NA	NA	Insufficient[f]
Quality of Life: 2; 285; RCT	Medium[a]	NA	NA	NA	NA	Insufficient[f]
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Downgraded for lack of consistency

[c] Downgraded for unclear precision

[d] Downgraded for unclear magnitude of effect.

[e] Insufficient SOE because inconsistent findings were reported.

[f] Insufficient SOE because although two studies assessed this outcome, severity of baseline distress was defined differently for all outcomes other than PTSD.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SOE = strength of evidence

Table G26. Strength of evidence for subgroup effects of severity of exposure to trauma

Outcome: Number of Studies, Number of Subjects	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 0; 0	NA	NA	NA	NA	NA	Insufficient
PTSD symptom severity: 1; 2,443	Medium[a]	Unknown[b]	Direct	Not reported[c]	Not reported	Insufficient[d]
Depression symptom severity:0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Downgraded as a single study

[c] Downgraded for unclear precision

[d] Insufficient SOE because findings reported by only one medium risk of bias trial and magnitude and precision not reported.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SOE = strength of evidence

Table G27. Strength of evidence for subgroup effects of type of trauma

Outcome: Number of Studies, Number of Subjects	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Incidence of PTSD: 1; 137	Medium[1]	Unknown[2]	Direct	Not reported[3]	Not reported	Insufficient[a]
PTSD symptom severity: 1; 137	Medium[1]	Unknown[2]	Direct	Not reported[3]	Not reported	Insufficient[a]
Depression symptom severity: 0;0	NA	NA	NA	NA	NA	Insufficient
Quality of Life: 0; 0	NA	NA	NA	NA	NA	Insufficient
Return to work/return to active duty or ability to work: 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of self-injurious or suicidal thoughts, attempts, or behaviors (including suicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Incidence of aggressive or homicidal thoughts, attempts, or behaviors (including homicide): 0; 0	NA	NA	NA	NA	NA	Insufficient
Perceived utility: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Unmasked RCT

[b] Downgraded as a single study

[c] Downgraded for unclear precision

[d] Insufficient SOE because: 1) findings reported by only one medium risk of bias trial; 2) no overall test of interaction (group-by-type of trauma-by-time) was done.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SOE = strength of evidence

Key Question 4.

Table G28. Strength of evidence comparing emotional debriefing vs. educational debriefing vs. placebo

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Overall rate of harms: 1; 236; RCT	Low[a]	NA[b]	Direct	Not reported	In a subgroup with hyperarousal at baseline, those receiving emotional debriefing has significantly higher PTSD scores than those in the control group at 6 week follow-up (p=0.005)[c]	Insufficient
Overall dropout rate because of adverse events: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Single-blind RCT (outcome assessor masked)

[b] Downgraded as single study.

[c] This subgroup analysis involved a significant test for interaction, but no significant differences were found at 2 weeks or 6 months, and the former result might be a chance finding. Downgraded as post-hoc analysis of subgroup with mixed results across time points.

Abbreviations: CI = confidence interval; NA = not applicable; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial

Table G29. Strength of evidence comparing light versus deep sedation

Outcome: Number of Studies; Number of Subjects; Design	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Magnitude of Effect: Summary Effect Size (95% CI)	Strength of Evidence
Overall rate of harms: 1; 137; RCT	Medium[a]	NA[b]	Direct	Not reported	No difference in mortality or incidence of adverse events	Insufficient[c]
Overall dropout rate because of adverse events: 0; 0	NA	NA	NA	NA	NA	Insufficient

[a] Open label RCT (outcome assessor masked), overall attrition > 20%, unclear how dropouts were handled in intention-to-treat analysis

[b] Downgraded as single study.

[c] Insufficient SOE because no data reported.

Abbreviations: CI = confidence interval; NA = not applicable; RCT = randomized controlled trial; SOE = strength of evidence

Appendix H. Sensitivity Analyses

KEY QUESTION 1

Cognitive Behavioral Therapy (CBT)

Sensitivity Analyses: Including the high risk of bias study Bryant, 1999

Figure H1. Mean change from baseline to end of treatment in PTSD incidence rates for CBT compared with supportive counseling

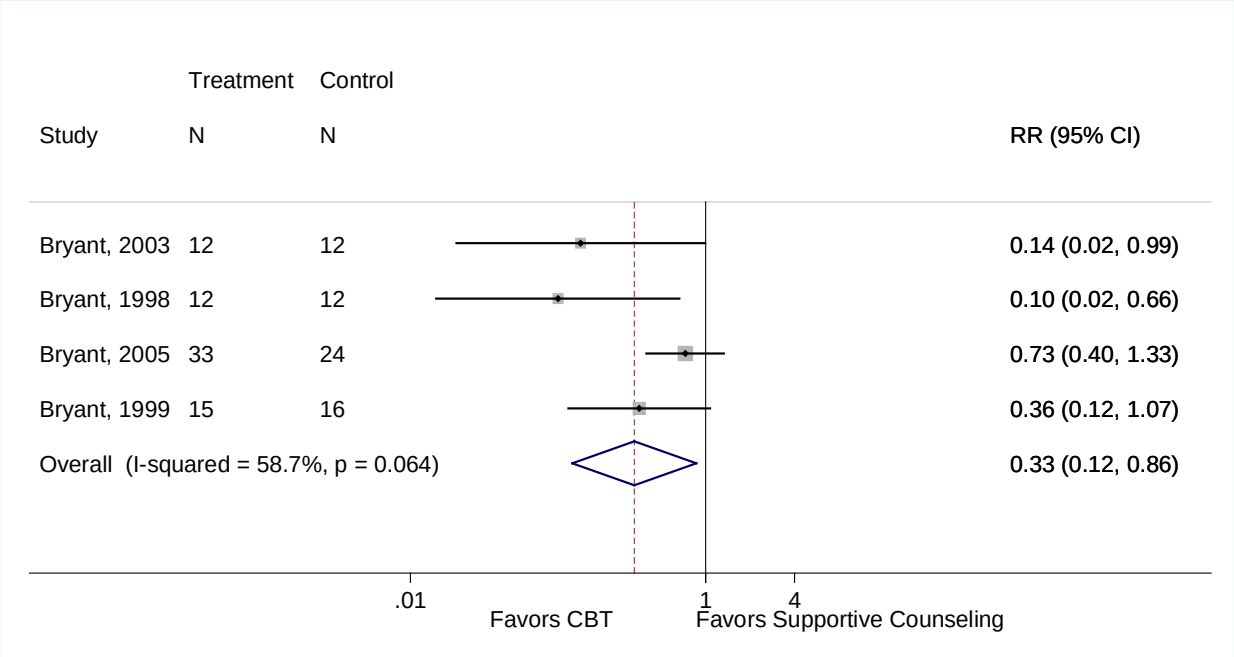


Figure H2. Mean change from baseline to 6-month followup in PTSD incidence rates for CBT compared with supportive counseling

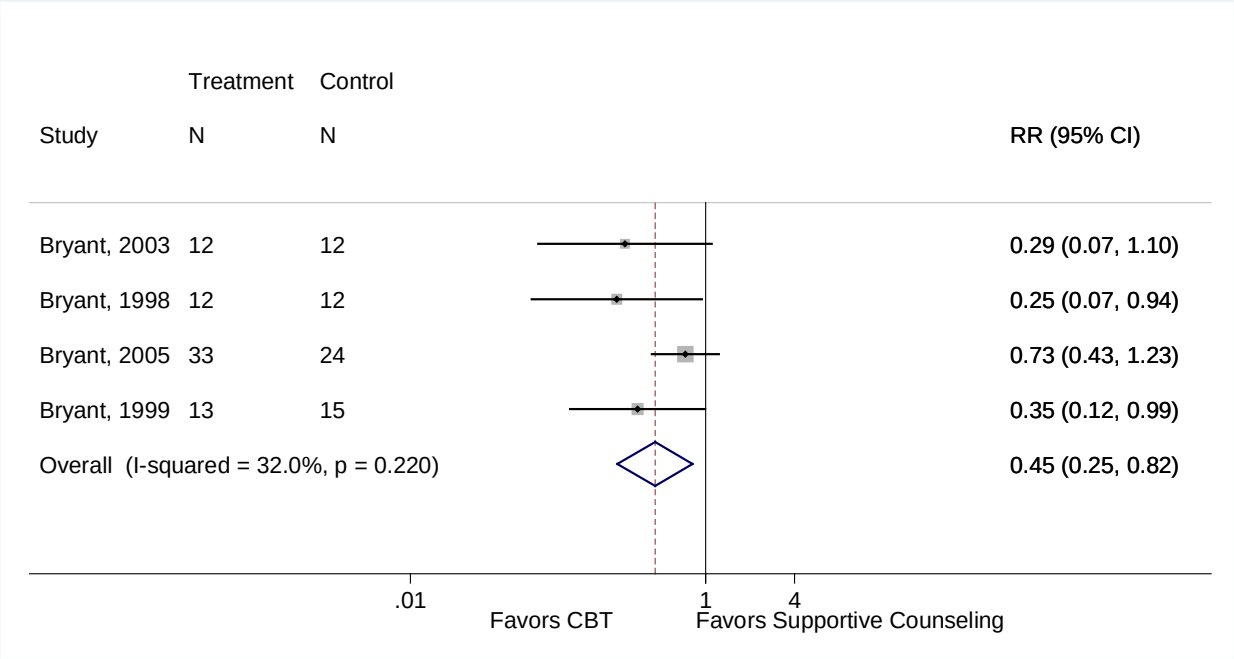


Figure H3. Mean change from baseline to end of treatment in IES Avoidance Subscale symptom scores for CBT compared with supportive counseling

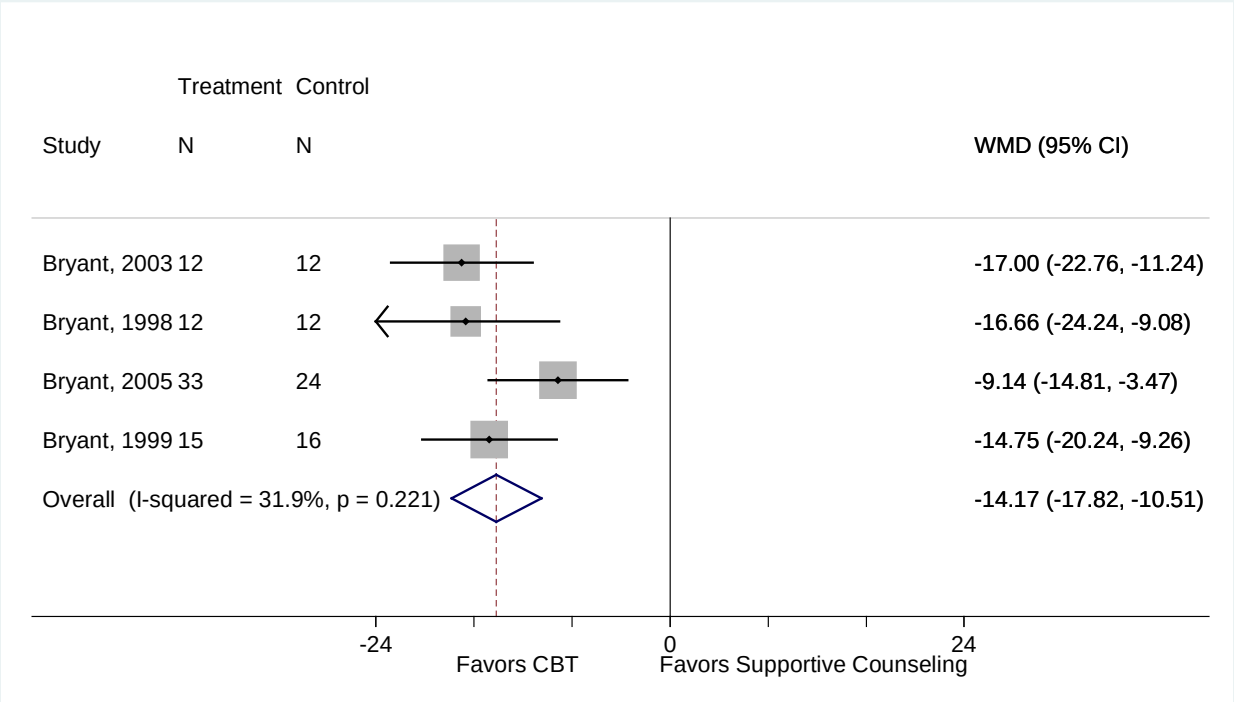


Figure H4. Mean change from baseline to 6-month follow-up in IES Avoidance Subscale symptom scores for CBT compared with supportive counseling

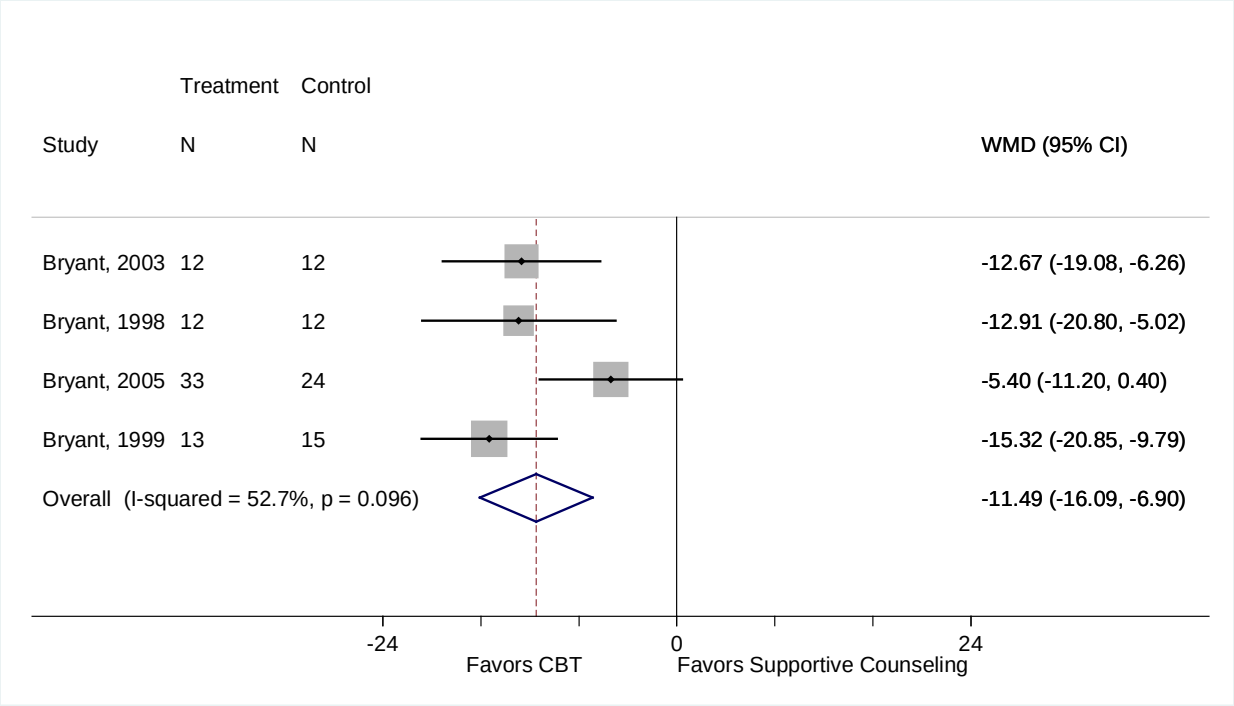


Figure H5. Mean change from baseline to end of treatment in IES Intrusion Subscale symptom scores for CBT compared with supportive counseling

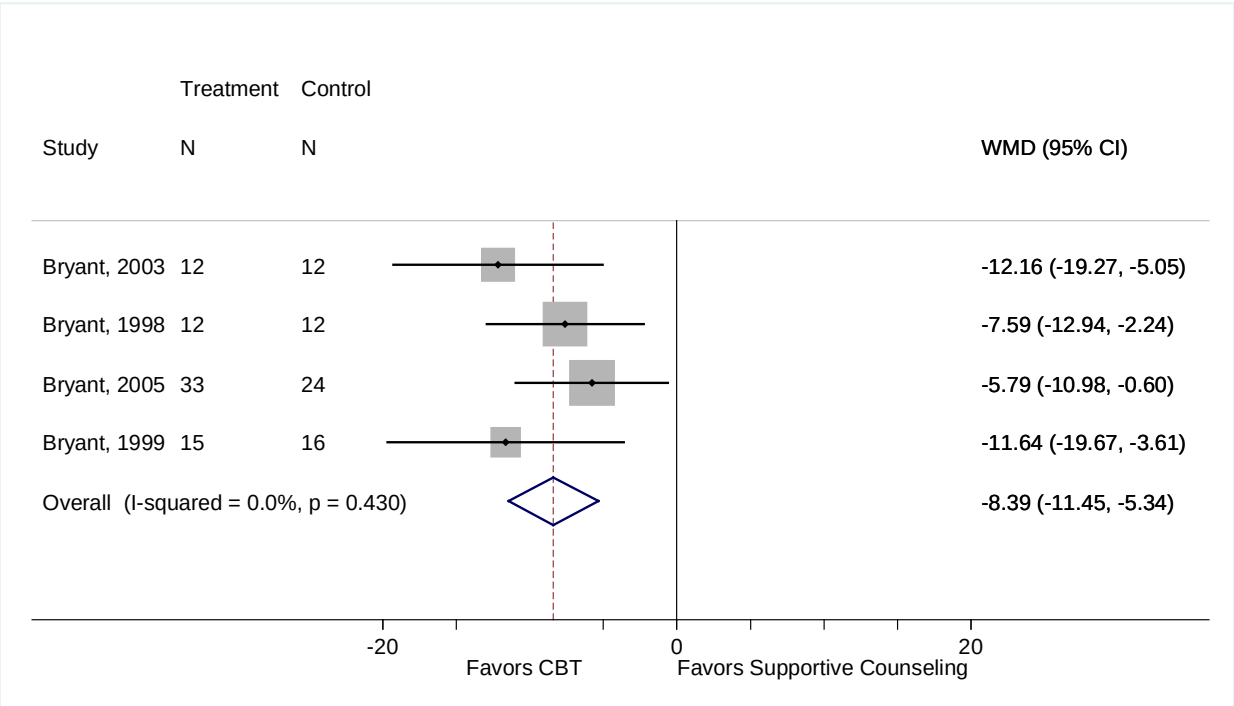


Figure H6. Mean change from baseline to 6-month follow-up in IES Intrusion Subscale symptom scores for CBT compared with supportive counseling

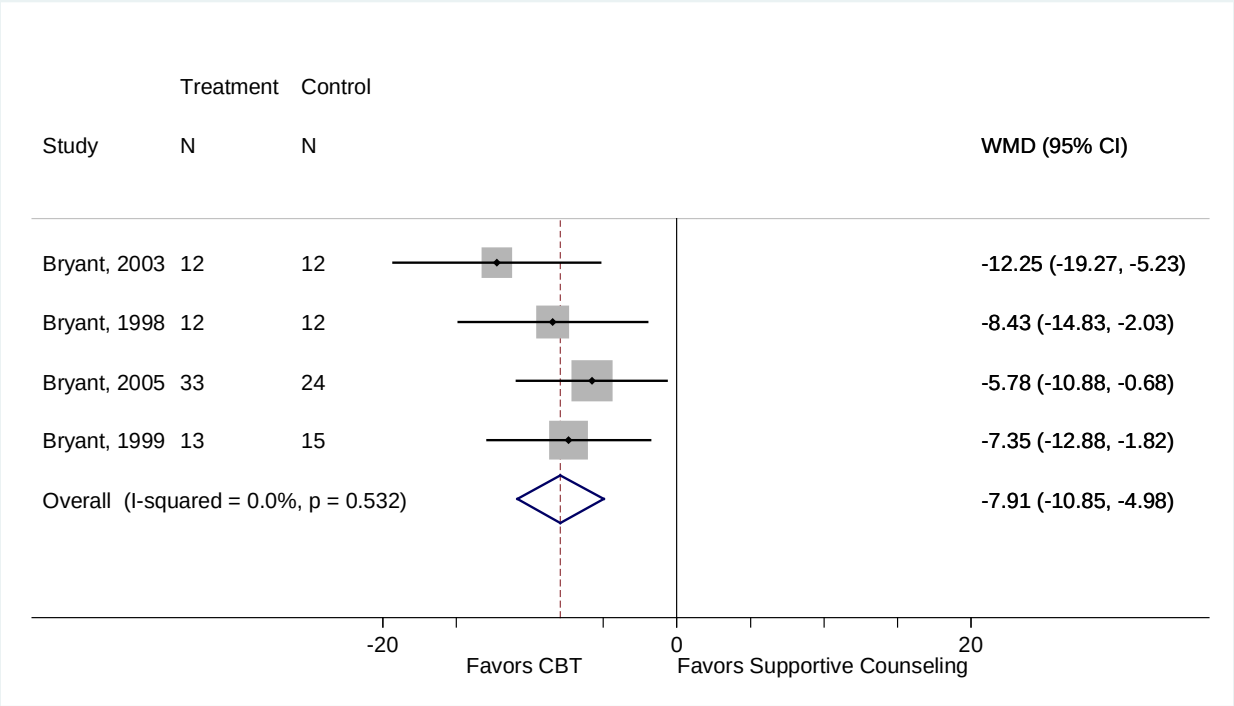


Figure H7. Mean change from baseline to end of treatment in anxiety symptom scores for CBT compared with supportive counseling

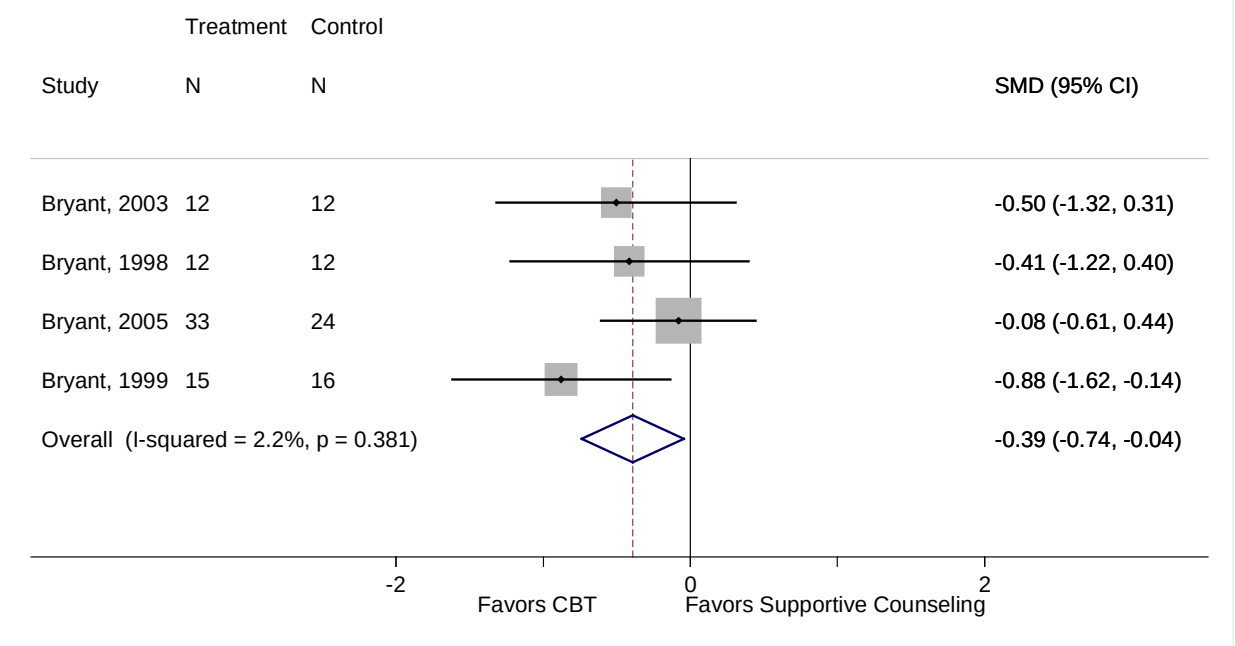


Figure H8. Mean change from baseline to 6-month follow-up in anxiety symptom scores for CBT compared with supportive counseling

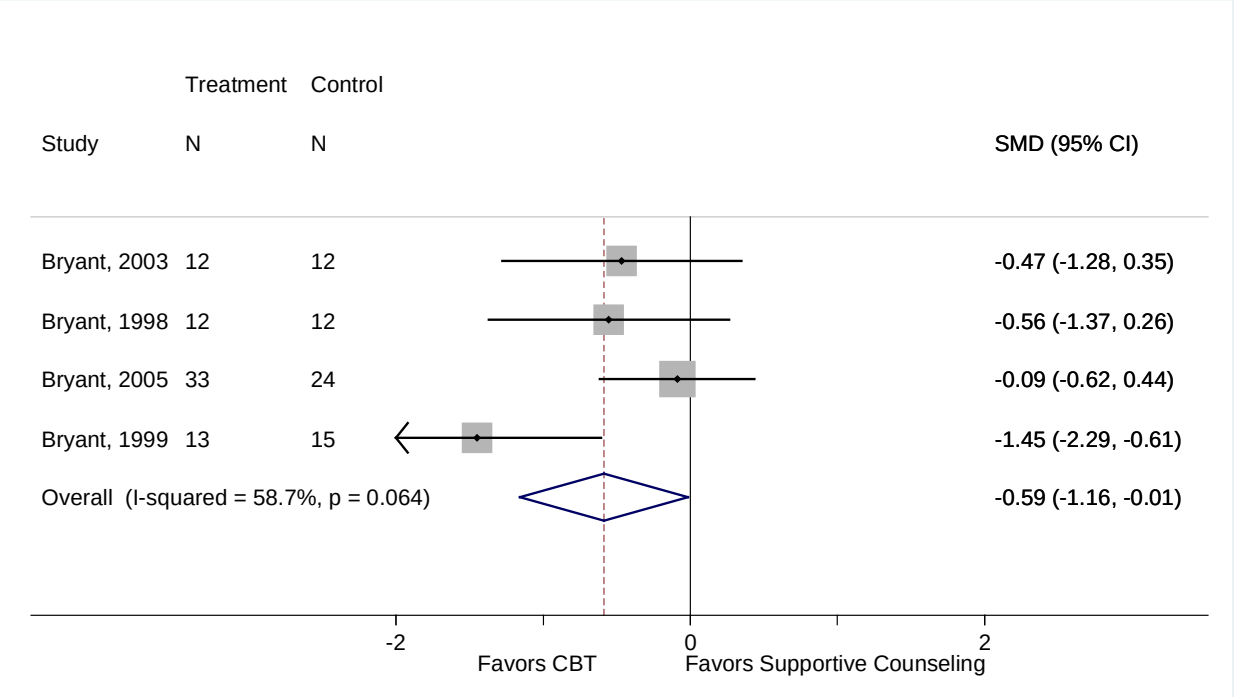


Figure H9. Mean change from baseline to end of treatment in depression symptom scores for CBT compared with supportive counseling

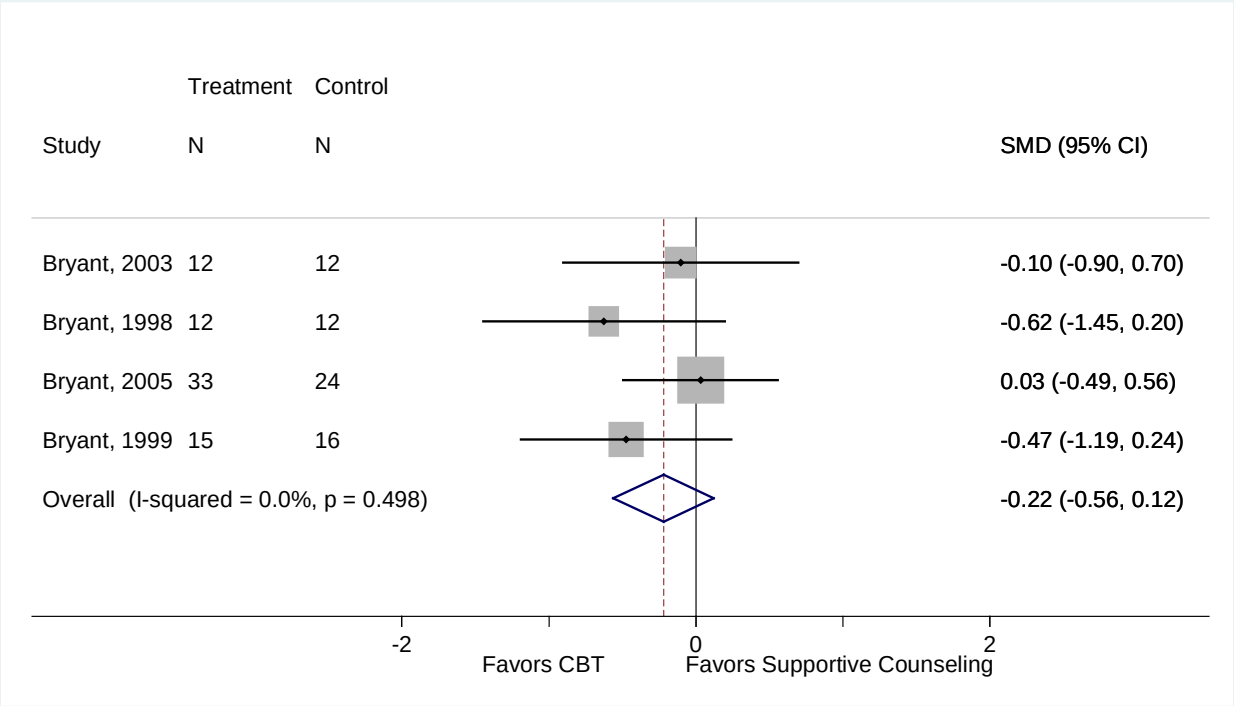
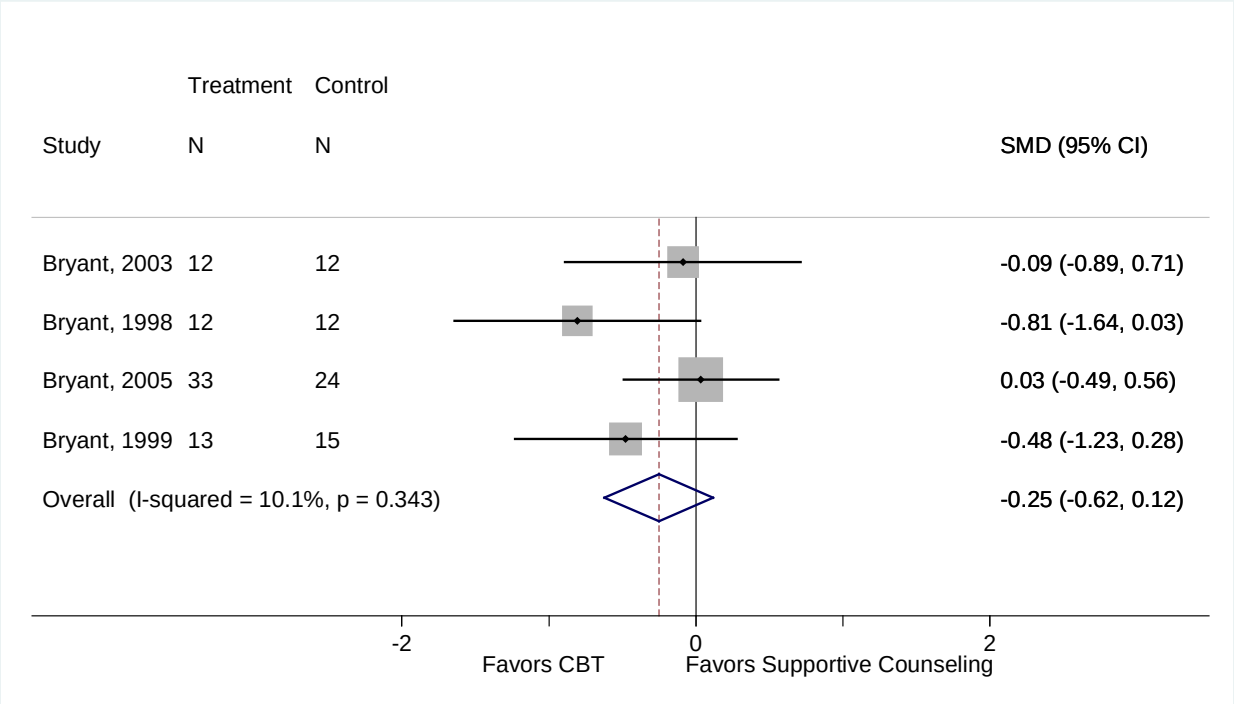


Figure H10. Mean change from baseline to 6-month follow-up in depression symptom scores for CBT compared with supportive counseling



Appendix I. Abbreviations and Acronyms

5-HT	5-hydroxytryptamine
AHRQ	Agency for Healthcare Research and Quality
AMPA	alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
ASD	Acute stress disorder
ASDI	Acute Stress Disorder Interview
BAI	Beck Anxiety Inventory
BDI	Beck Depression Inventory
BDI-2	Beck Depression Inventory-2
BOCF	baseline observation carried forward
BPM	beats per minute
CABG	coronary artery bypass grafting
CAM	Complementary and alternative medicine
CAPS	Clinician Administered PTSD Scale
CAPS-2	Clinician Administered PTSD Scale-2
CBT	Cognitive behavioral therapy
CBT+Hypnosis	CBT combined with hypnosis
CC	Collaborative care
CER	comparative effectiveness review
CI	Confidence interval
CIDI-PTSD	Composite International Diagnostic Interview PTSD module
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CISD	Critical incident stress debriefing
CISM	Critical incident stress management
COPD	Chronic obstructive pulmonary disease
COPE	Creating Opportunities for Parent Empowerment
CPT	Cognitive processing therapy
CR	Cognitive restructuring
CRF	corticotropin-releasing
CT	Cognitive therapy
DASS	Depression and Anxiety Stress Scales
DASS-21	Depression and Anxiety Stress Scales-21
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision
Educ	educational
EMBASE	Excerpta Medica Database
EMDR	Eye movement desensitization and reprocessing therapy
EPDS	Edinburgh Postnatal Depression Scale
GABA	gamma-aminobutyric acid
GHQ-12	12-item General Health Questionnaire
HADS-A	Hospital Anxiety and Depression Rating Scale-Anxiety subscale
HADS	Hospital Anxiety and Depression Rating Scale
HPA	hypothalamic-pituitary-adrenal
ICU	intensive care unit
IES	Impact of Event Scale

IES-A	Impact of Event Scale-Avoidance subscale
IES-I	Impact of Event Scale-Intrusion subscale
IES-R	Impact of Event Scale-Revised
IOM	Institute of Medicine
IPA	International Pharmaceutical Abstracts
IPT	Interpersonal therapy
ITT	intention-to-treat analysis
KQ	Key Question
LOCF	last observation carried forward
MAOIs	Monoamine oxidase inhibitors
MeSH	Medical Subject Headings
MIDI	Migraine Disability Index Post-Traumatic Stress Disorder
MINI-PTSD	Mini-International Neuropsychiatric Interview-Post-Traumatic Stress Disorder Module
MVA	Motor vehicle accidents
n	Number of participants
NA	not applicable
NCS-R	National Comorbidity Survey - Replication
NMDA	N-methyl-d-aspartate
NNT	number needed to treat
NR	not reported
NRCT	nonrandomized controlled trial
NS	not significant
NVVRS	National Vietnam Veterans Readjustment Survey
POD	post-operative day
PCL	Posttraumatic Stress Disorder Checklist
PCL-C	Posttraumatic Stress Disorder Checklist-Civilian Version
PDS	Posttraumatic Stress Diagnostic Scale
PE	Prolonged exposure therapy
PFA	Psychological first aid
PHQ-9	Patient Health Questionnaire, 9-item version
PHQ-Depression	Patient Health Questionnaire for Depression
PHSI-P	Post-Hospital Stress Index for Parents
PICOTS	Populations, Interventions, Comparators, Outcomes, Timing, and Settings
PILOTS	Published International Literature on Traumatic Stress
POMS	Profile of Mood States
PRISMA	Preferred Reporting Items for Systematic Review and Meta-analyses
PSDS-SR	Posttraumatic Stress Diagnostic Scale-Self Report
PSS	Posttraumatic Stress Scale
PSS-SR	Posttraumatic Stress Diagnostic Scale-Self Report
PTSD	Prevention of Posttraumatic Stress Disorder
PTSS-10	Posttraumatic Stress Symptom 10 Question Inventory
QOL	quality of life
RCT	randomized controlled trial
RR	relative risk
SC	Supportive counseling

SD	standard deviation
SE	standard error
SF-36	Medical Outcomes Study Health Survey – Short Form 36
SHB	Self-help booklet
SIPs	Scientific Information Packets
SI-PTSD	Structured Interview for PTSD
SMD	standardized mean difference
SNRIs	Serotonin and norepinephrine reuptake inhibitors
SOE	strength of evidence
SRC	Scientific Resource Center
SSRI	Selective serotonin reuptake inhibitor(s)
STAI	State-Trait Anxiety Inventory
TCAs	Tricyclic antidepressants
TEP	Technical Expert Panel
TISS	Therapeutic Intervention Scoring System
TRiM	Trauma Risk Management
UC	Usual care
VA/DoD	US Department of Veterans Affairs and Department of Defense
UK	United Kingdom
UN	United Nations
US	United States
USPSTF	U.S. Preventive Services Task Force
W-DEQ	Wijma Delivery Expectancy/Experience Questionnaire
WL	waitlist
WMD	Weighted mean difference
WTCD	World Trade Center Disasters
yr(s)	year(s)