Comparative Effectiveness Research Review Disposition of Comments Report

Research Review Title: *Interventions for the Prevention of Posttraumatic Stress Disorder (PTSD) in Adults After Exposure to Psychological Trauma*

Draft review available for public comment from July 27, 2012 to August 24, 2012.

Research Review Citation: Gartlehner G, Forneris CA, Brownley KA, Gaynes BN, Sonis J, Coker-Schwimmer E, Jonas DE, Greenblatt A, Wilkins TM, Woodell CL, Lohr KN. Interventions for the Prevention of Posttraumatic Stress Disorder (PTSD) in Adults After Exposure to Psychological Trauma. Comparative Effectiveness Review No. 109. (Prepared by the RTI-UNC EPC under Contract No. 290-2007-10056-I.) AHRQ Publication No. 13-EHC062-EF. Rockville, MD: Agency for Healthcare Research and Quality; April 2013. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Comments to Research Review

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The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

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Published Online: April 2, 2013

Commentator & Affiliation	Section	Comment	Response
TEP #1	Methods	Yes. One comment re the risk of bias criteria (e.g. pages 212 Stein and 214 Zohar) for studies of psychopharmacology. It is not customary (or even appropriate in my opinion) to expect that therapist fidelity be rated in drug studies. While treatment manuals have been developed for "fidelity" in drug administration (including by this reviewer), it is rare and superfluous. What would be more useful in rating "bias" would have been a measure of patient compliance such as pill count monitoring or blood levels. Thus I would caution against penalizing a drug study on this criterion.	Thank you for your suggestion. We have confirmed that none of our assigned risk of bias ratings for studies of pharmacological interventions were based on treatment fidelity or medication adherence.
TEP #1	Results	Yes to all. However, it would be helpful to give a total score on bias - what did studies need to score in order to be judged as low, medium or high? The tables aren't clear on this. (Was it given elsewhere and I missed it perhaps?)	We did not use a numerical scoring system to determine the risk of bias. Instead, we assessed critical domains for each study design (see methods). For example, for RCTs we assessed randomization, allocation concealment, blinding, loss to followup, and statistical analysis. If the study had a fatal flaw in any of these domains, we rated it as high risk of bias. Reasons for high risk of bias ratings are presented in the appendix of the report.
TEP #1	Discussion	This was done thoroughly.	Thank you.
TEP #1	Conclusion	This was done thoroughly.	Thank you.
TEP #1	General	Yes to all. It should be a valuable contribution which hopefully will stimulate further research into this most important question.	Thank you.
TEP #1	General	Reviewer's response to "Clarity and Usability" item: Yes.	Thank you.
Peer Reviewer #2	Executive Summary	As the authors note (p. ES-14, lines 17-19), "little or no evidence was available for preventive interventions following terrorist attacks, sexual assault, natural disaster, or combat", yet these are precisely the types of events for which we need data. And some data do exist for these in the high bias studies, so again, this reviewer urges you to consider including these summaries in the executive summary. The studies included include childbirth and illnesses, certainly important, but not what we typically think of as leading to PTSD and not the focus on prevention. It really is not helpful to conclude 'insufficient evidence' because only one study; this reviewer urges you to consider grouping studies and forming some conclusions if there is data.	We have added a table with results of high risk of bias studies to the full report to make it easier for readers to get an overview of findings from these studies. In the detailed synthesis of each KQ, we have already grouped studies by interventions looking across different populations. If possible we further grouped by follow-up times (e.g., combining outcomes of 3 and 5 months) In most cases, however, we are hesitant to make groups larger (e.g. all psychological interventions) because conclusions would not be meaningful anymore.
Peer Reviewer #2	Executive Summary	More minor points: the citations differ in the executive summary from the text to the tables and it is confusing.	We have corrected the in-text citations so that citations in the text match those used in the tables.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	General	Overall, the authors should be commended on a comprehensive literature review, synthesis of the literature, and report. It is very well-written, easy to follow, important, and timely. Terms and methods are delineated. It is indeed a sad commentary how few studies meet the specified criteria, and how few have been conducted in the United States despite a high prevalence of trauma and PTSD. This reviewer agrees that these results should be a clear call to action for US funders and researchers. This reviewer is of the opinion this is the most important message from this report.	Thank you.
Peer Reviewer #2	General	It is commendable that the authors set a high bar and specified inclusion criteria for studies. However, the fact that so few studies met these criteria, with the result that the report can draw next to no conclusions, requires some flexibility. The fact that so few studies met this criteria should be taken 1) as a state of the stage of development for PTSD research, and 2) as the nature of the beast with trauma survivors. As PTSD only became an official diagnosis in 1986, it is not surprising that large well-controlled *prevention* studies are scarce as the literature is filling with RCTs of the treatment of chronic PTSD. As the authors note, early intervention by definition means that recent trauma survivors are the study participants, and therefore likely to be transient. It is also the nature of the beast that PTSD sufferers are avoidant. The 2008 IOM report punished studies for this, as the current authors do, and was criticized. Notably, the recent 2012 IOM report did not set such stringent inclusion criteria and included many of the studies the current authors omitted. Therefore, the main criticism is that the report does not have much to say, as is, because so many studies were excluded. It is this reviewer's recommendation that the summaries included throughout the report, even for those excluded for high bias, be included in the executive summary. They can be included under the heading of high bias studies to clearly delineate them, but it just seems silly to exclude what they have to teach us when there are so few.	We appreciate this helpful comment. We have added a table with results of high risk of bias studies to the full report to make it easier for readers to get an overview of findings from these studies as well.
Peer Reviewer #2	General	The other criticism is that this is not really a report of prevention of PTSD. Rather it is a report of early interventions for PTSD, or treatment of ASD.	Studies that included subjects with a diagnosis of PTSD were not eligible for inclusion in this review. Although we did not exclude studies that included subjects with ASD, treatment of ASD was not a primary focus of this report. The studies included in this review focused on those exposed to a traumatic event who may be at risk for developing PTSD.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #2	General	In summary, due to the state of the literature and the nature of PTSD and trauma survivors as research participants, this reviewer urges the authors to "lower the bar" to produce a report that is more helpful in its synthesis. It could be made clear where the authors are being more lenient and set the bar higher as an aspirational goal for the future when there are more studies to include. As it is now, and it would be a shame, but this report could be considered a colossal waste of effort if it can make no conclusions.	Our criteria for rating the risk of bias are based on established guidance by the AHRQ Evidence-based Practice Center program. Loosening the criteria or including studies that we considered high risk of bias would not change our confidence in the results. When rating the strength of evidence, outcomes based on these studies would still be rated as insufficient to draw conclusions. However, to be more explicit about findings from high risk of bias studies, we have added a table with results of high risk of bias studies to the full report to make it easier for readers to get an overview of findings from these studies as well.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Introduction	The introduction is thorough and comprehensive, yet free of jargon and easy to understand. The authors articulate a clear justification for the review and for the questions they have chosen to explore. The introduction could use a modern conceptual scheme for early intervention for trauma. To lend some clarity to the varied intervention strategies reviewed, they should consider categorizing preventative interventions using the Institute of Medicine (IOM) framework (Munoz et al., 1996), which conceptualizes prevention interventions based on who they target: (1) universal prevention targets a whole population (applicable high risk occupations, such as the military); (2) selective prevention targets all members of groups at presumed equal risk (e.g., all individuals who have been exposed regardless of the degree of their distress and impairment, that is, their putative need and risk); and (3) indicated prevention targets individuals who have been exposed to trauma and they have significant and impairing pre-clinical symptoms (e.g., they are suffering at a sufficient pre-clinical level and they are at risk for developing chronic PGD). Until recently, the modal prevention strategy following trauma was selective, targeting anyone exposed regardless of risk and distress/impairment. Early selective prevention approaches following loss and trauma, such as grief counseling or critical incident stress debriefing, have been found to have no empirical or conceptual support (see Litz et al., 2002). By contrast, indicated prevention entails targeting individuals who are suffering and impaired to significant degree but are by definition pre-clinical because not enough time has passed for a diagnosable condition to be present. Indicated prevention reduces the incidence of mental disorders and promotes recovery and functioning. The best evidence supports the effectiveness of indicated prevention interventions that target subclinical distress, rather than selective prevention interventions (Feldner et al., 2007; Litz et al., 2002; Wittouck et al., 2011).	Thank you.
Peer Reviewer #3	Methods	The authors conducted an exhaustive literature search that is explicitly and clearly detailed. They have clearly gone to great lengths to make the search sufficiently inclusive (including a search of unpublished work as well) with the exception of non-English articles (unfortunate, but they explain in the discussion that this was due to financial and time constraints). Goals and methods were well articulated and clearly presented. Diagnostic criteria and outcome measures were appropriate and clearly defined. Procedures for evaluation and analysis of studies were extensive and well-detailed within the report. Unfortunately, the stringent exclusion criteria (although justifiable), yielded an extremely limited sample of only 15 studies, making it very difficult to draw few, if any, well-supported conclusions.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Results	Results were presented clearly and with appropriate level of detail. Tables and figures provided access to more detailed information in a well organized and clear format. Key questions were addressed in a thorough and organized way. Unfortunately for the field, the primary finding of the entire report was that there is insufficient evidence to support most conclusions in response to the key questions. While many studies were excluded early in the study based on initial exclusion criteria, even more potentially relevant studies were further excluded after being determined to have "high-risk of bias." In areas, where studies with "low or moderate risk of bias" were absent, the authors made the determination to discuss the studies with "high risk of bias," while noting that caveat. It would have been nice to see similarly consideration given to studies even when one or two related studies with low or moderate risk were available, particularly because conclusions from those low-moderate risk studies were then determined to provide insufficient evidence because they were only single studies. I resonate with the stringently conservative criteria used to assess sufficient evidence, however, given the limited evidence available, it would have been helpful for the authors to consider the implication of these so-called high-risk studies if integrated with the studies of lower risk (of course with all the appropriate caveats – as a secondary type of discussion/analysis); at least as they might be utilized inform direction for future more rigorous research/replication. 2 specific questions: KQ2 – A study of CISD with robbery victims was rated as "low" strength of evidence, whereas everywhere else in the report, single studies were rated as "insufficient" strength of evidence when there were no other studies supporting this conclusion. It would be helpful for the authors to explain why this single-study was given a different determination (was there a large effect size? Etc). KQ4 – The second study reported on within the findings discusses risk of mortality related to sedation prior to intubation. It is not made sufficiently clear how this study relates to prevention of PTSD and seems quite different than the harm of exacerbated PTSD symptoms that are typically discussed when considering harm in this literature.	KQ2: We have changed the rating to insufficient. KQ 4: We appreciate the reviewer's query about whether this mortality is reasonably considered an adverse event (AE) in reviewed interventions to prevent the development of PTSD symptoms. In general, harms can be viewed as either an unexpected worsening of underlying symptoms (PTSD exacerbation as the reviewer offers, or increase in depressive severity, as might be observed in depressive illness) or as a deleterious response to the medication itself (e.g., increased risk of death in group with a particular intervention, as noted by reviewer, or increased risk of seizure, as might be seen with hyper-therapeutic doses of bupropion). This conceptualization of an adverse event is consistent with how AEs are defined in mental health literature—for example, in children with MDD, whether a treatment leads to an increased risk of death (whether by suicide or by medication toxicity, for example) would be a key AE to monitor.
Peer Reviewer #3	Discussion	The implications and limitations are discussed adequately. An additional statement related to the breadth of literature omitted in this review that might present an inherent limitation to this kind of work would be welcome. A separate "future research section" is absent, but rather is integrated throughout the discussion; however the suggestions tend to be more theoretical and less practical. It would be nice to see some suggestions for directions for future research. There are a number of typos in this section (p. 63, lines 3 &4, p.76, lines 26 & 34, p.77, lines 8 & 55)	The issue of the large number of studies not reviewed because of high risk of bias is discussed in the discussion section. We have revised the research gaps section to add specific recommendations about research on targeted prevention.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #3	Conclusion	The report is very well structured, organized, and easy to navigate. Conclusions can inform policy and practice although more practical detailed suggestions as to how would be useful.	These suggestions are listed in the sections on Applicability and Research Gaps.
Peer Reviewer #3	General	The authors have conducted a rigorous, thoughtful, well-conceived and well-designed review of the literature on interventions for the prevention of PTSD in adults exposed to psychological trauma. The review provides an essential critical overview and assessment of this complex and muddied area of research from which practice recommendations are near to impossible to glean for all trauma types. The report is meaningful even though the implications are justifiably limited because of the paucity of sufficiently valid empirical evidence, as demonstrated by this report. The questions posed are appropriate, explicitly stated, and easy to follow.	Thank you.
Peer Reviewer #4	Executive Summary	On p. ES-1, line 26, the rate of PTSD in adults who have been traumatized is substantial but the atypical response. This also should be distinguished from the rate in children--it seems from the available data that PTSD is the atypical response in traumatized adults but not in children. On the same page, line 15, the authors might want to note that adults are exposed to potentially traumatic events as well as extreme traumatic events to stress subjectivity of response.	The focus of this report was on adults, not children, and we would suggest not discussing PTSD in children as part of this report. We added the word “subjective” in line 20 to underscore the reviewer’s second comment here.
Peer Reviewer #4	Executive Summary	Regarding key questions, should they be worded as "adults who directly experienced or were exposed to" for greater precision?	We do not believe that re-wording the Key Questions will be any more informative to readers. Exposure to psychological trauma can be conceptualized as direct experience of the trauma or indirect exposure to it.
Peer Reviewer #4	Introduction	p. 1, line 57 same issue as above: "directly expedrienced or were exposed to"	The text has been revised.
Peer Reviewer #4	Introduction	p. 10, mention might be made to sub-clinical forms of PTSD experienced in the aftermath of traumatization for many exposed individuals.	It is somewhat unclear where in the text the reviewer thought that this distinction might be useful, as the focus of this section of the report is on interventions to prevent PTSD. In addition, the report did not focus on subclinical forms of PTSD.
Peer Reviewer #4	Introduction	p. 11, line 1: change to "substancial number of adults"	We have changed “individuals” to “adults”.
Peer Reviewer #4	Introduction	p. 11, line 12. psychological trauma can be more than an identifiable event in that it might be ongoing or might be due to emotions generated at the time of exposure. I suggest you might want to more clearly distinguish the source event(s) from the aftermath.	The sentence beginning with “Unlike other psychiatric disorders …” and the following sentence have been deleted. We have added several paragraphs to both the ES and to the Introduction describing the different strategies of universal vs. targeted prevention.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #4	Introduction	p. 11, lines 43 on, same comment as above about wording.	We have replaced “a traumatic event” with “psychological trauma” to reflect the fact that trauma might be ongoing rather than discrete.
Peer Reviewer #4	Introduction	p. 12, line 44, population at risk, suggest adding those who have been previously traumatized and those who have previously had PTSD.	We did not create separate categories for persons who had been traumatized previously or those who previously had PTSD. However, if a study included a subgroup analysis based on either of those groups, we would have included them in our review because they are subsumed by our existing subgroup category scheme. The subgroup, “persons who had been previously traumatized” would have been included in our subgroup, “Personal risk for PTSD”. Indeed, we included one study that looked at the subgroup of “previous child abuse”, as part of the “Personal risk of PTSD” category. If a study had done a subgroup analysis by “Previous PTSD”, we would have included it, as part of the category, “Psychiatric comorbidities”.
Peer Reviewer #4	Methods	p. 16, line 40, add POW, slavery or other captivity to the list of traumas. Seems very important that bias in studies was taken into consideration.	We have added these traumas to the list in table 3.
Peer Reviewer #4	Results	Detail is considerable and appropriate. Seems very comprehensive and descriptive of findings. Categorization detailed and descriptive.	Thank you.
Peer Reviewer #4	Discussion	Implications of the major findings are clearly stated and limitations are adequately described.	Thank you.
Peer Reviewer #4	General	This is a topic of significance that is clinically meaningful. It is especially important given that interventions can be helpful or harmful and both ends of the spectrum are addressed in this report.	Thank you.
Peer Reviewer #4	General	Yes to all. The findings of this review are unfortunately not optimistic about current interventions but they do point the way to the urgent need for additional research that is more methodologically sound. The findings of this review should be widely disseminated in order to curtail the use of techniques and interventions that are not effective and that might be harmful to those who have been traumatized.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Executive Summary	The text in page 12 lines 29-30 cites a statement from the IOM (2008) report that "up to a third" of trauma exposed individuals develops PTSD. The phrase "up to a third" is imprecise and appears to overdramatize the impact of PTSD as a public health problem. The paragraph that follows gives the most recent epidemiological U.S. estimates available. The three items of information – percentages experiencing trauma, the IOM reference of proportion of victims with PTSD and the NCS-R percentages of PTSD in the USA came from different sources, created at different time periods and possibly based on different editions of the DSM. I suggest that the NCS-R (2000) should be used as the source for estimates of both exposure to trauma and PTSD.	Thank you for your suggestion. We have deleted the 2008 IOM statement mentioned in your comment to avoid overdramatizing the impact of PTSD. We now cite two additional, recently published articles that provide updated estimates of lifetime and current prevalence of PTSD based on the NCS-R (2000). However, we were unable to locate any NCS-R (2000) estimates of lifetime trauma prevalence or the proportion of trauma victims with PTSD.
Peer Reviewer #5	Executive Summary	The text in lines 41-44 makes the assumption that, unlike other psychiatric disorders, PTSD might be more readily prevented because the cause – an identifiable traumatic event --- allows to identified exposed people at risk for PTSD. This assumption is highly questionable. This is because the prevalence of lifetime PTSD is 6.8%, according to the NCS-R. The percentage of trauma exposed is >80% in the NCS-R. This means that <10% of trauma exposed (lifetime) are at risk of PTSD. Offering treatment to all those who are exposed is clearly wasteful.	In the draft, we did not draw an explicit distinction between universal and targeted prevention approaches. We now make that distinction explicit in the ES and full report, and we describe our rationale for evaluating both universal and targeted prevention interventions in the full report.
Peer Reviewer #5	Executive Summary	The first sentence states that the goal of the review is to evaluate interventions "to prevent PTSD in adults." This focus later extends to include related constructs. The report should explicitly discuss this extension.	As outlined in the methods of the full report, we are interested in other patient-relevant outcomes as well. The prevention of PTSD can be viewed as the primary outcome.
Peer Reviewer #5	Executive Summary	KQ 1 (lines 20-23) includes, in addition to interventions "to prevent PTSD", another class of interventions "to improve health outcomes." The latter is a vague construct that is never defined in this report.	We talk more about health outcomes in the methods of the full report. Because of space limitations, we need to keep the methods in the ES brief.
Peer Reviewer #5	Executive Summary	Page 14 Figure A. The "Outcomes" Box includes 10 constructs. This seems to be too many. Some of the listed outcomes are vague (e.g., resilience). None of the other constructs (that is, other than "incidence of PTSD", the obvious outcome needing no further definition), are explicitly defined in this document.	The outcomes have been defined by the Technical Expert Panel.
Peer Reviewer #5	Executive Summary	Pages 15,16 Methods. The methods, as outline, are very impressive. The only problem is in the list of outcomes in Table A, which includes, in addition to the 10 in Figure A, 2 more for a total of 12. [The second outcome, "Incidence and Severity of symptoms (e.g. sleep disturbance, anxiety)" is problematic, as I discuss below.] With perhaps no more than a single exception the studies were conducted on *clinical samples*, a fact that is unrecognized in the report. Results from samples of persons coming to treatment might not apply to members of the general community, who suffered traumatic experiences of the same type.	Many thanks for this comment. We are addressing this point as a limitation in the revised report.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Executive Summary	The general conclusion of the report, stated in the second sentence of the Discussion, is sobering: there is inadequate evidence to draw conclusions on whether or not interventions to prevent PTSD and related problems work. The exceptions, where meager evidence exists, support ineffectiveness of some popular interventions (e.g. debriefing) and possibly some limited advantage of CBT over SC. This is a disappointing, though justified, judgment on the state of science in this field, according to the standards adhered to in the evaluation of the evidence. The authors should consider adding a statement that this judgment does not apply to interventions to treat *chronic PTSD*, a topic not covered in this report.	We have added a sentence to the end of the conclusions.
Peer Reviewer #5	Executive Summary	The text in page 25, lines 33-39 states that the primary outcomes of the report---prevention of PTSD (including reduction of PTSD symptoms) --- was assessed in only a few studies and that several studies reported only on the rates of various "posttraumatic stress symptoms without establishing the incidence of PTSD." The report's critique of studies that reported only rates of various individuals PTSD symptoms is that PTSD symptoms "must be viewed as intermediate endpoints" and that "whether such findings can be extrapolated to differences in the incidence of PTSD remains unclear…". Calling PTSD symptoms (in the absence of information on PTSD incidence) "intermediate endpoint" is unclear and, I believe, incorrect. Symptoms of PTSD are diagnostically ambiguous. They characterize other anxiety disorders and depression and are used in the official definition of these disorders. They are also common symptoms of non-specific distress. Without pre-exposure measurement, it is entirely unclear that these non-specific symptoms, which are common in the general population, resulted from the identified trauma that is the focus of the intervention. These symptoms cannot be considered "intermediate endpoints", (that is, intermediate between the traumatic event and PTSD; caused by the event and causing PTSD.) Non-specific distress has long been a subject of sociological research (e.g. distributions across sub groups of the population, such as social classes, minority, and gender) and psychological/psychiatric research (e.g. their stability and relationship with personality traits). This review would benefit from clarifying this point or deleting this part of the text.	We agree with the reviewer that PTSD symptoms, because of their lack of specificity, cannot be considered intermediate endpoints. We have deleted that sentence.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #5	Executive Summary	The text on page 29 last paragraph cautions that "Preventing PTSD may present a set of unique challenges, because …" clinicians cannot predict when or where events will occur…." This contradicts in spirit the optimistic statement in the "Background" section (page 12, lines 35-44), asserting that exposed people at risk of PTSD can be identified and PTSD prevented, in contrast with people at risk for other psychiatric disorders. This should be resolved, possibly by deleting both statements. Appropriate services should be accessible to victims who want them. Clearly, only a small fraction of people exposed to traumatic events is at risk for PTSD and efforts to identify who is at risk are not feasible.	We have deleted the sentence that begins, "Unlike other psychiatric disorders …" and the following sentence that begins, "Therefore, the people at risk of developing PTSD …" We have now drawn an explicit distinction between universal and targeted prevention approaches in the ES and full report and have provided a justification for evaluating both types of interventions in the full report. We have added a paragraph to the discussion section on the importance of developing instruments to identify persons, among those who are exposed to a traumatic event or series of traumatic events, those who will develop the psychiatric disorder of PTSD. While we agree that, to date, efforts to identify those at risk have been disappointing, we do not believe that there is sufficient evidence to say that it is not feasible.
Peer Reviewer #5	Executive Summary	The text on page 30 first paragraph suggests that the focus of early intervention research should change to "mitigating symptoms severity and the impact that these symptoms have on functional outcomes…" This suggestion is based on the assumption that functioning problems among trauma exposure (e.g. unemployment, family problems, alcohol abuse) result from PTSD symptoms. This assumption is untested and is probably wrong. Interventions to address such functional problems in trauma victims merit research attention. Military veterans with and without PTSD have high rates of such problems. However, these functioning problems are likely to be independent of PTSD symptoms. There is no evidence that the causal pathway is as assumed here. Early interventions for these problems before they become chronic should receive high priority.	The text has been revised.
Peer Reviewer #5	General	My comments cover only the Executive Summary of the report. Nonetheless, I reviewed most of the document, including the extensive Appendices that summarize the characteristics of the studies, the evaluation of their methodologies and their evidential value. I found the document to be thorough and competently done.	Thank you.

Commentator & Affiliation	Section	Comment	Response
Katherine Li	References	More focus should be given to psychosocial support, considering how important it is in promoting resilience. The only mention to it is in the reference list as part of the name of a study. Tecic T, Schneider A, Althaus A, et al. Early short-term inpatient psychotherapeutic treatment versus continued outpatient psychotherapy on psychosocial outcome: a randomized controlled trial in trauma patients. J Trauma. 2011 Feb;70(2):433-41. PMID: 21057336.	Unfortunately, only one study that met our inclusion criteria specifically addressed psychosocial concerns, and this study was rated as having a high risk of bias. Therefore, we are not able to comment on the relationship between psychosocial support and resilience or the relationship between resilience and the prevention of PTSD.
Sreedhar Tirunagari	General	n/a	N/A
NIMH	General	Throughout the report, an important distinction between universal and indicated prevention is not made. It appears that the approach taken is one of universal precaution. Contemporary scientific and state-of-the-art clinical efforts in this area have moved beyond universal prevention based on a large epidemiologic literature describing post traumatic symptoms (experienced by many/all) and disorder (experienced by a minority). Thus, the majority opinion in the field is that universal prevention of PTSD is neither feasible nor warranted. It is worth noting that the field currently lacks tools for differentiating between sub-groups with different trajectories (those who spontaneously recover versus those who develop chronic PTSD). AHRQ may wish to undertake an additional review focused on prevention among high risk trauma survivors who carry the greatest public health burden.	The introduction now contains two paragraphs to clarify this. In the introduction, under Condition and Preventive Strategies in the ES and under Prevention Strategies in the full report, we include a paragraph explaining the difference between universal and targeted prevention. In the section on the Scope of this Review in the full report, we added a paragraph explaining why we focus on studies of both universal and targeted prevention.
NIMH	General	It appears that the authors utilized a very high standard for potential bias in this report. Out of 2,438 potential studies identified, only 15 were ultimately used. The authors cite several factors that may introduce bias (e.g., loss study of participants in the follow up) and may be quite challenging after a mass trauma. The authors might consider including those studies that lost participants in follow up if the studies meet other bias criteria. Additionally, there may be robust but somewhat less restrictive criteria that might be employed to capture the large body of evidence from research trials.	Our criteria for rating the risk of bias are based on established guidance by the AHRQ Evidence-based Practice Center program. Loosening the criteria or including studies that we considered high risk of bias would not change our confidence in the results. When rating the strength of evidence, outcomes based on these studies would still be rated as insufficient to draw conclusions.
NIMH	General	Other areas to address include the inconsistent metrics applied to the inclusion/exclusion of findings from studies. Notably, this is the case with the Critical Incident Stress Debriefing (CISD) debriefing findings. The authors conclude that there is a lack of evidence supporting debriefing approaches, yet indicate that there is evidence for CISD to reduce acute symptoms from a single trial. In light of the potential harmful effects of debriefing, and the literature indicating that it is not helpful for longer term outcomes, we suggest framing the CISD findings within the context of the larger literature.	Thanks for pointing out this issue. We have revised this section substantially.

Commentator & Affiliation	Section	Comment	Response
NIMH	General	We suggest adding "Universal" to the title, i.e.,: "Universal Interventions for the Prevention of Posttraumatic Stress Disorder (PTSD) in Adults After Exposure to Psychological Trauma."	We have made the distinction between universal and targeted interventions in the ES and the body of the full report.
NIMH	Executive Summary	We suggest deleting the sentence "Some evidence, however, indicates that early critical incident stress debriefing (within 10 hours) might be effective for reducing the severity of PTSD symptoms." This appears to originate from a partial result of one study, and the potential harm finding is not reported side by side with this statement. Also see table F. (pp. V; ES-13). Other mentions of this finding throughout the report should also be modified or deleted; the CISD finding from one study is not a prevention finding.	We have deleted this sentence because the finding it reports was based on insufficient evidence about early CISD's efficacy.
NIMH	Executive Summary	We suggest that the statement "debriefing appears to be an ineffective intervention to prevent PTSD" be inserted wherever CISD or other similar interventions are mentioned. (p. VI)	We make this clear in several sections of the report, and do not think that it will be helpful to the reader to repeat this every time these interventions are mentioned in the text.
NIMH	Executive Summary	Regarding the sentence: "Therefore, the people at risk of developing PTSD, that is, those exposed to trauma, can be identified, and preventive interventions can be offered to them shortly after exposure." (p. ES-1) Although exposure places people at risk, this statement overlooks a large and robust literature on risk confirming that exposure itself is one of the weakest risk predictors and use of this as a criterion would be relevant only perhaps for universal screening interventions. (p. ES-2)	We have deleted the sentence beginning with "Unlike other psychiatric disorders,.." and the following sentence beginning with "Therefore, the people at risk..." We have now explicitly described the two distinct prevention strategies, universal and targeted prevention, in the ES and full report and provided the rationale for evaluating both types of interventions in the full report.
NIMH	Executive Summary	The inclusion criteria required that interventions had to be administered in the first three months after the traumatic event, and individuals with PTSD were excluded. It is possible to be diagnosed with PTSD only after one month of the trauma. Those who have not developed PTSD within that timeframe are generally considered to be at low-risk for developing the disorder. The group of trauma survivors at highest risk for chronic and debilitating PTSD, as well as complex co-morbid mental and behavioral health outcomes, are those who *do* meet or approach diagnostic criteria within the first few months of their exposure. Additionally, a significant portion of the group at highest risk will spontaneously lose their diagnosis, i.e., recover without formal intervention. There is limited scientific and public health value of an evidence review limited to prevention among low-risk trauma survivors. (p. ES-4)	As described above, we now make the distinction between universal and targeted prevention approaches and explain why we evaluate interventions that used either approach.

Commentator & Affiliation	Section	Comment	Response
NIMH	Executive Summary	Given what is known epidemiologically about the onset of PTSD symptoms and the natural course or trajectory of PTSD, as well as current diagnostic criteria and requirements, we suggest that this review acknowledge its focus on prevention among low-risk trauma survivors and relative exclusion of trials focused on preventing chronic and complicated/co-morbid PTSD among trauma survivors at high-risk for more serious outcomes. (p. ES-4)	We did not focus exclusively on prevention among low-risk trauma survivors. Studies that used the universal prevention approach and studies that used the targeted prevention approach were both eligible for inclusion in this review. We did not include studies that required that participants meet criteria for PTSD to be eligible for inclusion as those studies could be more accurately characterized as studies of treatment of PTSD. Our group recently conducted a comparative effectiveness review of treatment of PTSD and studies in which persons meeting criteria for PTSD one month after being exposed to trauma were eligible for inclusion in that review.
NIMH	Executive Summary	Regarding the statements: "Some evidence (discussed in KQ2), however, indicates that early critical incident stress debriefing (within 10 hours) might be effective for reducing the severity of PTSD symptoms. We had insufficient data (single study) to determine the efficacy of debriefing at 2- or 6-week follow-up, as well as at 11-month follow-up." (p. ES-8) As noted earlier, the reporting of this single finding is inconsistent with other reporting conventions used in the report. If single study findings are to be included, we suggest greater detail be reported about harm findings from Table F, and that positive findings for prolonged exposure (PE) and cognitive therapy (CT) be reported from single trials (see Shalev et al., PMID: 29169418) as well. (p. ES-8)	The text has been revised accordingly.
NIMH	Executive Summary	Also, is there evidence to suggest that findings from studies conducted in one group of trauma survivors would not hold up in other groups where the studies were not completed (e.g., terrorist attacks, sexual assault, natural disaster, combat)? Where there are studies completed in different trauma exposure groups with the same intervention, this seems to add to the evidence base. (p. ES-8)	We retrieved only one such study. It compares the efficacy of a modified prolonged exposure therapy for preventing PTSD and reducing PTSD symptoms among adults following exposure to different types of trauma.
NIMH	Executive Summary	The report states that there is insufficient evidence for whether sex modified the effect of early psychological interventions in the two trials cited. However, both citations are review articles rather than publications from individual trials where information on the magnitude of the estimated effect would likely be reported. We suggest looking at individual trials cited by review articles for information. In addition, it is possible that the wrong citations were included in the executive summary, as they do not match those cited in the full report (citations 15, 23 on ES-12 vs. citations 112, 123 on p. 59).	The citations in both the ES and full report should have referred to RCTs conducted by Rose et al., 1999 and Campfield et al., 2001, respectively. We have ensured that both sets of citations are correct.

Commentator & Affiliation	Section	Comment	Response
NIMH	Executive Summary	Although studies may not characterize or explicitly state the risk of harm, this information can be provided through pre- and post-symptom levels scores. Where an intervention may be harmful, one would at least expect to see an increase in scores, although this may reflect that some trial have focused on the most at-risk or ill survivors who might have experienced even greater distress/outcomes scores had the intervention not been provided. To the extent that any study reports a decrease in scores across measures, it suggests that there is no harm done with respect to symptom profiles. It would be helpful if this report reviewed those studies that provided such information. (pp. ES-12-13)	We believe that harms need to be explicitly assessed to be able to draw reliable conclusions. It would be impossible for us to determine whether an increase in pre-post scores is based on harmful effects or a lack of efficacy with a progression of the disease.
NIMH	Executive Summary	The following bullets are difficult to interpret and appear to conflict. • "Our meta-analyses of three studies comparing CBT with SC in individuals with acute stress disorder found no statistically significant difference between treatments for preventing PTSD (low SOE), reducing the severity of depression symptoms (low SOE), or reducing the severity of anxiety symptoms (moderate SOE). Results trended in favor of CBT and were generally imprecise." • "Our meta-analyses of three studies comparing CBT with SC in individuals with acute stress disorder found that persons who received CBT had greater reduction in severity of PTSD symptoms than those who received SC (moderate SOE)." (pp. ES-13-14)	We merged these two bullets into one and changed the language to make the findings clearer.
NIMH	Executive Summary	As noted earlier, the CISD finding does not seem appropriate to report in the following bullet: • "Early critical incident stress debriefing (CISD) in robbery victims is more efficacious in preventing symptoms of PTSD and reducing symptom severity than late CISD (low SOE)." (p. ES-14)	The text has been revised.
NIMH	Executive Summary	Regarding: "Some studies selected populations with acute stress disorder, which might have little applicability to populations exposed to psychological trauma who may or may not have acute stress symptoms at the time of the intervention." As noted earlier, unless the review declares that its focus is limited to universal interventions, it is misleading to suggest that presence of acute symptoms makes a trial not applicable. It is arguable inappropriate to intervene with asymptomatic trauma survivors. (p. ES-14)	We have revised that paragraph substantially. We now draw the distinction between universal and targeted prevention and indicate that findings from studies of universal prevention interventions may not be applicable to persons at high risk and that studies using targeted prevention interventions may not be applicable to populations exposed to trauma that are not differentiated by risk.
NIMH	Executive Summary	Regarding: "Our primary outcome measures were prevention of PTSD (couched as incidence of PTSD) and reduction of symptoms of PTSD. Few studies, however, assessed such endpoints." Many of the included trials should be dropped, as they are not relevant to preventing PTSD. (p. ES-14)	The text has been revised.

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NIMH	Executive Summary	Regarding: "Rates of various symptoms, however, must be viewed as intermediate endpoints. Whether such findings can be extrapolated reliably to differences in the incidence of PTSD remains unclear based on our results." These statements are imprecise, and it is misleading to suggest that symptoms should be used as a proxy for PTSD in clinical trials or practice. Posttraumatic stress symptoms are ubiquitous, i.e., a normative response to trauma whereas PTSD is a significant complex psychiatric illness. (p. ES-14)	The diagnosis of PTSD is defined by the number and severity of symptoms which individuals may experience in the aftermath of a traumatic event. As such, symptoms of PTSD are the only available indicator of the disorder prior to the required 1 month period of time to elapse post-trauma when the actual diagnosis can be made.
NIMH	Executive Summary	Again reference to single CISD finding seems inconsistent with the review conventions: "The single trial of CISD timing indicated that early CISD was more effective than late CISD in reducing the number of posttraumatic symptoms in victims of robbery. Whether these findings can be extrapolated to populations experiencing other traumas remains unclear." This is a finding (not *findings*), and we don't know if it's real and we don't see the potential harm data reported as in table F. (p. ES-15)	The text has been revised.
NIMH	Executive Summary	The following statements, "Although these participants did not have a diagnosis of PTSD per se (as 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" which are paraphrased elsewhere, argue for renaming the review as one of universal interventions. Based on strong epidemiological data, one should review universal and indicated prevention efforts individually unless they are combined as a single program in response to trauma. Universal intervention may be most useful as a way of identifying those at greatest risk (screening) and in need of assessment and possible preventive intervention – the goals of universal post trauma intervention would be quite different from preventing PTSD. (p. ES-16)	We appreciate this comment. In the revised report we will be more explicit about studies that used universal and indicated prevention. We agree with the reviewer that this is an important point to consider.
NIMH	Executive Summary	The research gaps identified did not include one of the greatest barriers to more robust and efficient trials, i.e., prediction of those at greatest risk. (p. ES-17)	We have added a section on that topic to research gaps.
NIMH	Executive Summary	Regarding: "These may include combat-exposed military personnel and various types of first responders." We suggest inserting a statement identifying the great potential to learn about prevention of PTSD by working with other high risk groups (e.g., first responders including police and fire), as well as emergency department and trauma centers that see hundreds of thousands of acute injury and trauma patients each year. (p. ES-18)	We have added a statement to the ES.

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NIMH	Executive Summary	Regarding: “One could argue that the threshold for obtaining a diagnosis of PTSD is sufficiently high enough that many trauma-exposed individuals, who may have substantial amount of symptoms and impairment as a result, may not be able to receive treatment and support because that do not meet all of the criteria required to obtain a diagnosis.” While this is a fair statement, it should be made clear that ~8 million adults in the U.S. each year have a diagnosis of PTSD, making prevention an important goal. (p. ES-19)	The text has been revised to incorporate this statistic.