Evidence-based Practice Center Systematic Review Protocol

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

Amendment Date(s): November 8, 2012; September 26, 2012; July 27, 2012

(Amendments Details—see Section VII)

I. Background and Objectives for the Systematic Review

Studies suggest that individuals experience a broad range of traumatic events throughout their lives, and that the frequency of these events may vary by the group studied, for example, civilian versus noncivilian samples. The fourth edition of the American Psychiatric Association’s Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) defines a traumatic event as an event experienced, witnessed, or confronted by a person that involves (a) actual or threatened death, (b) serious injury, or (c) a threat to the physical integrity of self or others. The DSM-IV-TR diagnosis of PTSD also requires that the person’s response to the event involve intense fear, helplessness, or horror. Traumatic events may 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. The full DSM-IV-TR criteria are listed in Table 1.

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

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Symptom or description</th>
</tr>
</thead>
</table>
| 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: Re-experiencing 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 | - Disturbance causes clinically significant distress or impairment in social, |
Prevalence of Traumatic Events

Studies conducted in the 1990s attempted to identify and describe the prevalence of traumatic events in nonclinical samples. Resnick et al. (1993) found that lifetime exposure to any type of traumatic event was 69 percent in a sample of 4,008 adult U.S. women. 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.

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. Several studies have examined the prevalence of traumatic events among college students. These studies all showed that exposure to traumatic events was relatively common, with lifetime prevalence ranging from 39 to 84 percent.

Development of PTSD and Rationale for Early Intervention to Prevent PTSD

Many theories focus on the role of disturbances in memory (i.e., problems with memory formation, retrieval, bias, saliency, etc.), and 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 memories are not properly integrated into memory, individuals may re-experience symptoms of PTSD.

Intense affect during a traumatic event and its accompanying physiological arousal have been associated with the development of PTSD. Dissociation or detachment during the event has also been found to be a significant predictor of PTSD. In extreme threat situations, strong affect can result in dissociation, and prevent 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 and/or may make the memory less accessible. 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. Some studies have shown that elevated levels of cortisol and adrenaline can disrupt the normal formation of memories, while others have found that stress hormones enhance memory consolidation.

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 cognitive schema. An individual exposed to a traumatic event tries to make sense of the experience but has difficulty fully integrating it into his/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.
The implications of these various theories provide a rationale for a myriad of early intervention strategies, but they are only one part of the puzzle. 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.

**Potential Preventive Interventions**

Potential preventive interventions span a variety of psychological and pharmacological domains. 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: psychological debriefing interventions, including critical incident stress debriefing (CISD) and critical incident stress management (CISM); psychological first aid (PFA); trauma-focused cognitive-behavioral therapy (CBT); cognitive restructuring therapy; cognitive processing therapy; exposure-based therapies; coping skills therapy (including stress inoculation therapy); psychoeducation; normalization; and eye movement desensitization and reprocessing (EMDR). These therapies are designed to prevent the onset of PTSD and development of trauma-related stress symptoms soon after exposure to a traumatic event.

**Psychological Debriefing, CISD, and CISM**

Psychological 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 typically offered in a single session within hours or days following the event to everyone exposed to the event. Although several variations of these single session interventions have been tested, the most common form of psychological debriefing is CISD.\(^14\)

**CISD** is a secondary prevention 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.\(^15,\,16\) 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 it.\(^17\) 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.\(^18\,\,19\) A 2002 update of a previous 1997 Cochrane Review assessed the effectiveness of brief, single-session psychological debriefing for the management of psychological distress after trauma and the prevention of PTSD.\(^21\)

CISD has expanded to become **CISM**, a multicomponent, comprehensive crisis intervention program that aims to reduce the severity of, and related impairment
associated with traumatic stress.\textsuperscript{18} CISM incorporates additional methods such as pre-incident training for people with high-risk occupations, one-on-one individual crisis support, demobilizing (i.e., information about coping and stress to large groups of emergency workers as they rotate off duty), and defusing (small-group interventions during which participants are asked to explore and discuss the incident and their emotional reactions to it).\textsuperscript{15} CISM also has a family support component whereby family members of the emergency personnel are debriefed. Lastly, there are additional procedures for referring people for psychological services.\textsuperscript{18}

\textit{PFA} is a systematic set of helping actions aimed at reducing initial posttrauma distress and supporting short- and long-term adaptive functioning. PFA is designed as an initial component of a comprehensive disaster/trauma response, and 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.\textsuperscript{22} PFA is concept-driven and 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 non-disaster field settings, including hospital trauma centers, rape crisis centers, and war zones.\textsuperscript{23}

\textit{CBT} uses principles of learning and conditioning to treat 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 either as group or individual therapy.\textsuperscript{24-26}

\textit{Exposure-based therapy} involves confrontation with frightening stimuli and 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 (\textit{in vivo} exposure). The aim is to extinguish the conditioned emotional response to traumatic stimuli (for the subject to learn that nothing “bad” will happen during traumatic events), which eventually reduces or eliminates avoidance of feared situations and the affect associated with it. Exposure therapy is typically conducted for 8 to 12 weekly or biweekly sessions lasting 60 to 90 minutes.\textsuperscript{24, 25, 27}

\textit{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 and increase awareness of dysfunctional trauma-related thoughts and correct or replace those thoughts with more
adaptive and/or rational cognitions. Cognitive restructuring generally takes place over 8 to 12 sessions of 60 to 90 minutes.\textsuperscript{24, 25}

*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, while more comprehensive interventions such as stress inoculation therapy require 10 to 14 sessions.\textsuperscript{24, 25}

*EMDR* combines imaginal exposure with the concurrent induction of saccadic eye movements that are believed to help reprogram brain function so that emotional impact of trauma can be resolved. In the EMDR process, the client 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 client to contemplate memory while focusing on rapid movement of clinicians’ fingers. After 10 to 12 eye movements (back and forth), the clinician asks the client 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.\textsuperscript{24, 28}

**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 PTSD prevention including propranolol, morphine, glucocorticoids, and selective serotonin reuptake inhibitors (SSRIs).\textsuperscript{11, 26}

*Propranolol*

A significant body of research suggests that PTSD is associated with hyperreactivity of the sympathetic nervous system, specifically the noradrenergic system. Studies have repeatedly shown that heart rates are elevated in the peritraumatic event period among persons exposed to trauma who develop PTSD, that stress-induced norepinephrine levels are higher among persons with PTSD, and that corticotrophin-releasing factor, which stimulates release of norepinephrine, is elevated among persons with PTSD.\textsuperscript{29}

Propranolol, a beta-adrenergic antagonist that crosses the blood-brain barrier, has been evaluated in several studies for its ability to prevent PTSD.\textsuperscript{30-32} So far results have failed to show any clear benefit of propranolol compared to 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.\textsuperscript{33} This
effect leads to various ethical concerns, considering that the long-term implications of emotional and episodic memories are not yet well understood.

**Morphine**

The opiate analgesic, morphine, has shown promise in preventing PTSD in persons experiencing physical injury from a traumatic event. In 155 adults hospitalized following traumatic injury, those prescribed higher doses of morphine had lower incidence of PTSD at 3-month follow-up. In 696 combat-injured U.S. military personnel serving in Iraq, the use of morphine during early trauma care was associated with significantly lower risk of a subsequent PTSD diagnosis. These studies highlight and support the importance of pain control in physically injured persons, but the potential role of opiates in prevention of PTSD following severe psychological trauma in the absence of painful physical injury remains unclear.

**Cortisol**

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 persons with PTSD. This has led to the hypothesis that exogenous administration of cortisol shortly after trauma may prevent PTSD by preventing development of HPA axis dysregulation.

Several naturalistic studies have found that patients who were administered glucocorticoids either during or immediately following the trauma were significantly less likely to develop PTSD than those who were not. These studies were conducted naturalistically in settings where multiple variables, including the administration of other medications and treatment procedures, could not be controlled.

**SSRIs**

SSRI (selective serotonin reuptake inhibitors) antidepressants 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. 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.

Table 2 provides a summary of the medications studied for the prevention or treatment of PTSD.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Class</th>
</tr>
</thead>
</table>

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)

Published Online: November 8, 2012
Class | Drug
---|---
Selective serotonin reuptake inhibitors | citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline
Serotonin and norepinephrine reuptake inhibitors | duloxetine, desvenlafaxine, and venlafaxine
Other second-generation antidepressants | bupropion, mirtazapine, nefazodone, and trazodone
Tricyclic antidepressants | imipramine, amitriptyline, and desipramine
Monoamine oxidase inhibitors | phenelzine, isocarboxazid, selegiline, and tranylcypromine
Alpha blockers | prazosin
Beta blockers | propranolol
Benzodiazepines | alprazolam, diazepam, lorazepam, and clonazepam
Anticonvulsants | topiramate, tiagabine, lamotrigine, carbamazepine, divalproex, and gabapentin
Nonbenzodiazepine sedatives/hypnotics | zolpidem, eszopiclone, rozerem, and zaleplon
Second-generation (atypical) antipsychotics | olanzapine and risperidone
Narcotic medication | morphine
Steroids | hydrocortisone
Opioid antagonists | naltrexone

**Emerging Interventions**

In addition to traditional psychological and pharmacological interventions, there is a growing variety of emerging interventions and approaches derived from complementary and alternative medicine (CAM). Among these are dietary supplements, yoga, and guided imagery. The use of CAM practices to prevent PTSD is relatively novel, and as a result, their efficacy remains unclear.

**Prevention Intervention Outcomes**

One of the primary outcomes in the PTSD prevention intervention literature is lack of trauma-related symptom development, which includes both clinician-rated and self-reported measures. In addition, we will consider other health outcomes such as symptom reduction; prevention/reduction of comorbid medical or psychiatric conditions (e.g., depressive symptoms, anxiety symptoms); improved quality of life; or ability to return to work or return to active duty. If we cannot find data on a particular health outcome of interest, we will include surrogate outcomes if evidence of a causal relationship between surrogate and health outcome is available.

**Summary of Existing Guidance**

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)
Published Online: November 8, 2012
A recent review assessed the evidence base for existing guidelines for PTSD from seven respected organizations in the United States, Australia, and Europe. These organizations include the American Psychiatric Association (APA), the U.S. Department of Veterans Affairs/Department of Defense (VA/Department of Defense), the National Institute of Clinical Excellence (NICE), the National Health and Medical Research Council (NHMRC), the International Society for Traumatic Stress Studies (ISTSS), the American Academy of Child and Adolescent Psychiatry (AACAP), and the Institute of Medicine (IOM). The review investigated whether each of the guidelines was based on existing evidence and concluded that the empirical data were insufficient to support many of the guidelines and recommendations put forth by these organizations.

Nonetheless, the clinical practice guidelines named above provide very similar recommendations regarding prevention of PTSD. Five of the seven sets of guidelines (VA/Department of Defense, APA, NICE, NHMRC, ISTSS for adults, and ISTSS for children and adolescents) address early preventive interventions for populations exposed to trauma. They each warn against the use of psychological debriefing interventions to prevent the onset of PTSD, and four (APA, NICE, NHMRC, and ISTSS for adults) describe alternative approaches. The NICE guidelines suggest offering “practical social and emotional support” to trauma survivors, while the NHMRC guidelines suggest provision of psychological first aid based on expert consensus and the ISTSS guidelines support “practical, pragmatic psychological support and information.” The APA guidelines state that the use of early supportive interventions, psychoeducation, and case management may be helpful for acutely traumatized individuals because they “promote engagement in ongoing care and may facilitate entry into evidence-based psychotherapeutic and psychopharmacological treatments [II].” In addition, the APA guidelines report that there is only minimal evidence that early supportive care alone can lead to long-term reductions in PTSD symptoms in populations of patients exposed to multiple recurrent traumas. On the other hand, there is no evidence of harms due to early supportive care.

**Rationale and Objective of the Review**

Psychological trauma is common and leads to PTSD in a substantial number of individuals exposed to trauma. Prevention of PTSD, therefore, has the potential to reduce a significant burden of individual and societal suffering. Unlike most psychiatric disorders, the precipitating cause of PTSD, psychological trauma, is an identifiable event that has a known time and place of onset. Therefore, the people at risk of developing PTSD, i.e., those exposed to trauma, can be identified and preventive interventions can be offered to them shortly after exposure.

In spite of evidence that some early 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 like it should help, and also that not enough consideration is given to scientific evidence when weighing intervention benefits and harms.
The objective of this review is to evaluate systematically the evidence on the general and comparative effectiveness and risk of harms of early interventions to prevent PTSD in people who have experienced psychological trauma. The report will also take into account the unique nature of different types of trauma and moderators affecting the impact of traumatic exposure. We will develop an analytic framework that will help conceptualize interventions to prevent PTSD.

This evidence review will be part of a collection of reports produced by the Agency for Healthcare Research and Quality for a three-part series focusing on the treatment of PTSD in populations exposed to trauma. These reports will critically assess the comparative effectiveness of selected interventions aimed at treating symptoms of PTSD in adults and children, and of interventions to prevent the development of PTSD in adults exposed to psychological trauma.

Note: This Protocol includes revisions to the Key Questions suggested by our Key Informants and revisions to the PICOTS (specifically the minimum sample size of 100 for prospective cohort studies, the addition of MAOIs and nonbenzodiazepine sedatives/hypnotics to the list of pharmacological interventions, and changing the name of the pharmacological interventions table) suggested by members of our Technical Expert Panel and the project team. We posted the draft Key Questions for public comment on January 4, 2012 and received one comment on January 8, but it applied to another report in progress supported by AHRQ that addresses the psychological and pharmacological treatments for adults with PTSD.

II. Key Questions (KQs)

KQ 1: For adults exposed to psychological trauma, what is the absolute effectiveness or comparative effectiveness 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 do 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 versus not having the diagnosis)?

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

Population, Interventions, Comparators, Outcome measures, Timing, and Setting (PICOTS) criteria for the preceding KQs are:

Source: www.effectivehealthcare.ahrq.gov
Published Online: November 8, 2012
• **Population(s):**
  
  − Adults exposed to psychological trauma (to include interpersonal or domestic violence/abuse, sexual abuse/assault/rape, combat/military-related trauma, crime-related events, terrorism, natural disasters, injury, life-threatening illness or medical procedures, witnessing a traumatic event, being a refugee, and asylum seeking) at risk of developing PTSD.
  
  − Subgroups of interest include:
    
    o Demographic groups (defined by age, ethnic and racial groups, and sex)
    
    o Populations with psychiatric comorbidities
    
    o Populations with different personal risks of developing PTSD

• **Interventions**
  
  − Psychological interventions including:
    
    o Trauma-focused CBT
    
    o Cognitive restructuring and cognitive processing therapy
    
    o Exposure-based therapies
    
    o Coping skills therapy (including stress inoculation therapy)
    
    o Psychological first aid
    
    o Psychoeducation
    
    o Normalization
    
    o EMDR
    
    o Psychological debriefing
    
    o CISD
    
    o CISM
  
  − Pharmacological interventions including:
    
    o SSRIs: citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline
    
    o Serotonin–norepinephrine reuptake inhibitors (SNRIs: duloxetine, desvenlafaxine, and venlafaxine)
    
    o Other second-generation antidepressants (bupropion, mirtazapine, nefazodone, and trazodone)
- Tricyclic antidepressants (imipramine, amitriptyline, and desipramine)
- MAOIs (phenelzine, isocarboxazid, selegiline, and tranylcypromine)
- Alpha blockers (prazosin)
- Beta blockers (propranolol)
- Benzodiazepines (alprazolam, diazepam, lorazepam, clonazepam, and temazepam)
- Anticonvulsants/mood stabilizers (topiramate, tiagabine, lamotrigine, carbamazepine, divalproex, and gabapentin)
- Nonbenzodiazepine sedative/hypnotics (zolpidem, eszopiclone, rozerem, and zaleplon)
- Atypical antipsychotics (olanzapine and risperidone)
- Narcotic medication (morphine)
- Steroids (hydrocortisone)
- Opioid antagonists (naltrexone)
  - Emerging interventions
    - CAM e.g., dietary supplements, yoga, guided imagery

- Comparators
  - Psychological treatments (listed above) with one another
  - Pharmacological treatments (listed above) with one another
  - Psychological treatments with pharmacological treatments (listed above)
  - Pharmacological treatments with placebo
  - Psychological treatments with waiting list assignment, usual care, or no intervention

- Outcomes
  - Final outcomes
    - Incidence of PTSD
    - Incidence and severity of symptoms: assessor-rated or self-rated symptoms (e.g., sleep disturbance, anxiety)

\(^a\) At least one PTSD-related outcome has to be addressed for a study to be eligible.
- Incidence and severity of comorbid 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
  - Adverse effects of intervention(s)
    - Adverse effects (e.g., 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)
    - Dropout rate (overall dropout rate, dropout because of adverse effects, dropout because of lack of efficacy)

- **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

- **Setting**
  - Any setting

### III. Analytic Framework

Figure 1 depicts the analytic framework for the comparative effectiveness of psychological and pharmacological interventions to prevent of PTSD in adults. The KQs are displayed within the context of the population, intervention, comparator, outcome, timing, and setting described in the previous section. Beginning with a population of adults exposed to one or more traumatic events, the figure illustrates the absolute and comparative effects of early preventive interventions on incidence of PTSD or health outcomes, including incidence and severity of trauma-related symptoms, incidence and severity of comorbid conditions, quality of life, quality of interpersonal or social functioning.
functioning, ability to return to work or duty, incidence of self-injuries, suicidal thoughts, attempts, and behaviors, and incidence of aggressive or homicidal thoughts, attempts, and behaviors (KQ 1). Timing of intervention as a potential mediator of these interventions is explored in KQ 2. Type of traumatic exposure and characteristics of subgroups as potential moderators of these interventions are explored in KQ 3. Subgroups within the overall population will be identified based on age, sex, race and ethnicity, psychiatric comorbidities, and personal risk of PTSD.

KQ 4 addresses the absolute and comparative risks of harms and adverse events from these interventions.

**IV. Methods**

**A. Criteria for Inclusion/Exclusion of Studies in the Review.** Table 3 presents the inclusion/exclusion criteria for this review. We do not repeat all of the PICOTS information related to the inclusion/exclusion criteria; Table 3 supplements the information outlined above in the PICOTS.
### Inclusion

| Population | Adults exposed to psychological trauma, as defined above in the PICOTS |
| Geography | No limits |
| Time period | 1980 to present; searches to be updated after draft report goes out for peer review |
| Study duration | No limits |
| Settings | As defined above in the PICOTS |
| Interventions | Early interventions (any time ranging from immediately to 3 months after exposure) for the prevention of PTSD, as defined above in the PICOTS |
| Control Interventions | Early interventions (any time ranging from immediately to 3 months after exposure) for the prevention of PTSD, as defined above in the PICOTS |
| Outcomes | As listed above under the PICOTS |

### Exclusion

<table>
<thead>
<tr>
<th>Publication language</th>
<th>English</th>
<th>All other languages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admissible evidence (study design and other criteria)</td>
<td>Original research</td>
<td>Case series</td>
</tr>
<tr>
<td>For KQs 1 through 4 eligible study designs include:</td>
<td>• Randomized controlled trials.</td>
<td>Case reports</td>
</tr>
<tr>
<td>• Prospective controlled cohort studies</td>
<td></td>
<td>• Systematic reviews and meta-analyses</td>
</tr>
</tbody>
</table>

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 |
| | | • Systematic reviews and meta-analyses |
| | | • Nonsystematic reviews |
| | | • Editorials |
| | | • Letters to the editor |
| | | • Studies rated high risk of bias during quality assessment |
| | | • Studies with historical, rather than concurrent, control groups |
| | | • Pre-post studies without a separate control group |

---

*a* Due to limited time and resources, we will only include studies published in English.

Abbreviations: KQ = key question; PICOTS = populations, interventions, comparators, outcomes, timing, and setting; TEP = Technical Expert Panel.
B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the KQs. We will systematically search, review, and analyze the scientific evidence for each KQ. We will take the following steps to perform the literature search.

1. To identify articles relevant to each KQ, we will begin with a focused MEDLINE search using a variety of terms, medical subject headings (MeSH), and major headings and limiting the search to English-language and human-only studies. Relevant terms are listed in Table 4. We will also search the Cochrane Library, the Cochrane Central Trials Registry, the Published International Literature on Traumatic Stress database, the Cumulative Index to Nursing and Allied Health Literature database, PsycINFO, the International Pharmaceutical Abstracts database, EMBASE, and Web of Science by using analogous search terms. We will conduct quality checks to ensure that known studies (i.e., studies included in the previous review on treatment of adult PTSD and those identified during Topic Nomination and Refinement) are identified by the search. If they are not, we will revise and rerun our searches.

2. We will search the literature published in 1980 and later. This 1980 search date was selected based on the introduction/definition of PTSD as a clinical entity and based on 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.

3. We will search the “gray literature” for unpublished studies relevant to this review and will include studies that meet all the inclusion criteria and contain enough methodological information for assessment of internal validity/quality. Sources of gray literature include ClinicalTrials.gov, the FDA Web site, and pharmaceutical companies’ dossiers (for pharmacotherapies of interest). AHRQ’s Scientific Resource Center will manage the process of submitting requests for scientific information packets, which contain information about pharmacotherapies of interest from relevant drug manufacturers.

4. We will review our search strategy with the Technical Expert Panel (TEP) and supplement it as needed according to their recommendations. In addition, to attempt to avoid retrieval bias, we will manually search the reference lists of landmark studies and background articles on this topic to look for any relevant citations that electronic searches might have missed.
5. We will also conduct an updated literature search (of the same databases searched initially) concurrent with the peer review process. We will investigate any literature the peer reviewers or the public suggest and, if appropriate, will incorporate them into the final review. Appropriateness will be determined by the same methods described above.
Table 4. PubMed proposed literature search terms


| Limits | Humans; English; All Adult: 19+ years |

C. Data Abstraction and Data Management. Two trained research team members will independently review all titles and abstracts identified through searches for eligibility against our inclusion/exclusion criteria. Studies marked for possible inclusion by either reviewer will undergo a full-text review. For studies without adequate information to determine inclusion or exclusion, we will retrieve the full text and then make the determination. All results will be tracked in an EndNote® bibliographic database (Thomson Reuters, New York, NY).

We will retrieve and review the full text of all titles included during the title/abstract review phase. Two trained team members will independently review each full-text article for inclusion or exclusion based on the eligibility criteria described above. If both reviewers agree that a study does not meet the eligibility criteria, the study will be excluded. If the reviewers disagree, conflicts will be resolved by discussion and consensus or by consulting a third member of the review team. As described above, all results will be tracked in an EndNote database. We will record the reason why each excluded publication did not satisfy the eligibility criteria so that we can later compile a comprehensive list of such studies.
For studies that meet our inclusion criteria, we will abstract important information into evidence tables. We will design data abstraction forms to gather pertinent information from each article, including characteristics of study populations, settings, interventions, comparators, study designs, methods, and results. Trained reviewers will extract the relevant data from each included article into the evidence tables. A second member of the team will review all data abstractions for completeness and accuracy.

D. **Assessment of the Risk of Bias of Individual Studies.** To assess the risk of bias (internal validity) of studies, we will use predefined criteria based on guidance provided by AHRQ and the University of York Centre for Reviews and Dissemination. In general terms, results of a study with low risk of bias are considered to be valid. A study with medium risk of bias is susceptible to some bias but probably not sufficient enough to invalidate its results. A study with high risk of bias has significant methodological flaws (e.g., stemming from serious errors in design or analysis) that may invalidate its results. We will consider the risk of bias for each relevant outcome of a study.

Two independent reviewers will assess the risk of bias for each study. Disagreements between the two reviewers will be resolved by discussion and consensus or by consulting a third member of the team. We will rate studies that meet all criteria as having “low risk of bias”. “Medium risk of bias” ratings will be given to studies that presumably fulfill all quality criteria but do not report their methods sufficiently to answer all of our questions. We will give a “high risk of bias” rating to studies that have a fatal flaw (defined as a methodological shortcoming that leads to a very high risk of bias) in one or more categories and will exclude them from our analyses.

E. **Data Synthesis.** If we find three or more similar studies for a comparison of interest, we will consider quantitative analysis (i.e., meta-analysis) of the data from those studies. We will also consider conducting mixed treatment comparisons meta-analysis using Bayesian methods to compare the pharmacologic interventions with each other if we identify a sufficient number of studies with a common comparator (e.g., placebo). For all analyses, we will use random-effects models to estimate pooled or comparative effects. In order to determine whether quantitative analyses are appropriate, we will assess the clinical and methodological heterogeneity of the studies under consideration following established guidance. We will do this by qualitatively assessing the PICOTS of the included studies, looking for similarities and differences. If we conduct quantitative syntheses (i.e., meta-analysis), we will assess statistical heterogeneity in effects between studies by calculating the chi-squared statistic and the $I^2$ statistic (the proportion of variation in study estimates due to heterogeneity). The importance of the observed value of $I^2$ depends on the magnitude and direction of effects and on the strength of evidence for heterogeneity (e.g., p-value from the chi-squared test, or a
confidence interval for \( I^2 \)). If we include any meta-analyses with considerable statistical heterogeneity in this report, we will provide an explanation for doing so, considering the magnitude and direction of effects. We will also examine potential sources of heterogeneity using sensitivity analysis or analysis of subgroups. We plan to stratify analyses and/or perform subgroup analyses when possible and appropriate to examine clinical heterogeneity. Planned stratifications or categories for subgroup analyses include the subgroups listed in the analytic framework and geographic location of studies. When quantitative analyses are not appropriate (e.g., due to heterogeneity, insufficient numbers of similar studies, or insufficiency or variation in outcome reporting), we will synthesize the data qualitatively.

F. Grading the Evidence for Each KQ. We will grade the strength of evidence based on the guidance established for the Evidence-based Practice Center Program.\(^4\) 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 5 describes the grades of evidence that can be assigned. Grades reflect the strength of the body of evidence to answer KQs on the comparative effectiveness, efficacy, and harms of the interventions included in this review. Two reviewers will assess each domain for each key outcome, and differences will be resolved by consensus. We will grade the strength of evidence for the outcomes deemed to be of greatest importance to decision makers and those most commonly reported in the literature. We expect these to include PTSD symptom reduction, quality of life, disability/functional impairment, and adverse events.

Table 5. Definitions of the grades of overall strength of evidence\(^4\)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate</td>
<td>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.</td>
</tr>
<tr>
<td>Low</td>
<td>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.</td>
</tr>
<tr>
<td>Insufficient</td>
<td>Evidence either is unavailable or does not permit estimation of an effect.</td>
</tr>
</tbody>
</table>

G. Assessing Applicability. We will assess applicability of the evidence following guidance from the Methods Guide for Effectiveness and...
Comparative Effectiveness Reviews. We will use 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 (e.g., few women may be enrolled in the studies); race/ethnicity of enrolled populations; few studies enrolling subjects with exposure to certain types of trauma; or few studies distinguishing/reporting the type of traumatic exposure for a heterogeneous population.

V. References


Source: www.effectivehealthcare.ahrq.gov
Published Online: November 8, 2012


VI. Definition of Terms
Absolute effectiveness: the effectiveness of an intervention relative to a non-active control group, i.e., either assigned to a waitlist group or receiving a placebo intervention.
Absolute risk of harms: an intervention’s risk of harms relative to a non-active control group, i.e., either assigned to a waitlist group or receiving a placebo intervention.

Intensity: the length and number of treatment sessions for a psychological intervention; the equivalent of dosage for pharmacological interventions.

Perceived utility: the extent to which recipients of an intervention subjectively find value in and/or express satisfaction with the intervention.

Resilience: the ability to cope with adversity, such as traumatic exposures, and adapt to challenges or change.\textsuperscript{48}
### VII. Summary of Protocol Amendments

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Original Protocol</th>
<th>Revised Protocol</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>11/8/2012</td>
<td>III</td>
<td>The previous revision made to Figure 1 on 9/26/2012 did not make it clear that KQ 3 addressed the effectiveness of interventions among subgroups, rather than the entire target population of the review.</td>
<td>The text “( KQ 3)” was moved to follow “Subgroups” immediately in the “Population at risk…” box was revised as follows: “Subgroups (KQ 3)”.</td>
<td>The team decided that the subgroup focus of KQ 3 could be made clearer in the Analytic Framework with this revision.</td>
</tr>
<tr>
<td>9/26/2012</td>
<td>II</td>
<td>The term “absolute effectiveness” was used in the KQs.</td>
<td>“Absolute effectiveness” has been replaced by “efficacy”.</td>
<td>The team decided after submitting the draft report that “efficacy” was a more readily understood term than “absolute effectiveness”.</td>
</tr>
<tr>
<td>9/26/2012</td>
<td>II</td>
<td>In the description of PICOTS, the description of eligible intervention types (i.e., psychological, pharmacological, and emerging) did not take into account other interventions not specifically named.</td>
<td>The following sub-bullets have been added below each eligible intervention type: 1) “Other clearly defined psychological interventions” under “Psychological interventions”; 2) “Other clearly defined pharmacological interventions” under “Pharmacological interventions”; and 3) “Other...</td>
<td>The team had originally planned to consider interventions not specifically named in the PICOTS for potential inclusion, but this was not made clear in the original version of the list.</td>
</tr>
<tr>
<td>Source: <a href="http://www.effectivehealthcare.ahrq.gov">www.effectivehealthcare.ahrq.gov</a></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Published Online: November 8, 2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>clearly defined emerging interventions” under “Emerging Interventions”.</th>
<th></th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Note</th>
<th>Changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>9/26/2012</td>
<td>III</td>
<td>In Figure 1, it was unclear which KQ the subgroups listed in the “Population at risk…” box pertain to.</td>
<td>The “Population at risk…” box was revised as follows: “Population at risk: Adults exposed to psychological trauma (KQ 3)”. This revision was necessary to respond to a peer reviewer’s comment suggesting that we clarify that the subgroups listed in the “Population at risk…” box of Figure 1 are the focus of KQ 3.</td>
</tr>
<tr>
<td>9/26/2012</td>
<td>III</td>
<td>In Figure 1, there was a typographical error in the “Timing, intensity…” box: the word “Intervention” should be entirely lowercase.</td>
<td>The typographical error was corrected. This error was unintentional.</td>
</tr>
<tr>
<td>9/26/2012</td>
<td>IV</td>
<td>No description of ineligible intervention types was provided in Table 3, which presents the CER’s eligibility criteria.</td>
<td>The following exclusion criterion has been added to the “Interventions” and “Control Interventions” rows in Table 3: “Undefined or non-clinical interventions”. The team had originally planned to consider only clearly-defined, clinical interventions, but this was not made clear in the PICOTS or in the original version of Table 3.</td>
</tr>
<tr>
<td>9/26/2012</td>
<td>VI</td>
<td>The term “absolute effectiveness” was included under “Summary of Terms”.</td>
<td>“Absolute effectiveness” has been replaced by “efficacy”. The team decided after submitting the draft report that “efficacy” was a more readily understood term than “absolute effectiveness”.</td>
</tr>
<tr>
<td>7/27/2012</td>
<td>I</td>
<td>The original description of EMDR was outdated.</td>
<td>Investigators conducting a concurrent CER of treatments for adult PTSD used the same original description of EMDR in their project protocol.</td>
</tr>
</tbody>
</table>

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)

Published Online: November 8, 2012
**EMDR** combines imaginal exposure with the concurrent induction of saccadic eye movements that are believed to help reprogram brain function so that emotional impact of trauma can be resolved. In EMDR, the patient is asked to hold the distressing image in mind, along with the associated negative cognition and bodily sensations, while engaging in saccadic eye movements. After approximately 20 seconds, the therapist asks the patient to “blank it out,” take a deep breath, and note any changes occurring in the image, sensations, thoughts or emotions. The process is repeated until desensitization has occurred (i.e., and received suggestions during their public comment period to update its description. Following this guidance, the EMDR description is revised for this project’s protocol to be consistent with concurrent CER of treatments for adult PTSD.
patient reports little or no distress on Subjective Units of Distress Scales), at which time the patient is asked to hold in mind a previously identified positive cognition, while engaging in saccadic eye movements, and rating the validity of this cognition while going through the procedure as outlined above. The saccadic eye movements were initially theorized to both interfere with working memory and elicit an orienting response, which lower emotional arousal so that the trauma can be resolved. The eye movements, or other alternative parallel stimulation, have since been found in dismantling studies to be unnecessary in achieving desensitization.
Although earlier versions of EMDR consisted of 1 to 3 sessions, current standards consist of 8 to 12 90-minute weekly sessions.\textsuperscript{24,28}

<table>
<thead>
<tr>
<th>Date</th>
<th>Section</th>
<th>Issue Description</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/27/2012</td>
<td>I</td>
<td>In Table 2, temazepam was missing from the list of benzodiazepines studied for the prevention or treatment of PTSD.</td>
<td>Temazepam has been added to Table 2.</td>
</tr>
<tr>
<td>7/27/2012</td>
<td>I</td>
<td>In Table 2, the SSRI escitalopram was unintentionally listed a second time as “citalopram”.</td>
<td>“Citalopram” has been deleted from the list of SSRIs in Table 2.</td>
</tr>
<tr>
<td>7/27/2012</td>
<td>II</td>
<td>One of the drug classes listed in the description of PICOTS was “anticonvulsants/mood stabilizers”.</td>
<td>The drug class is now listed as “anticonvulsants”.</td>
</tr>
<tr>
<td>7/27/2012</td>
<td>II</td>
<td>In the description of PICOTS, escitalopram was unintentionally listed a second time as “citalopram” (see Amendment for Section I, Table 2).</td>
<td>“Citalopram” has been deleted from the PICOTS.</td>
</tr>
<tr>
<td>7/27/2012</td>
<td>III</td>
<td>Analytic Framework’s list of outcomes was missing “resilience.”</td>
<td>The team identified resilience as an outcome of interest early in the project’s timeline, but resilience</td>
</tr>
</tbody>
</table>

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)
Published Online: November 8, 2012
VIII. Review of KQs
For all EPC reviews, KQs are reviewed and refined as needed by the EPC with input from Key Informants and the TEP to assure that the questions are specific and explicit about what information is being reviewed. In addition, for Comparative Effectiveness Reviews, the KQs are posted for public comment and finalized by the EPC after review of the comments.

IX. Key Informants
Key Informants are the end users of research, including patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Within the EPC program, the Key Informant role is to provide input into identifying the KQs for research that will inform health care decisions. The EPC solicits input from Key Informants when developing questions for systematic review or when identifying high-priority research gaps and needed new research. Key Informants are not involved in analyzing the evidence or writing the report and have not reviewed the report, except as given the opportunity to do so through the peer or public review mechanism.

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 are invited to serve as Key Informants and those who present with potential conflicts may be retained. The Task Order Officer (TOO) and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts
Technical Experts comprise a multidisciplinary group of clinical, content, and methodologic experts who provide input in defining populations, interventions, comparisons, or outcomes as well as identifying particular studies or databases to search. They are selected to provide broad expertise and perspectives specific to the topic under development. Divergent and conflicted opinions are common and perceived as health scientific discourse that results in a thoughtful, relevant systematic review. Therefore, study questions, design, and/or methodological approaches do not necessarily represent the views of individual technical and content experts. Technical Experts provide information to the EPC to identify literature search strategies and recommend approaches to specific issues as requested by the EPC. Technical Experts do not perform analysis of any kind nor contribute to the writing of the report, and they have not reviewed the report, except as given the opportunity to do so through the public review mechanism.

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 are invited to serve as Technical Experts.
and those who present with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers
Peer Reviewers are invited to provide written comments on the draft report based on their clinical, content, or methodologic expertise. Peer review comments on the preliminary draft of the report are considered by the EPC in preparation of the final draft of the report. Peer Reviewers do not participate in writing or editing of the final report or other products. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual Reviewers. The dispositions of the peer review comments are documented and will, for Comparative Effectiveness Reviews and Technical Briefs, be published 3 months after the publication of the Evidence report.

Potential Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than $10,000. Peer Reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.

XII. EPC Team Disclosures
With the exception of the following, the team had no interests to disclosure:

- Lead Clinical Investigator’s Statement of Disclosure of Business and Professional Interest:
  - Member, Binge Eating Disorder Association Scientific Advisory Board
- Co-Investigator A’s Statement of Disclosure of Business and Professional Interest:
  - Editorial Board for Medscape Psychiatry and Mental Health, a continuing medical education organization

XIII. Role of the Funder
This project was funded under Contract No. 290 2007 10056 I from the Agency for Healthcare Research and Quality, U.S. Department of Health and Human Services. The TOO reviewed contract deliverables for adherence to contract requirements, including the objectivity and independence of the research process and the methodological quality of the report. The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.
### Appendix A. PTSD outcome measures

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Description</th>
</tr>
</thead>
</table>
| **Clinician-Administered PTSD Scale (CAPS)**<sup>24, 49</sup> | • Gold standard for PTSD assessment and diagnosis for military and civilian and trauma survivors.  
  • 30-item structured interview that corresponds to the DSM-IV criteria for PTSD.  
  • Can be used to make a current or lifetime diagnosis of PTSD or to assess symptoms over the past week.  
  • In addition to PTSD symptoms, CAPS assesses the impact of symptoms on social and occupational functioning, improvement in symptoms since a previous CAPS administration, overall response validity, overall PTSD severity, and frequency and intensity of five associated symptoms (guilt over acts, survivor guilt, gaps in awareness, depersonalization, and derealization).  
  • Can be used to make a current or lifetime diagnosis of PTSD or to assess symptoms over the past week.  
  • 45- to 60-minute administration by trained (para) professionals. |
| **Clinician-Administered PTSD Scale Part 2 (CAPS-2)**<sup>49</sup> | • Assesses 1-week symptom status. |
| **Davidson Trauma Scale (DTS)**<sup>50, 51</sup> | • 17-item, self-rating scale used to assess DSM-IV PTSD criteria (B-D).  
  • Each item corresponds to a DSM-IV symptom of PTSD, and each symptom is rated in terms of frequency and severity.  
  • Can be used to screen clients at initial evaluation, evaluate psychopathology in trauma victims, assess the effectiveness of treatment, and predict treatment success.  
  • Scale covers the following types of trauma: accident, combat, sexual, criminal assault, natural disaster, torture, burns, loss of property, near-death experiences, and bereavement.  
  • Approximately 10-minute administration. |
| **Diagnostic Interview Schedule (DIS)**<sup>4</sup> | • Assesses DSM III-R/IV symptomatology and can be used for PTSD diagnosis.  
  • Semistructured interview.  
  • Requires patient to associate each symptom with a specific traumatic event.  
  • 15-minute administration by lay-trained interviewers. |
| **Impact of Events Scale (IES)**<sup>52</sup> | • 15-item self-reported measure used to assess the frequency with which experiences of "intrusions," "avoidance," and emotional numbing related to stressful events occurred in the last week.  
  • A total distress score is calculated by summing all 15 item responses. |
| **Impact of Events Scale-Revised (IES-R)**<sup>53</sup> | • 22-item self-report measure that assesses subjective distress caused by traumatic events.  
  • Items correspond directly to 14 of the 17 DSM-IV symptoms of PTSD. |
| **Los Angeles Symptom Checklist (LASC)**<sup>24</sup> | • 43-item self-report measure used to assess PTSD symptoms and associated features, including signs of distress and functional problems. |
| **Minnesota Multiphasic Personality Inventory, Keane PTSD Scale**<sup>34</sup> | • Self-report questionnaire.  
  • Originally composed of 29 items, revised for MMPI-2 by deleting 3 item repetitions.  
  • 46 MMPI items.  
  • Norms available for different populations. |
| **Mississippi Scale for Combat-related PTSD (M-PTSD)**<sup>24</sup> | • 35-item self-report questionnaire used to assess DSM-III combat-related PTSD and related features (depression, suicidality, and substance abuse).  
  • 10- to 15-minute administration. |

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)  
Published Online: November 8, 2012
<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Modified PTSD Symptom Scale (MPSS-SR)</td>
<td>17-item self-report measure that assesses the 17 DSM-III-R symptoms of PTSD. This scale is a modification of the PTSD Symptom Scale. The major modifications are that the items are not keyed to any particular traumatic event and that the MPSS-SR includes severity ratings in addition to the original measure’s frequency ratings for each item. It can be used to make a preliminary determination of the diagnosis of PTSD using either DSM-III-R criteria or a frequency, severity, or total score cutoff scores. It can be scored as a continuous measure of PTSD symptom severity.</td>
</tr>
<tr>
<td>Penn Inventory for Posttraumatic Stress Disorder</td>
<td>26-item self-report questionnaire primarily used with male patients, including accident victims, veterans, and general psychiatric patients. It does not assess all of the 17 DSM symptoms of PTSD and includes items that are not directly related to DSM criteria (e.g., self-knowledge).</td>
</tr>
<tr>
<td>Posttraumatic Diagnostic Scale (PTDS)</td>
<td>17 questions, including 12-item checklist of traumatic events used to assess DSM-IV PTSD criteria. Assesses frequency of PTSD symptoms in the past month and self-ratings of impairment across 9 areas of functioning. Has been validated across several populations, including combat veterans and sexual and nonsexual-assault survivors.</td>
</tr>
<tr>
<td>PTSD Checklist (PCL)</td>
<td>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). 5- to 10-minute administration.</td>
</tr>
<tr>
<td>PTSD Interview (PTSD-I)</td>
<td>Structured clinical interview. Patients given a copy of scale to read along with interviewer and asked to give subjective ratings for each symptom. Administered by trained subprofessionals.</td>
</tr>
<tr>
<td>PTSD Symptom Scale-Interview (PSS-I)</td>
<td>17-item semistructured interview 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. Interviewees are asked about symptoms they have experienced in the past 2 weeks. Approximately 20-minute administration.</td>
</tr>
<tr>
<td>PTSD Symptom Scale-Self-report Version (PSS-SR)</td>
<td>17-item scale used to diagnose PTSD according to DSM-III-R criteria. Assess the severity of PTSD symptoms (consist of the same 17 items as the PSS-I).</td>
</tr>
<tr>
<td>Structured Interview for PTSD (SI-PTSD or SIP)</td>
<td>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. Item responses can be used to make a determination about whether client's symptoms meet DSM criteria B, C, and D for PTSD. 20- to 30-minute administration.</td>
</tr>
<tr>
<td>Structured Clinical Interview (SCID) PTSD Module</td>
<td>Semistructured interview used to assess the prevalence, absence, and subthreshold presence of PTSD used across trauma populations. It consists of separate modules corresponding to categories of diagnoses. 25-minute administration.</td>
</tr>
</tbody>
</table>

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)
Published Online: November 8, 2012
<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Description</th>
</tr>
</thead>
</table>
| Symptom Checklist-90-Revised (SCL-90-R) | • 90-item self-report questionnaire used to assess a broad range of psychological problems, symptoms of psychopathology, patient progress, and treatment outcomes.  
• 12 to 15-minute administration. |