Evidence-based Practice Center Systematic Review Protocol

Project Title: Interventions Addressing Children Exposed to Trauma: Part 2 – Trauma Other Than Child Maltreatment and Family Violence

I. Background and Objectives for the Systematic Review

The Agency for Healthcare Research and Quality (AHRQ) is supporting two systematic reviews on children's exposure to trauma. The first in the series focuses on the comparative effectiveness of interventions that address child exposure to trauma in the form of maltreatment (physical, sexual, and emotional/psychological abuse, and neglect). This review, the second in the series, addresses the prevention and treatment of traumatic stress symptoms, including those of post-traumatic stress disorder (PTSD), for children exposed to traumatic events other than child maltreatment. Interventions for children exposed to family violence (i.e., intimate partner violence and other forms of violence exposure in the home) are not covered by either review given the heterogeneity in this population and the interventions used to treat family violence exposure. That is, children who witness but do not directly experience interpersonal violence represent different clinical populations in terms of the nature of the relationship disturbance and implications for treatment. Although the background and discussion below provide a comprehensive overview of the prevalence and types of trauma, sexual trauma and maltreatment will be addressed by the child maltreatment review.

Given the high occurrence rate of psychological trauma among children and adolescents,[1] traumatic stress in childhood has attracted considerable clinical and research interest. Although there is little doubt that symptoms of traumatic stress alone can cause impairment in children, there is considerable controversy surrounding the diagnosis of syndromes of traumatic stress symptoms in them. PTSD is an anxiety disorder that can be diagnosed in children at least 1 month after exposure to a traumatic event. The *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (hereafter *DSM-IV*) diagnosis of childhood PTSD is the same as that for an adult; however, several exceptions are noted within some of the symptom cluster criteria.[2] A child with PTSD may re-experience the traumatic event by having frequent memories of it (or in young children, reenacting the event through play), having upsetting and frightening dreams, or developing repeated physical or emotional symptoms when reminded of the event. Children with PTSD may also show symptoms such as loss of interest in daily activities; headaches, stomachaches, or other physical symptoms; excessive worry; and sleep or concentration problems.[2]

Prevalence of Traumatic Stress in Children

Traumatic events are common in childhood. In one longitudinal study of more than 1,400 children 9 to 16 years of age, 68 percent of children reported at least one traumatic event (with 37% experiencing more than one), and 13.4 percent of those experiencing trauma developed some post-traumatic symptoms. However, only 0.5 percent of these trauma-exposed children met the full criteria for PTSD.[1] In a survey of adolescents 12 to 17 years of age, the 6-month prevalence for PTSD was 6.3 percent in girls and 3.7 percent in boys.[3] The prevalence of PTSD in younger children is largely unknown; however, several studies have assessed the prevalence of PTSD in young children exposed to various types of violence (abuse, car crashes, and natural

disasters) with high reported rates of PTSD. The rates of PTSD vary considerably in such studies and may be related to the severity, chronicity, and type of trauma.

Types of Trauma

Children can be exposed to many types of trauma, ranging from inflicted trauma, unintentional trauma, natural disasters, war, and neighborhood violence. One longitudinal study reported that 25 percent of its sample was exposed to or victimized by violence (excluding sexual trauma), 11 percent was exposed to sexual trauma, and 32 percent was exposed to other types of trauma (diagnosed with a physical illness, 11%; serious accident, 11.6%; natural disaster, 11.1%; fire, 5.9%).[1] The Adverse Childhood Experiences Study showed high rates of childhood trauma exposure in a large adult population.[4] In this population, 65 percent recalled adverse childhood experiences, many of which could be defined as traumatic events. These experiences included emotional abuse (11%), physical abuse (28%), sexual abuse (21%), battered mother (13%), household drug/alcohol abuse (27%), household mental illness (17%), parent separation or divorce (23%), and incarcerated household member (5%).[4] PTSD rates vary by type of traumatic exposure, with 35 percent of children exposed to community violence[5] and half of those affected by interpersonal violence.[6] Road crashes, another common form of childhood trauma, were associated with rates of PTSD ranging from 13 to 25 percent between 4 and 12 months after a road crash.[7] Children with agency-reported abuse had much higher rates of PTSD when compared with children without reported abuse.[8] Trauma from natural disasters frequently leads to PTSD; for example, one study reported a PTSD rate of 35 percent for children surviving an earthquake.

Risk and Protective Factors of Traumatic Stress in Children

Not all trauma-exposed children develop traumatic stress syndromes. Several risk and protective factors play a role in the development of syndromes such as PTSD. In one study of terrorism exposure, children more directly affected by terrorism were more likely to report PTSD. Likewise, those with more frequent reminders of traumatic experiences were more likely to experience PTSD, and those with support-seeking behavior were less likely to report PTSD.[9] The severity of injuries resulting from motor vehicle crashes has been shown to be associated with the development of PTSD. Previous trauma and pre-existing anxiety disorders increase the risk of PTSD.[1] A variety of genetic and neurobiological factors play a role in the development of PTSD.[10] The developmental age, number of trauma exposures, family systems, and neighborhood factors may play a role in the development of PTSD after trauma.

Clinical Presentation of Post-traumatic Stress Disorder and Associated Impairment

Clinicians often face several challenges in recognizing and diagnosing PTSD in children.[11] Because misdiagnosis of PTSD as other psychiatric conditions such as bipolar disorder is common, clinicians need to be careful in assessing children for several key features of PTSD. To establish the diagnosis, a clinician needs to establish that a traumatic event preceded onset of the disorder, which he or she can determine either through compelling evidence or by reports given by the child or the child's caregiver. This conclusion might be difficult given that avoidance of the trauma is a core feature of PTSD in children, and a parent might deny the trauma if he or she

is the perpetrator, is ashamed or embarrassed about the trauma, or is unaware of it. In some instances, referral of the child for a forensic evaluation might be necessary.

Second, clinical diagnosis of PTSD in children requires the presence of three distinct symptom clusters: 1) symptoms of re-experiencing the trauma, 2) emotional numbing and persistent avoidance of trauma reminders, and 3) persistent symptoms of hyperarousal. Young children might exhibit different behaviors, such as opposition, fears unrelated to the traumatic event itself, and separation anxiety. Although acute stress disorder (ASD) can be diagnosed in children immediately after the traumatic event, at least 1 month is required to make a PTSD diagnosis in children.

Studies have indicated that childhood PTSD is associated with a high degree of impairment during childhood that can carry into adolescence and adulthood. For example, childhood PTSD increases the risk of several comorbid mental disorders such as depression, substance abuse, and conduct disorder.[12] Suicidality is a particularly grave concern for children with PTSD.[12-14] Decreased functioning in several domains (social, home, school, relational) by children and adolescents with PTSD also has been observed (e.g., lower academic achievement[15]).

Diagnostic Issues

Much debate has surrounded the validity of the *DSM-IV* diagnostic criteria for PTSD in children.[11,16] Part of the debate stems from the number of symptoms required within each symptom cluster to make a formal diagnosis. This is particularly so with the emotional numbing/avoidance symptom criteria, in that young children often are not developmentally able to report on these emotions nor do their parents have awareness of their children's internal states.[17-19]

Currently, several experts in the field of child PTSD are considering possible age-related subtypes of PTSD in preschool or school-aged children for inclusion in the forthcoming *DSM-V*, particularly given that the *DSM-IV* criteria were developed and tested on adults and only adolescents ages 15 years or older.[20] Although it is known, for example, that preschool children can experience traumatic events, community studies have found PTSD prevalence rates much lower than expected. One possible explanation for the low rates involves the strict *DSM-IV* diagnostic criteria that might not be developmentally appropriate for this age group.[16] Thus, an alternative algorithm for PTSD in young children has been proposed and refined[21-23] and endorsed by field experts.[24] This alternative algorithm might also apply to school-aged children, who have also exhibited lower-than-expected prevalence of PTSD based on *DSM-IV* criteria. Because few studies have empirically tested the proposed algorithm on school-aged children, however, it is not known whether the *DSM-V* should incorporate alternative criteria for PTSD diagnosis in this age group.

Alternatively, several experts in the field of childhood traumatic stress believe that a diagnosis of developmental trauma disorder (DTD) more adequately captures the reality of clinical presentations of children and adolescents exposed to chronic interpersonal trauma and faulty caregiver systems. These experts believe that children suffering from DTD have disrupted affect regulation, attention, cognition, perception, and interpersonal relationships and may not meet criteria for the traditional diagnosis of PTSD. The criteria for DTD include exposure to multiple or prolonged adverse events and experiences of affective and physiological dysregulation, attentional and behavioral dysregulation, self and relational dysregulation, and

post-traumatic spectrum symptoms for at least 6 months that cause functional impairment in at least two areas of functioning (scholastic, familial, peer group, legal, health, or vocational).

Interventions

The continued uncertainties of trauma identification and PTSD diagnosis increase the clinical challenges of addressing this population appropriately. Interventions designed to prevent or treat traumatic stress symptoms exist within the domains of psychotherapy, pharmacotherapy, complementary and alternative treatments, and other therapies such as systems or combination therapies. To provide a comprehensive review, we include all intervention domains for questions of prevention as well as treatment; although some of the intervention examples specified below focus solely on the prevention of traumatic stress symptoms, others may be relevant for the prevention or treatment of traumatic stress symptoms, and still others focus solely on the treatment of traumatic stress symptoms. For children who have been exposed to trauma, but have not yet developed symptoms, interventions are intended to prevent the onset of traumatic stress symptoms or PTSD. For children already experiencing such symptoms, treatments are intended to result in remission of PTSD, a reduction of symptoms, and improved functioning.

We also note settings when relevant. Interventions other than pharmacotherapy may be carried out at an individual, family, or group level. They may be carried out in various settings (including the outpatient vs. inpatient setting) or in the community, schools, or classrooms. Many programs attempt to bring one of a variety of psychotherapeutic techniques into the home. In these circumstances, the training that parents and children receive differs very little from general psychotherapeutic techniques. The goal of these interventions, rather, is to improve access and outcomes in populations that are traditionally harder to reach such as ethnic minorities, rural populations, or people of low socioeconomic status.[25] In addition to attempting to prevent PTSD or traumatic stress symptoms, these interventions are often directed at associated symptoms such as aggression or delinquency.

Psychotherapy: interventions for preventing or treating post-traumatic stress disorder or traumatic stress symptoms in children

Several different psychotherapeutic interventions may be used to address symptoms of traumatic stress; some of these interventions, or their components (e.g., teaching relaxation skills), have the potential to be effective at preventing traumatic stress symptoms when implemented after exposure to a traumatic event.

Cognitive Behavioral Therapy (CBT) is a form of psychotherapy used to treat many psychiatric problems, including depression, anxiety, and PTSD. CBT combines elements of cognitive therapy and behavioral therapy. In CBT, maladaptive thought patterns are identified and targeted through cognitive restructuring, and maladaptive behaviors are targeted through behavioral techniques that may include exposure/desensitization, relaxation skills, and stress inoculation training or teaching an individual how to reduce anxiety. In addition to the more traditional use of CBT with individuals who are experiencing symptoms of traumatic stress, its components may be appropriate for use with children exposed to traumatic events.

Trauma-Focused CBT (TF-CBT) is a psychotherapeutic technique that has specifically adapted CBT for use with children exposed to trauma and those presenting symptoms of traumatic stress. In TF-CBT, children and parents learn skills to help process thoughts and

feelings related to traumatic life events and to manage and resolve distressing thoughts, feelings, and behaviors also related to those same events. Components of treatment include psychoeducation about trauma; parenting skills; relaxation skills; coping skills to deal with trauma-related thoughts, feelings, and behaviors; and child exposure tasks via narratives, drawings, or other imaginal methods. Safety and social skills training may also be a component of treatment.[26]

Child-Parent Psychotherapy (CPP) is a relationship-based treatment that integrates modalities derived from psychodynamic, attachment, trauma, cognitive-behavioral, and social learning theories. The child-parent relationship is used to target the child's improvement in emotional, cognitive, and social domains of functioning. The interventions focus on promoting affect regulation in the child and in the parent; changing maladaptive behaviors in the child, the mother, and their interaction; supporting and encouraging developmentally appropriate interactions and activities; and assisting the child and the mother in creating a joint trauma narrative.[27] CPP has more traditionally been implemented with populations in which there were clinical concerns about the child's behavior or the mother's parenting after the child witnessed or overheard marital violence and also with maltreating families. However, this intervention may also be appropriate for children soon after exposure to other traumatic events.

Skills Training in Affective and Interpersonal Regulation/Narrative Story-Telling (STAIR/NST) is a two-module treatment focused on reducing symptoms of PTSD and other trauma-related symptoms (including depression and dissociation) and on building and enhancing specific social and emotional competencies that are frequently disturbed in youths who have experienced multiple traumas and/or sustained trauma. This intervention might also be used to prevent the development of traumatic stress symptoms when implemented after exposure to a traumatic event. STAIR/NST includes 10 treatment sessions conducted in group or individual format that target social and emotional competency building. The sessions focus on developing emotional regulation and social skills, positive self-definition exercises, and goal setting and achievement. The NST phase of treatment is conducted in six individual sessions that focus on the emotional processing of traumas in detail while developing a positive life narrative and future plan.

Trauma and Grief Component Therapy (TGCT) is a group treatment program for traumatically bereaved older school-aged children and adolescents. The target population includes youths affected by community violence, school violence, gang violence, war/ethnic cleansing, and natural and manmade disasters. TGCT has several areas of focus, including the processing of traumatic experiences, coping with reminders of trauma and loss, coping with post-traumatic adversities, managing traumatic grief, and resuming developmental progression. This intervention may be appropriate for children exposed to traumatic events and for those experiencing traumatic stress symptoms.

Psychotherapeutic interventions have also been developed specifically for use in the schools.

Cognitive Behavioral Intervention for Trauma in Schools (CBITS) is a skills-based, group intervention for children exposed to trauma who are typically between the ages of 10 and 15 years; it may be appropriate not only for intervening early after exposure to a traumatic event but also for treating traumatic stress symptoms. The CBITS program consists of 10 group sessions designed to provide education about reactions to trauma, teach relaxation skills, provide cognitive therapy to challenge upsetting thoughts, teach social problem solving, and work on processing traumatic memories and grief. These skills are learned through the use of drawings and by talking in both individual and group settings. Between sessions, children complete

assignments and participate in activities that reinforce the skills they have learned. Parent and teacher education sessions are also included.

Psychotherapy: interventions for treating post-traumatic stress disorder or traumatic stress symptoms in children

Dialectical Behavior Therapy (DBT) is a psychotherapeutic approach that helps clients learn to both regulate and tolerate their emotions and may be appropriate for treating traumatic stress symptoms. Concrete skills are taught and practiced, including mindfulness practices from Eastern medicine. DBT combines standard cognitive behavioral techniques for emotion regulation with concepts of distress tolerance, acceptance, and mindfulness.[28]

Structured Psychotherapy for Adolescents Responding to Chronic Stress (SPARCS) is based on DBT. SPARCS is a group intervention designed to address the needs of chronically traumatized adolescents who may be living with ongoing stress and is intended to take place in a variety of settings, including schools, agencies, and residential treatment centers; it has been shown to decrease PTSD symptoms.[29] These adolescents may experience problems in several areas of functioning, including difficulties with affect regulation and impulsivity, self-perception, relationships, somatization, dissociation, numbing, and avoidance. SPARCS is predominantly cognitive-behavioral; key components of the program include mindfulness, problem solving, relationship building/communication skills, and distress tolerance.

Parent-Child Interaction Therapy (PCIT) is a treatment that targets improvement in the quality of the parent-child relationship. Parents are taught skills that facilitate the establishment of a nurturing and secure relationship with their child while increasing the child's prosocial behavior and decreasing negative behavior. The treatment includes a Child-Directed Interaction that is similar to play therapy, with the goal of strengthening the parent-child relationship, and a Parent-Directed Interaction, in which parents learn to use behavior management techniques as they play with their child. PCIT has been adapted for children who have experienced trauma[30, 31] and is most appropriate as a treatment of traumatic stress symptoms rather than addressing prevention of traumatic stress symptoms after exposure to a traumatic event.

Eye Movement Desensitization and Reprocessing (EMDR) is a psychotherapeutic approach in which the patient attends to past memories, present triggers, or anticipated future experiences while simultaneously moving his or her eyes back and forth following the therapist's fingers as they move across the patient's field of vision. Graduated imaginal exposure to the traumatic event(s) is combined with having the child visually track the therapist's hand movements. The theoretical basis for EMDR is that PTSD symptoms result from insufficient processing or integration of sensory, cognitive, and affective components of the traumatic memory, and the eye movements are proposed to facilitate information processing and integration, thereby allowing patients to fully process traumatic memories.[32] EMDR is an intervention that targets individuals who experience symptoms of traumatic stress.

Pharmacotherapy: interventions for preventing post-traumatic stress disorder or traumatic stress symptoms in children

Medication use in children who have experienced acute trauma or during their exposure to trauma to prevent the development of PTSD is intended to target memory consolidation and physiologic hyperarousal. A similar rationale supports use of the opioid analgesic morphine in

the acute care setting in the prevention of PTSD, especially in the pediatric intensive care setting. In addition to treating the pain from invasive medical procedures, morphine diminishes the memory consolidation that may accompany this pain. In addition, other medications, such as the alpha-agonist clonidine, are intended to diminish the physiologic symptoms of hyperarousal immediately following or during a traumatic event. Other medications that target physiologic hyperarousal and memory consolidation may also be used to prevent PTSD in exposed children.

Pharmacotherapy: interventions for treating post-traumatic stress disorder or traumatic stress symptoms in children

Selective serotonin-reuptake inhibitors, or SSRIs, are a class of antidepressants that are among the most studied medications for PTSD treatment in children. SSRIs work by inhibiting the reuptake of serotonin and, therefore, increase the amount of serotonin in the synaptic cleft available to receptors on the postsynaptic neuron. Because they are the first-line treatments for PTSD in adults, they are some of the most common medications used to treat PTSD in children as well. However, there has been no clear indication established for SSRI use as monotherapy (i.e., without psychotherapy) in children with PTSD.
Some studies conducted with the SSRIs sertraline and citalopram have indicated some therapeutic benefit in children and adolescents. In contrast, there have been few studies of fluoxetine or other SSRIs aimed at improving PTSD in children.

Other antidepressants. Atypical antidepressants, such as bupropion, venlafaxine, and mirtazapine, are also commonly used to treat PTSD symptoms or PTSD-associated symptoms. Imipramine is a tricyclic antidepressant that has shown promise as a PTSD treatment and was used frequently before the development of the SSRIs; however, cardiac side effects have significantly limited its use. In addition, the restricted diet that patients on monoamine oxidase inhibitors (MAOIs) must follow has also limited the use of MAOIs as a PTSD treatment.

Other medications. Because childhood PTSD is so often associated with other comorbid mental conditions, numerous other medications are used to treat PTSD and have been studied. These medications are thought to work through various mechanisms.

- *Stimulants* such as methylphenidate and its derivatives and amphetamine preparations are used to treat PTSD-related symptoms of inattention and externalizing behaviors that are often confused with or misdiagnosed as attention deficit hyperactivity disorder (ADHD). Because PTSD often causes hyperarousal and associated physiologic changes, medications that treat these physiologic effects have also been studied in patients with PTSD. As mentioned earlier, the alpha agonist clonidine is thought to mainly target hyperarousal symptoms in PTSD. Propranolol, a beta-adrenergic blocking agent, has also had promising results as a treatment for PTSD in childhood.
- *Antipsychotics* have also been studied as a PTSD treatment because of their effects on comorbid aggression or psychotic symptoms. These medications include risperidone and quetiapine. In addition, clozapine has been shown to reduce both hallucinations and flashbacks to a traumatic event while reducing the number of medications required to treat children with PTSD. Because PTSD can often be accompanied by severe behavior problems and mood fluctuations, the mood stabilizers valproic acid, carbamazepine, and lithium have been studied in children with PTSD and are frequently used clinically.

- *Benzodiazepines*, another class of medication, have also been used to treat the severe anxiety that often accompanies PTSD. Medications in this class include clonazepam, diazepam, alprazolam, and lorazepam. The American Association of Child and Adolescent Psychiatry (AACAP) has advocated that these medications not be used to treat PTSD in children because of the risk for long-term cognitive effects, sedation, and the potential for tolerance and addiction.

Complementary and alternative interventions for preventing or treating post-traumatic stress disorder or traumatic stress symptoms in children

Equine-Assisted Psychotherapy is a specialized experiential approach to psychotherapy that uses a horse as a therapeutic tool. The goal is to encourage client insight through horse examples, addressing self-esteem and personal confidence; communication and interpersonal effectiveness; trust, boundaries and limit setting; and group cohesion. Work is performed through the horse supports and encourages the identification and expression of emotions.[33]

Other interventions for preventing post-traumatic stress disorder and traumatic stress symptoms in children

Given that many traumatic events such as natural disasters or acts of terrorism can affect whole communities, community-based approaches have been developed to try to combat PTSD at its source or where chronic harm may be occurring. These approaches are outside of the traditional clinic setting and often allow clinicians an inside view of the context of the problem, which the patient is often unable to express during a clinic visit. These can be home- or school-based intervention programs or programs that partner with first responders or law enforcement to attempt to prevent or improve PTSD. Interventions may also encompass system-level, multicomponent, or other approaches (e.g., Web-based). Two interventions designed to intervene early after exposure to traumatic events are *Critical Incident Stress Debriefing* (CISD) and *Child-Development Community Policing* (CD-CP). CISD is an intervention that targets individuals who have recently been exposed to a traumatic event. CISD is one of the first interventions created for police officers, first responders, and emergency medical technicians to use in the field with a survivor of a traumatic event during the first 72 hours. The CD-CP program is a collaborative early intervention program that targets individuals exposed to violence and is the product of a partnership between mental health professionals at the Yale University Child Study Center and the New Haven Police Department. The goals of the program are to help children cope with traumatic events and prevent the development of traumatic stress symptoms.[34]

Other interventions for preventing or treating post-traumatic stress disorder and traumatic stress symptoms in children

Trauma Systems Therapy (TST) is targeted toward children and adolescents who are having difficulty regulating their emotions as a result of the interaction between the traumatic experience and stressors in the social environment. TST is appropriate for individuals who are experiencing traumatic stress symptoms, but it might also be relevant for preventing traumatic stress symptoms when implemented after exposure to a traumatic event. Interventions include a

focus on both the emotional regulation capacities of the traumatized child and the ability of the child's social environment and system of care to help the child manage his or her emotions or to protect the child from threat. Treatment modules include Home and Community Based Services, Services Advocacy, Emotional Regulation Skills Training, Cognitive Processing, and Psychopharmacology.

Other interventions for treating post-traumatic stress disorder and traumatic stress symptoms in children

Attachment, Self-Regulation and Competency (ARC) is designed to treat children and families who have experienced chronic trauma such as sexual abuse, physical abuse, or domestic violence, but is also relevant for children exposed to community violence. ARC interventions focus on building secure attachments, enhancing the child's self-regulatory capabilities, and increasing competencies across multiple domains.

Current Child Traumatic Stress Guidelines

Although there are no existing guidelines for other syndromes of childhood traumatic stress, three organizations—the AACAP, the International Society for Traumatic Stress Studies (ISTSS), and the National Institute for Health and Clinical Excellence (NICE)—have published guidelines on the treatment of PTSD during childhood and adolescence. These guidelines largely stem from expert consensus based on existing evidence and clinical practice rather than on formal comparative effectiveness reviews. These guidelines use different categories of interventions to summarize evidence and offer inconsistent recommendations for some treatment categories or interventions. For instance, the AACAP notes that SSRIs can be considered as a treatment for children and adolescents with PTSD; NICE concludes that there is insufficient evidence to recommend the use of any medication in young people with PTSD. Similarly, ISTSS considers the evidence on EMDR to be insufficient to make a definitive recommendation for the acute period; NICE suggests that EMDR shows promise despite the lack of rigorous testing in randomized controlled trials. The guidelines suggest agreement on some issues. For example, both AACAP and ISTSS agree on the importance of considering comorbid psychiatric conditions and school-based treatment approaches

Objectives

The limitations of existing guidelines underscore other clinical dilemmas. Clinicians require better guidance on the comparative benefits of pharmacotherapy and nonmanualized treatment modalities such as psychodynamic or play therapy. Similarly, clinicians require better guidance on whether specific therapies could cause retraumatization or more harm. Our proposed systematic review will evaluate the comparative effectiveness of a broad array of interventions for benefits and harms.

The challenges of the diagnostic criteria for PTSD signal the need for a comprehensive review of interventions for children with traumatic stress symptoms or PTSD. Because the diagnostic criteria for PTSD were created for adults and tested only in adolescents aged 15 years or older, they may not be entirely relevant for younger children. Often, younger children are unable to express signs and symptoms in words and are more likely to externalize or express

themes during play or in drawings. In addition, many children who do not meet criteria for a diagnosis of PTSD will have symptoms that significantly impair daily functioning. Our systematic review will address the question of whether children without a formal diagnosis of PTSD but with traumatic stress symptoms may benefit from treatment. Another clinical concern is whether outcomes of interventions vary by the presence of comorbid diagnoses such as depression, disruptive behavior disorders, ADHD, other anxieties, learning disabilities, and psychosis. Our review will evaluate evidence of effectiveness for subgroups that have such comorbidities.

Another treatment dilemma is access to services for PTSD. In areas without large academic medical centers or large population centers, the treatment approach is limited to what resources are available in the immediate vicinity. Often providers are trained in only one modality of therapy or were trained many years before and have not kept abreast of recent advances in treatment. Access to school-based and community-based resources is often lacking in rural or underserved areas and often depends on the political and sociocultural climate of the area. In addition, financial factors such as price of medication, insurance coverage, and other issues of access come into play when choosing a treatment modality. In patients and families with limited resources and with limited psychological mindedness, acceptance and participation may be a challenge for proven therapies.

Our review will evaluate the extent to which outcomes of interventions vary by rural/urban locale and socioeconomic status.

A comprehensive review will also help to identify a broad range of modalities, including those with limited dissemination, and may contribute to better uptake of effective interventions in areas with limited access to services for PTSD.

II. The Key Questions

Introduction

Several comments were received regarding the narrow inclusion of a single outcome for Key Question (KQ 1). In response, we have added all outcomes examined in KQ 2 to the outcomes examined in KQ 1. The list of outcomes in both KQ 1 and KQ 2 has been expanded to include additional physical health conditions (including obesity, cardiovascular disease, and asthma), co-occurring substance use conditions, risk-taking behavior, and healthy development measures. We have changed several characteristics in KQ 3 to include rural/urban location and *sex* instead of *gender* in response to comments received as well. These changes have been incorporated in the new KQs listed below.

KQ 1: What is the comparative effectiveness of different types of pharmacotherapy, psychotherapy, complementary and alternative therapies, or other therapies such as combined therapy for children ages 0–17 years exposed to trauma other than maltreatment? Outcomes include the following:

- Prevention of traumatic stress symptoms or syndromes (e.g., PTSD, ASD, DTD)
- Prevention of or reduction in mental health conditions or symptoms (e.g., depression, anxiety)

- Prevention or reduction in physical health conditions or symptoms (e.g., sleep disorders, eating disorders, pain, overweight or obesity, asthma, cardiovascular problems, gastrointestinal problems, headaches)
- Reduction in risk-taking behaviors (including substance use), behavioral problems (including conduct disorder and ADHD), or criminal activities
- Healthy development, including improvements in interpersonal/social functioning or signs of developmental regression
- School-based functioning
- Improvements in quality of life
- Decreased suicidality

KQ 2: What is the comparative effectiveness of different types of pharmacotherapy, psychotherapy, complementary and alternative therapies, or other therapies such as combined therapy for children ages 0–17 years with traumatic stress symptoms from trauma other than maltreatment and who are experiencing traumatic stress symptoms? Outcomes include the following:

- Remission of PTSD
- Reduction in severity or number of traumatic stress syndromes or symptoms
- Prevention of or reduction in co-occurring mental health conditions or symptoms (e.g., depression, anxiety)
- Prevention or reduction in co-occurring physical health conditions or symptoms (e.g., sleep disorders, eating disorders, pain, overweight or obesity, asthma, cardiovascular problems, gastrointestinal problems, headaches)
- Reduction in risk-taking behaviors (including substance use), behavioral problems (including conduct disorder and ADHD), or criminal activities
- Healthy development including improvements in interpersonal/social functioning or signs of developmental regression
- School-based functioning
- Improvements in quality of life
- Decreased suicidality

KQ 3: Do interventions for prevention or treatment of traumatic stress symptoms vary in their effectiveness by characteristics of the child, treatment, or setting? Characteristics include the following:

- Child characteristics (KQ 3a)
  - Age group of child
  - Sex
  - Type and severity of trauma experienced (specific type and whether trauma is acute or chronic, single or multiple, direct or indirect)
  - Race/ethnicity
  - Urban (including inner cities)/suburban/rural locale
  - Insurance status

- Socioeconomic status
- Co-occurring mental or physical health conditions

- Treatment characteristics (KQ 3b)

  - Involvement of parent
  - Timing of treatment

- Setting (KQ 3c)

KQ 4: What are the harms (low adherence/dropouts, side effects, retraumatization) associated with specific types of therapies for preventing or treating traumatic stress symptoms?

Table 1. Population, intervention, comparators, outcomes, and setting (PICOS)

Domain	Description
Population	Children ages 0–17 years* who have been exposed to a trauma other than maltreatment. Specific types of trauma include terrorism, community violence, war, school violence, natural disasters, medical trauma, and death of loved ones. Children ages 0–17 years* who have been exposed to a trauma other than maltreatment and who have either traumatic stress symptoms or PTSD.
	Specific clinical interventions are described below. **Interventions for exposures** Psychotherapy • Cognitive behavioral therapy [CBT] • Hypnotherapy • Psychodynamic therapy • Community-/classroom-based interventions Pharmacotherapy • Selective serotonin reuptake inhibitors (SSRIs) • Tricyclic antidepressants (TCAs), • Benzodiazepines • Beta-blockers • Alpha-blockers • Mood stabilizers • Antipsychotics o Combined therapies o Other therapies **Interventions for treatment of symptoms** Psychotherapy (including groupings of trauma focused vs. non–trauma focused) • Cognitive behavioral therapy (CBT) • Parent-child interaction therapy (PCIT) • Child-parent psychotherapy (CPP) • Eye movement desensitization and reprocessing (EMDR) • Dialectical behavior therapy (DBT) • Complementary and alternative therapies (e.g., equine-assisted therapy) • Community-/classroom-based interventions

Source: www.effectivehealthcare.ahrq.gov
Published Online: March 26, 2012

Table 1. Population, intervention, comparators, outcomes, and setting (PICOS) (continued)

Domain	Description
Interventions	Pharmacotherapy • Selective serotonin reuptake inhibitors (SSRIs) • Tricyclic antidepressants (TCAs), • Benzodiazepines • Beta-blockers • Alpha-blockers • Mood stabilizers • Antipsychotics Combined therapy Other therapies
Comparator	The comparison condition as defined in the respective studies, including active controls (such as usual care) and inactive controls (such as waiting list groups).
Outcomes	**Outcomes for children exposed to trauma without traumatic stress symptoms** • Prevention of traumatic stress symptoms or syndromes (e.g., PTSD, ASD, DTD) • Prevention of or reduction in mental health conditions or symptoms (e.g., depression, anxiety) • Prevention of or reduction in physical health conditions or symptoms (e.g., sleep disorders, eating disorders, pain, overweight or obesity, asthma, cardiovascular problems, gastrointestinal problems, headaches) • Reduction in risk-taking behaviors (including substance use), behavioral problems (including conduct disorder and ADHD), or criminal activities • Healthy development, including improvements in interpersonal/social functioning or signs of developmental regression • School-based functioning • Improvements in quality of life • Decreased suicidality • Low adherence/dropouts • Side effects • Retraumatization **Outcomes for children with traumatic stress symptoms or PTSD** • Remission of PTSD • Reduction in severity or number of traumatic stress syndromes or symptoms • Prevention of or reduction in co-occurring mental health conditions or symptoms (e.g., depression, anxiety) • Prevention of or reduction in co-occurring physical health conditions or symptoms (e.g., sleep disorders, eating disorders, pain, overweight or obesity, asthma, cardiovascular problems, gastrointestinal problems, headaches) • Reduction in risk-taking behaviors (including substance use), behavioral problems (including conduct disorder and ADHD), or criminal activities • Healthy development, including improvements in interpersonal/social functioning or signs of developmental regression • School-based functioning • Improvements in quality of life • Decreased suicidality • Low adherence/dropouts • Side effects • Retraumatization

Source: www.effectivehealthcare.ahrq.gov
Published Online: March 26, 2012

Table 1. Population, intervention, comparators, outcomes, and setting (PICOS) (continued)

Domain	Description
Setting	• Includes studies conducted in the United States or internationally • Specialty (e.g., outpatient and inpatient primary care or mental health care settings) • Nonspecialty (e.g., schools, community-based providers, shelters) • Home-based settings and out-of-home care (e.g., residential treatment)

*At least 95% of the sample was required to be between 0 and 17 years of age.

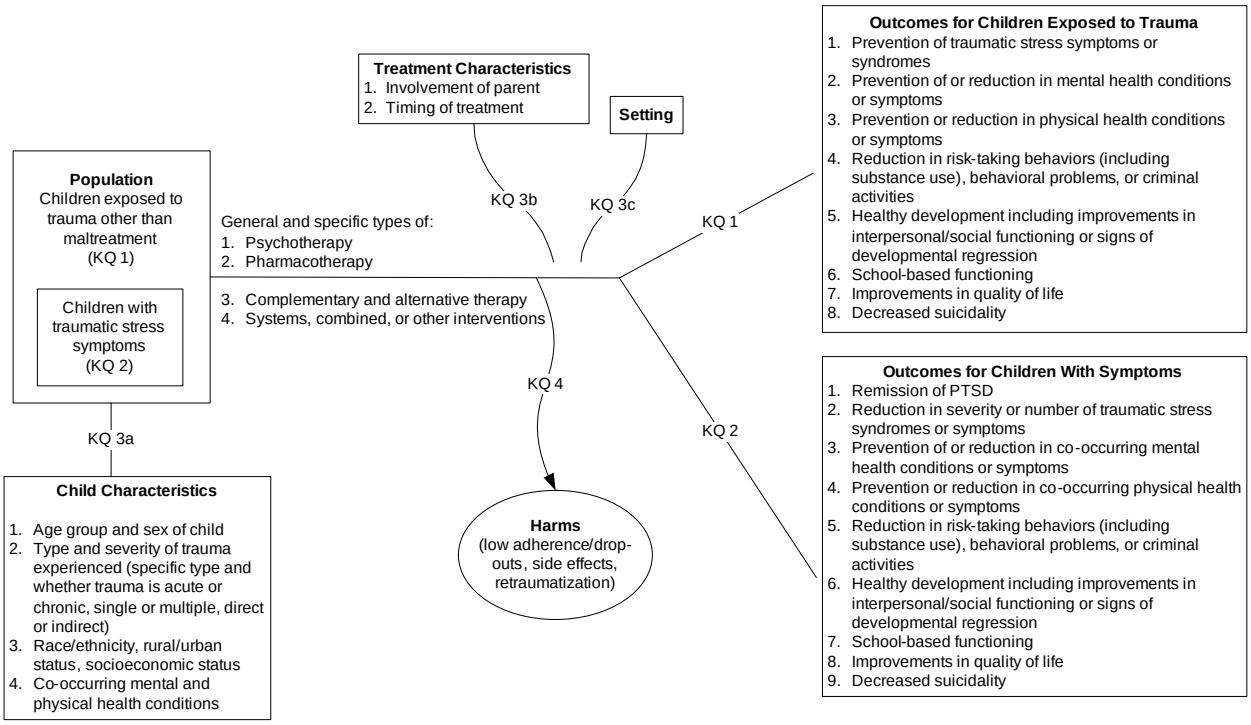
Abbreviations: ADHD = attention deficit hyperactivity disorder; ASD = acute stress disorder; DTD = developmental trauma disorder; PTSD = post-traumatic stress disorder

Source: www.effectivehealthcare.ahrq.gov
Published Online: March 26, 2012

III. Analytic Framework

Figure 1 depicts the KQs within the context of the PICOS described in the previous section.

Figure 1. Analytic framework for comparative effectiveness of interventions addressing children exposed to trauma other than maltreatment



Abbreviations: KQ = key question; PTSD = post-traumatic stress disorder

IV. Methods

A. Criteria for Inclusion/Exclusion of Studies in the Review. Criteria for inclusion and exclusion of studies are based on the PICOS model outlined in Section II, as well as the study-specific inclusion criteria listed in Table 2.

Source: www.effectivehealthcare.ahrq.gov
Published Online: March 26, 2012

Table 2. Study inclusion criteria

Category	Criteria for inclusion
Study design	Systematic reviews, randomized controlled trials, nonrandomized controlled trials, prospective cohort studies, and nested case-control studies
Study duration	No limits
Sample size	N ≥ 10
Geography	United States and international
Time of publication	1990 to present*
Language of publication	English
Risk of bias	Low or medium

*Search to be updated when the report is out for peer review.

B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies to Answer the Key Questions. We will systematically search, review, and analyze the scientific evidence for each KQ. The steps that we will take to accomplish the literature review are described below. To identify articles relevant to each KQ, we will begin with a focused MEDLINE® search on stress disorders using a variety of terms, medical subject headings (MeSH®), and major headings, limited to children, English, and human-only studies published from 1990 onward. Relevant terms are listed in Table 3. We will limit the search to studies published in English, because of limited resources; this may bias the report to include more studies from English-speaking countries. We will also search the Cochrane Library, EMBASE®, and PsycINFO® using analogous search terms. We will conduct quality checks to ensure that known studies are identified by the search. If they are not, we will revise and rerun our searches.

We will also search the gray literature for unpublished studies relevant to this review; we will include studies that meet all inclusion criteria and report enough methodological information to assess internal validity/quality. In addition, in an effort 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 might have been missed by electronic searches.

Methods for identifying gray literature will include a review of trial registries, specifically, ClinicalTrials.gov, Health Services Research Projects in Progress (http://www.nlm.nih.gov/hsrproj/), and the European Union Clinical Trials Register (https://www.clinicaltrialsregister.eu/). Further, AHRQ will also request Scientific Information Packets (SIPS) from the developers or distributors of the interventions identified in the literature review. SIPs allow an opportunity for the intervention developers and distributors to provide the Evidence-based Practice Center (EPC) with both published and unpublished data that they believe should be considered for the review. The EPC will review the information provided in the SIPs and gray literature. We will include studies that meet all inclusion criteria and contain enough information on the research methods used for our risk of bias assessment.

We will also conduct an updated literature search (of the same databases searched initially) concurrent with the peer review process. Any literature suggested by peer reviewers or public comment respondents will be investigated and, if appropriate, incorporated into the final review. Appropriateness will be determined by the same methods listed above.

Table 3. Literature search terms

Population	("Traumatizing"[tiab] OR "Traumatising"[tiab] OR "Trauma"[tiab] OR "Traumatic"[tiab] OR "Traumas"[tiab] OR "Traumatization"[tiab] OR "Traumatisation"[tiab] OR "Traumatized"[tiab] OR "Traumatised"[tiab] OR "peritraumatic"[tiab] OR "Stress Disorders, Traumatic"[MeSH] **OR** "Social Problems"[MeSH] **OR** "Wounds and Injuries/epidemiology"[MeSH] OR "Wounds and Injuries/prevention and control"[MeSH] OR "Wounds and Injuries/psychology"[MeSH] OR "Wounds and Injuries"[MeSH:NoExp]) AND "Adolescent"[MeSH] OR "Child"[MeSH] OR "Infant"[MeSH]
Interventions	At least one of the following: "Mental Health Services"[MeSH]; "Complementary Therapies"[MeSH]; "Psychotherapy"[MeSH]; "Monoamine Oxidase Inhibitors"[MeSH]; "Adrenergic alpha-Antagonists"[MeSH]; "Adrenergic beta-Antagonists"[MeSH]; "Serotonin Uptake Inhibitors"[MeSH]; "Benzodiazepines"[MeSH]; "Psychotropic Drugs"[MeSH]; "Adrenergic Uptake Inhibitors"[MeSH]; Citalopram; Escitalopram; Fluoxetine; Fluvoxamine; Paroxetine; Sertraline; Desvenlafaxine; Duloxetine; Venlafaxine; Bupropion; Mirtazapine; Nefazodone; Trazodone; Clonidine; Guanfacine; Propranolol; Phenelzine; tranylcypromine; Clomipramine; Imipramine; Topiramate; Tiagabine; Lamotrigine; Lithium; Carbamazepine; "Divalproex sodium"; Oxcabazepine; Aripiprazole; Olanzapine; Risperidone; Quetiapine; Clonazepam; Lorazepam; Alprazolam; Buspirone; Propranolol; Estazolam; Flurazepam; Temazepam; Triazolam; Chlordiazepoxide; Clorazepate; Diazepam; Oxazepam; Prazepam; Quazepam
Limits	Humans English language 1990 onwards **AND at least one of the following:** "Randomized Controlled Trial"[Publication Type]; "Randomized Controlled Trials as Topic"[MeSH]; "Single-Blind Method"[Mesh]; "Double-Blind Method"[Mesh]; "Random Allocation"[MeSH]; "meta-analysis"[Publication Type]; "meta-analysis as topic"[MeSH Terms]; "meta-analysis"[All Fields]; "Comparative Study"[Publication Type]; "comparative study"; "trial"[tiab]; "Cohort Studies"[MeSH]; "cohort effect"[MeSH Term]; cohort*[tiab]; ("review"[Publication Type] AND "systematic"[tiab]); "systematic review"[All Fields]; ("review literature as topic"[MeSH AND "systematic"[tiab])

C. Data Abstraction and Data Management. All titles and abstracts identified through our literature searches will be independently reviewed for eligibility against our inclusion/exclusion criteria by two trained members of the research team. 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® (Thomson Reuters, New York, NY) database.

We will retrieve and review the full text of all articles included during the title/abstract review phase. Each full-text article will be independently reviewed by two trained members of the research team for inclusion or exclusion on the basis of the eligibility criteria described earlier. 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. All results will be tracked in an EndNote database. We will record the reason that each excluded full-text publication did not satisfy the eligibility criteria so that we can later compile a comprehensive list of such studies.

For studies that meet inclusion criteria, we will abstract relevant 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, as specified in the PICOS. Trained reviewers will extract the relevant data from each included article into the evidence tables. All data abstractions will be reviewed for completeness and accuracy by a second member of the team.

D. Assessment of Methodological Risk of Bias of Individual Studies. To assess the risk of bias of studies, we will use criteria described in the AHRQ *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[35] We will use questions specified in the RTI Item Bank[36] and the Cochrane Risk of Bias tool.[37] We will assess the potential for selection bias, performance bias, attrition bias, detection bias, and reporting bias. Results of this assessment will be summarized in a rating of low, medium, or high risk of bias for individual outcomes. In general, a study with a low risk of bias has a strong design, measures outcomes appropriately, uses appropriate statistical and analytical methods, reports low attrition, and reports methods and outcomes clearly and precisely. Studies with a medium risk of bias are those that do not meet all criteria required for low risk of bias. These studies may have some flaws in design or execution (e.g., imbalanced recruitment, high attrition) but they provide information (say, through sensitivity analysis) to allow the reader the ability to evaluate and determine that those flaws are not likely to cause major bias. Missing information often leads to ratings of medium as opposed to low. Studies with a high risk of bias are those with at least one major flaw that is likely to cause significant bias and thus might invalidate the results. Major flaws preclude the ability to draw causal inferences between the intervention and the outcome. Examples include poor randomization for randomized controlled trials or failure to control for confounding for observational studies. Studies with a high risk of bias will be considered in this review only if we are unable to answer the KQs with the available studies with low or medium risk of bias.

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.

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. For all meta-analyses, we will use random-effects models to estimate pooled effect sizes using Comprehensive Meta-Analysis[38] (Biostat, Inc., Englewood, NJ) software. To determine whether quantitative analyses are appropriate, we will assess the clinical heterogeneity of the population in studies under consideration following established guidance.[39] We will do this by qualitatively assessing the PICOS] of the included studies, looking for similarities and differences. If we conduct quantitative syntheses, 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 by using sensitivity analysis or analysis of subgroups. We plan to perform subgroup analyses when possible and appropriate to examine clinical heterogeneity.

Planned population subgroup analyses for outcomes listed in KQ 1 are specified in KQ 2. When quantitative analyses are not appropriate (e.g., because of heterogeneity, insufficient numbers of similar studies, or insufficiency or variation in reporting), we will synthesize the data qualitatively.

F. Grading the Evidence (SOE) for Individual Outcomes. We will grade the strength of evidence on the basis of guidance established for the EPC Program.[35,40] Developed to grade the overall strength of a body of evidence, this approach incorporates four key domains: risk of bias (including study design and aggregate quality), consistency, directness, and precision of the evidence. The grades of evidence that can be assigned are described in Table 4. Grades reflect the strength of the body of evidence to answer the KQs on the comparative effectiveness and harms of the interventions in this review. Two reviewers will assess each domain for each key outcome listed in the framework, and conflicts will be resolved by consensus.

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

Grade	Definition
High	High confidence that the evidence reflects the true effect: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Moderate confidence that the evidence reflects the true effect: Further research may change our confidence in the estimate of the effect and may change the estimate.

Low	Low confidence that the evidence reflects the true effect: Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate.
Insufficient	Evidence either is unavailable or does not permit estimation of an effect.

Source: Owens et al., 2010[40]

G. Assessing Applicability. We will assess the applicability both of individual studies and of the body of evidence.[35] For individual studies, we will examine conditions that may limit applicability based on the PICOS structure. Such conditions may be associated with heterogeneity of treatment effect and the ability to generalize the effectiveness of an intervention to use in everyday practice. Examples include the following:

- Population: narrow eligibility criteria
- Intervention: intensity and delivery of the interventions
- Comparator: use of substandard comparators
- Outcomes: use of composite outcomes that mix outcomes of different significance to patients
- Timing: studies of different duration that may have various implications for applicability

We will abstract and report key characteristics that may affect applicability into evidence tables. To assess the applicability of a body of evidence, we will consider the consistency of results across studies that represent an array of different populations.

V. References

1. Copeland WE, Keeler G, Angold A, et al. Traumatic events and posttraumatic stress in childhood. Arch Gen Psychiatry 2007 May;64(5):577-84. PMID: 17485609.
2. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 4th ed. Text rev. Washington, DC: American Psychiatric Association; 2000.
3. Kilpatrick DG, Ruggiero KJ, Acierno R, et al. Violence and risk of PTSD, major depression, substance abuse/dependence, and comorbidity: results from the National Survey of Adolescents. J Consult Clin Psychol 2003 Aug;71(4):692-700. PMID: 12924674.
4. Dube SR, Anda RF, Felitti VJ, et al. Childhood abuse, household dysfunction, and the risk of attempted suicide throughout the life span: findings from the Adverse Childhood Experiences Study. JAMA 2001 Dec 26;286(24):3089-96. PMID: 11754674.
5. Berman SL, Kurtines WM, Silverman WK, et al. The impact of exposure to crime and violence on urban youth. Am J Orthopsychiatry 1996 Jul;66(3):329-36. PMID: 8827256.
6. Famularo R, Fenton T, Kinscherff R, et al. Psychiatric comorbidity in childhood post traumatic stress disorder. Child Abuse Negl 1996 Oct;20(10):953-61. PMID: 8902292.
7. Mehta S, Ameratunga SN. Prevalence of post-traumatic stress disorder among children and

adolescents who survive road traffic crashes: a systematic review of the international literature. J Paediatr Child Health 2011 Apr 29 [Epub ahead of print]. PMID: 21535287.

8. Scott KM, Smith DR, Ellis PM. Prospectively ascertained child maltreatment and its association with DSM-IV mental disorders in young adults. Arch Gen Psychiatry 2010 Jul;67(7):712-9. PMID: 20603452.
9. Scrimin S, Moscardino U, Capello F, et al. Trauma reminders and PTSD symptoms in children three years after a terrorist attack in Beslan. Soc Sci Med 2011 Mar;72(5):694-700. PMID: 21255892.
10. Gillespie CF, Phifer J, Bradley B, et al. Risk and resilience: genetic and environmental influences on development of the stress response. Depress Anxiety 2009;26(11):984-92. PMID: 19750552.
11. Cohen JA, Bukstein O, Walter H, et al. Practice parameters for the assessment and treatment of children and adolescents with post traumatic stress disorder. J Am Acad Child Adolesc Psychiatry 2010;49(4):414-30. PMID: 20410735.
12. Fergusson DM, Horwood LJ, Lynskey MT. Childhood sexual abuse and psychiatric disorder in young adulthood: II. Psychiatric outcomes of childhood sexual abuse. J Am Acad Child Adolesc Psychiatry 1996 Oct;35(10):1365-74. PMID: 8885591.
13. Brent DA, Oquendo M, Birmaher B, et al. Familial pathways to early-onset suicide attempt: risk for suicidal behavior in offspring of mood-disordered suicide attempters. Arch Gen Psychiatry 2002 Sep;59(9):801-7. PMID: 12215079.
14. Brown J, Cohen P, Johnson JG, et al. Childhood abuse and neglect: specificity of effects on adolescent and young adult depression and suicidality. J Am Acad Child Adolesc Psychiatry 1999 Dec;38(12):1490-6. PMID: 10596248.
15. Saigh PA, Mroueh M, Bremner JD. Scholastic impairments among traumatized adolescents. Behav Res Ther 1997 May;35(5):429-36. PMID: 9149452.
16. Scheeringa MS. Developmental considerations for diagnosing PTSD and acute stress disorder in preschool and school-age children. Am J Psychiatry 2008 Oct;165(10):1237-9. PMID: 18829877.
17. Bryant B, Mayou R, Wiggs L, et al. Psychological consequences of road traffic accidents for children and their mothers. Psychol Med 2004 Feb;34(2):335-46. PMID: 14982139.
18. Scheeringa MS, Wright MJ, Hunt JP, et al. Factors affecting the diagnosis and prediction of PTSD symptomatology in children and adolescents. Am J Psychiatry 2006 Apr;163(4):644-51. PMID: 16585439.
19. Meiser-Stedman R, Smith P, Glucksman E, et al. The posttraumatic stress disorder diagnosis in preschool- and elementary school-age children exposed to motor vehicle accidents. Am J Psychiatry 2008 Oct;165(10):1326-37. PMID: 18676592.
20. Zeanah CH. Proposal to include child and adolescent age related manifestations and age related subtypes for PTSD in DSM-V. Arlington, VA: American Psychiatric Association; 2010. Available at: http://www.dsm5.org/Proposed%20Revision%20Attachments/DSM-5%20Child%20PTSD%20Review%2012-22-08.pdf. Accessed March 22, 2012.
21. Scheeringa MS, Zeanah CH, Drell MJ, et al. Two approaches to the diagnosis of posttraumatic stress disorder in infancy and early childhood. J Am Acad Child Adolesc Psychiatry 1995 Feb;34(2):191-200. PMID: 7896652.
22. Scheeringa MS, Peebles CD, Cook CA, et al. Toward establishing procedural, criterion, and discriminant validity for PTSD in early childhood. J Am Acad Child Adolesc Psychiatry 2001 Jan;40(1):52-60. PMID: 11195563.

23. Scheeringa MS, Zeanah CH, Myers L, et al. New findings on alternative criteria for PTSD in preschool children. J Am Acad Child Adolesc Psychiatry 2003 May;42(5):561-70. PMID: 12707560.
24. Task Force on Research Diagnostic Criteria: Infancy Preschool. Research diagnostic criteria for infants and preschool children: the process and empirical support. J Am Acad Child Adolesc Psychiatry 2003 Dec;42(12):1504-12. PMID: 14627886.
25. De Arellano MA, Waldrop AE, Deblinger E, et al. Community outreach program for child victims of traumatic events: a community-based project for underserved populations. Behav Modif 2005 Jan;29(1):130-55. PMID: 15557481.
26. Cohen JA, Mannarino AP, Deblinger E. Treating trauma and traumatic grief in children and adolescents. New York: Guilford Press; 2006.
27. Lieberman AF, Van Horn P, Ippen CG. Toward evidence-based treatment: child-parent psychotherapy with preschoolers exposed to marital violence. J Am Acad Child Adolesc Psychiatry 2005 Dec;44(12):1241-8. PMID: 16292115.
28. Linehan M. Cognitive-behavioral treatment of borderline personality disorder. New York: Guilford Press; 1993.
29. Weiner DA, Schneider A, Lyons JS. Evidence-based treatments for trauma among culturally diverse foster care youth: treatment retention and outcomes. Child Youth Serv Rev 2009;31(11):1199-205.
30. Zisser A, Eyberg SM. Treating oppositional behavior in children using parent-child interaction therapy. In: Kazdin AE and Weisz JR, eds. Evidence-based psychotherapies for children and adolescents. 2nd ed. New York: Guilford Press; 2010:179-93.
31. Eyberg S. Parent-child interaction therapy: integration of traditional and behavioral concerns. Child Fam Behav Ther 1988;10(1):33-46.
32. Shapiro F. Eye movement desensitization and reprocessing: basic principles, protocols, and procedures. New York: Guilford; 2001.
33. Schultz PN, Remick-Barlow GA, Robbins L. Equine-assisted psychotherapy: a mental health promotion/intervention modality for children who have experienced intra-family violence. Health Soc Care Community 2007 May;15(3):265-71. PMID: 17444990.
34. Berkowitz SJ, Marans SM. The child development-community policing program: a partnership to address the impact of violence. Isr J Psychiatry Relat Sci 2000;37(2):103-14. PMID: 10994294.
35. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality; February 2011. AHRQ Publication No. 10(11)-EHC063-EF. Chapters available at: www.effectivehealthcare.ahrq.gov.
36. Viswanathan M, Berkman ND. Development of the RTI item bank on risk of bias and precision of observational studies. J Clin Epidemiol 2012 Feb;65(2):163-78. PMID: 21959223.
37. Higgins JPT, Altman DG. Assessing risk of bias in included studies. Cochrane Handbook for Systematic Reviews of Interventions. Hoboken, NJ: John Wiley & Sons, Ltd; 2008:187-241.
38. Borenstein M, Hedges L, Higgins J, et al. Comprehensive meta-analysis version 2. Englewood, NJ: Biostat; 2005.
39. West SL, Gartlehner G, Mansfield AJ, et al. Comparative Effectiveness Review Methods: Clinical Heterogeneity. Methods Research Report (Prepared by RTI International-University

of North Carolina Evidence-based Practice Center under Contract No. 290-2007-10056-I). Rockville, MD: Agency for Healthcare Research and Quality; September 2010. AHRQ Publication No: 10-EHC070-EF. Available at: http://www.ncbi.nlm.nih.gov/books/NBK53310/pdf/TOC.pdf.

40. Owens DK, Lohr KN, Atkins D, et al. AHRQ series paper 5: grading the strength of a body of evidence when comparing medical interventions—Agency for Healthcare Research and Quality and the Effective Health-Care Program. J Clin Epidemiol. 2010 May;63(5):513-23. PMID: 19595577.
41. Lieberman AF, Van Horn P. Psychotherapy with infants and young children: repairing the effects of stress and trauma on early attachment. New York: The Guilford Press; 2008.

VI. Definition of Terms

Not applicable.

VII. Summary of Protocol Amendments

None.

VIII. Review of Key Questions

For all EPC reviews, key questions were reviewed and refined as needed by the EPC with input from Key Informants and the Technical Expert Panel (TEP) to ensure that the questions are specific and explicit about what information is being reviewed. In addition, for Comparative Effectiveness Reviews, the key questions were 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 Key Questions 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 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 methodological 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 healthy 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 do analysis of any kind nor contribute to the writing of the report and 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 methodological 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 has no interests to disclose:

- Content expert A discloses the following business and professional interests:

  Principal Investigator of a CDC-funded translational research study examining effective dissemination and implementation of a dependency court improvement model to improve child well-being (developed in Miami, FL). The model is multidimensional, comprising a) improved systems integration across the judiciary, child welfare, and child mental health, and b) evidence-based treatment for the very young child and his/her primary caregiver adapted for the court setting. Because the model is intended to have broad applicability for communities with different service landscapes, it does not specify a single intervention approach. The particular evidence-based treatment under investigation

in the translational research study is Child-Parent Psychotherapy,[27,41] as that is the treatment model used at the originating site in Miami.

- Co-investigator A discloses the following business and professional interests:

  Faculty member in the Department of Psychiatry at the University of North Carolina at Chapel Hill.

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 Task Order Officer 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.