Magellan Clinical Practice Guideline

For the Assessment and Treatment of Patients with

Posttraumatic Stress Disorder and Acute Stress Disorder

Magellan Clinical Practice Guideline Task Force

Thomas G. Carlton, M.D.
Nancy D. Donachie, M.D.
Gary M. Henschen, M.D., F.A.P.A.
Pamela E. Kumar, B.S.N.
Kathryn Kvederis, M.D., D.F.A.P.A.
Louis A. Parrott, M.D., Ph.D.
Clifton A. Smith, D.O., M.S., F.A.P.A.
Fatimah A. Tahil, M.D., M.P.H., D.F.A.P.A., F.A.P.M.

Table of Contents

Purpose of This Document

This document is an introduction and update to Magellan Healthcare's (Magellan's) adopted clinical practice guideline (CPG) for the assessment and treatment of patients with posttraumatic stress disorder and acute stress disorder. Magellan has adopted the following American Psychiatric Association (APA) guidelines : *Clinical Practice Guideline for the Assessment and Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder (2004); Treating Patients with Acute Stress Disorder and Posttraumatic Stress Disorder: A Quick Reference Guide (2004);* and the *APA Guideline Watch : Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder (2009).* The APA guideline is a research-based document covering psychiatric management of patients with posttraumatic stress disorder (PTSD) and acute stress disorder (ASD), including psychotherapy and pharmacotherapy, clinical features and epidemiology, and treatment planning. The APA guideline watch provides additional information made available after publication of the guideline.

The purpose of this document is to provide an introduction, as well as a summary, of recommendations from a literature review conducted through December 2015, and highlights from various sources. The rationale for this summary, presented in table format, is to avail clinicians of evidence- and consensus-based guidance on assessment and treatment of PTSD and ASD in one location for ease of use and reference. However, clinicians also should obtain and become familiar with the adopted APA guidelines.

This guideline presents the results of published, peer-reviewed studies including clinical trials, systematic reviews and meta-analyses. Many are early studies, not yet reproduced, and some are very small, or include a narrow population of participants. Clinicians should exercise caution when interpreting results of these studies, especially when the authors describe study results as insignificant, or where suggestions, rather than conclusions, are based on the results of the studies. Clinicians should note that some are international studies including the use of medications that are not available in the United States or are "off label" for a particular condition.

Clinicians are cautioned to assess studies for relevance to the treatment of any given patient. Some factors to consider are the age, gender and culture of patients; age at the time of exposure to trauma; the nature of the traumatic event(s); the duration of exposure to trauma; and whether patients experienced multiple traumatic events. Applying studies of male combat veterans to female adolescent victims of childhood sexual assault *and vice versa* could be problematic.

As with all guidelines, this document augments, not replaces, sound clinical judgment. As a matter of good practice, clinically sound exceptions to this practice guideline are in the member's treatment record, with documentation of the clinical reasoning for making the exception. Magellan periodically requests treatment records from providers in order to monitor compliance with clinical practice guidelines. Additionally, this guideline does not supersede Food and Drug Administration (FDA) determinations or other actions regarding withdrawal or approval of specific medications or devices, and their uses. It is the responsibility of the treating clinician to remain current on medication/device alerts and warnings issued by the FDA and other regulatory and professional bodies, and to incorporate such information in his or her treatment decisions.

Obtaining Copies of the APA Guidelines

Copies of the *Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder, Treating Patients with Acute Stress Disorder and Posttraumatic Stress Disorder: A Quick Reference Guide* and *Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder* may be obtained through the APA at http://psychiatryonline.org/guidelines or by calling 1-800-368-5777, or by U.S. mail at:

American Psychiatric Publishing, Inc.
1000 Wilson Blvd., Suite 1825
Arlington, VA 22209-3901

Provider Feedback

Magellan welcomes feedback on our clinical practice guidelines. All suggestions and recommendations are considered in our ongoing review of the guidelines. Please submit comments to:

Clinical Operations Coordinator
Re: CPG
Magellan Healthcare
6950 Columbia Gateway Dr.
Columbia, Maryland 21046
CPG@MagellanHealth.com

Executive Summary

(Discussion of changes/new information in this updated guideline)

Posttraumatic Stress Disorder (PTSD)

General/Assessment

A recent prospective longitudinal study of U.S. Marines investigated whether reduced heart rate variability (HRV) before combat deployment may be a contributing risk factor for PTSD after deployment (Minassian et al., 2015). Researchers defined HRV as the "quantitative assessment of variation in heartbeat intervals," an index of autonomic nervous system function (Minassian et al., p. 980). This study assessed active duty Marines (n=2160) both one month before deployment as well as 3-6 months after their return from active service. Researchers found a modest association between lower HRV prior to deployment and increased risk of PTSD upon return. They concluded that reduced HRV "may contribute to vulnerability and resilience to PTSD along with known risk factors, such as combat exposure and preexisting stress and trauma symptoms" (Minassian et al., p. 985). They further noted that **if supported in future studies**, this association "sheds light on the interplay between complex biological systems and the psychological and functional consequence of trauma and may provide new opportunities for prevention" (Minassian et al., p. 985).

According to research, the prevalence rate of PTSD among individuals actively serving in wars, e.g., Afghanistan and Iraq, is approximately 8%, and veterans may suffer from PTSD symptoms for years after their war experience (Stecker et al., 2014). According to researchers, only about 25% of veterans seek treatment despite extensive outreach by various government agencies. A longitudinal assessment of gender differences in the development of PTSD among U.S. military personnel deployed in support of the operations in Iraq and Afghanistan **suggested** that women have no significantly different risk for developing PTSD than men after experiencing combat (Jacobson et al., 2015).

In a review of literature considering recommendations and guidelines of medical societies from Germany and abroad, authors noted higher risk of PTSD when trauma is inflicted deliberately rather than as the results of natural catastrophes and accidents (Frommberger et al., 2014).

A recent study analyzing information obtained from 1987 to 2011 on Vietnam veterans (n=2400) found that "Male Vietnam war theater veterans who had PTSD were about 87% more likely to die between 1987 and 2011 than those without PTSD – even after adjusting for demographic, social and economic factors" (Medscape, 2015). Authors found that PTSD was associated with a greater risk of death from cancer, traffic accidents, suicide, murder and accidental factors. Noting that Vietnam veterans are the majority of living veterans in the U.S., they emphasized the importance of studying the long-term mental and physical health effects of their war experiences to provide better care for veterans (Medscape, 2015).

Past studies have linked PTSD to cardiovascular disease without conclusively linking PTSD and atherosclerosis (Medscape, 2015). A recent study, presented by Dr. Ahmadi at the American Psychiatric Association's 2015 annual meeting, included participants (n=246) with and without PTSD who underwent clinically indicated computed tomography (CT) angiography and assessment of the coronary distensibility index (CDI). Results from this study showed that impaired coronary distensibility was more prominent in patients with PTSD than in those without PTSD. Researchers **suggested** further studies investigating early diagnosis of PTSD and related coronary atherosclerosis (American Psychiatric Association, 2015).

Psychotherapy Treatments

A recent systematic review and meta-analysis assessed the efficacy, comparative effectiveness and adverse effects of psychological treatment for adults with PTSD (Cusack et al., 2015). This study included 64 trials including patients with severe PTSD. Evidence supported efficacy of the following: exposure therapy including manualized prolonged exposure (PE); cognitive therapy (CT); cognitive processing therapy; cognitive behavioral therapy (CBT)-mixed therapies; eye movement desensitization and reprocessing (EMDR); and narrative exposure therapy. To determine whether evidence supported the efficacy of specific types of interventions, authors first examined studies with inactive comparison groups, e.g., usual care, followed by examination of studies with active comparison groups. In most instances, head-to-head evidence from this meta-analysis was insufficient in determining whether the different psychotherapies differed in effectiveness. Moderate strength of evidence **suggested** the following: that exposure therapy was superior in reducing PTSD symptoms when compared to relaxation therapy; and that exposure therapy and cognitive therapy were similar in loss of PTSD diagnosis.

World Health Organization guidelines recommend the following for treatment of adults with PTSD: individual or group cognitive behavioral therapy (CBT) with a trauma focus; eye movement desensitization and reprocessing (EMDR); stress management; and psychoeducation. The guidelines noted moderate quality of evidence for individual CBT and EMDR, and low quality of evidence for group CBT and stress management (WHO, 2013).

A recent study tested the effectiveness of a brief, telephone-based, cognitive-behavioral intervention in the treatment of service members returning from Afghanistan and Iraq who screened positive for PTSD but had not engaged in PTSD treatment. Service members (n=300) were randomized to one of two conditions: intervention or control. Participants in the intervention condition received a brief telephone-based, cognitive behavioral therapy intervention administered by a psychologist that lasted 45-60 minutes while those in the control condition did not receive this intervention session. All participants received follow-up phone calls at one, three and six months to assess symptoms and utilization of treatment services. Participants who received the intervention attended twice as many PTSD treatment sessions as those in the control condition at one-month follow-up. Earlier engagement in treatment led to immediate symptom reduction. No differences were found at longer-term follow-up, suggesting additional intervention may be necessary to build upon the initial gains (Stecker et al., 2014).

A recent systematic review and meta-analysis found evidence supporting the efficacy of cognitive therapy, including cognitive processing therapy, to improve the symptoms of PTSD, improve depression and anxiety symptoms, and reduce disability for adults with PTSD. For loss of diagnosis, 50% more participants treated with cognitive therapy achieved this outcome compared with control groups. The strength of the evidence in these studies was moderate (Cusack et al., 2015). A recent randomized controlled trial comparing 7-day intensive and three months of standard weekly cognitive therapy with three months of weekly emotion-focused supportive therapy in the treatment of patients (n=121) with chronic PTSD found that intensive cognitive therapy was as effective as standard weekly cognitive therapy, and both were superior to emotion-focused supportive therapy (Ehlers et al., 2014). Researchers noted advantages, e.g., faster symptom reduction, with the intensive version of cognitive therapy. As patients with PTSD often have problems with concentration and memory, the intensive version "may help keep the therapeutic material fresh in patients' minds until the next session" (Ehlers et al., p. 303).

The Cusack et al. systematic review and meta-analysis (referred to in the paragraph above) found high strength of evidence for exposure therapy, including prolonged exposure, for improving PTSD symptoms. Compared with those in wait-list control groups, 66% more subjects treated with exposure therapy achieved loss of PTSD (Cusack et al., 2015). Cusack et al. acknowledged that the high benefits and strength

of evidence for exposure therapy supports its use as a first-line treatment for PTSD. However, they cautioned that factors, e.g., patient preference, access to treatment, and clinical judgment, be considered when selecting a treatment. They noted that both exposure therapy and cognitive processing therapy are not likely to be available in community-based mental health centers. Most of the studies included in the meta-analysis excluded patients with substance dependence or suicidality, affecting the choice of first treatment (Cusack et al., 2015).

Interpersonal psychotherapy (IPT), a non-exposure-based, non-cognitive behavioral treatment, has demonstrated antidepressant efficacy and promise in PTSD research (Markowitz et al., 2015). In a randomized, 14-week trial comparing IPT, prolonged exposure, and relaxation therapy in the treatment of patients (n=110) with severe, chronic PTSD, researchers found that IPT demonstrated that it was not inferior to exposure therapy, the "gold standard" PTSD treatment. Finding that ITP had higher response rates than prolonged exposure, researchers **suggested** that "PTSD treatment may not require cognitive behavioral exposure to trauma reminders" and "patients with comorbid major depression may fare better in Interpersonal Psychotherapy than Prolonged Exposure" (Markowitz et al., 2015, p. 2). Roy-Byrne noted, "The results of this trial add a new, non-CBT treatment armamentarium, showing that there is not 'one royal road to PTSD response'" (Roy-Byrne, 2015, p. 404). He pointed out a distinct advantage of IPT: how it focuses on and addresses a patient's emotional and interpersonal life.

The Cusack et al. recent systematic review and meta-analysis found low strength of evidence of EMDR for reducing PTSD symptoms due to some inconsistency and imprecision. However, moderate evidence in achieving loss of PTSD diagnosis as well as for improving depression symptoms was found for EMDR. Compared with subjects in wait-list control groups, 64% more subjects treated with EMDR experienced this outcome (Cusack et al., 2015).

Complementary and Alternative Treatments

A randomized clinical trial compared mindfulness-based stress reduction therapy with present-centered group therapy in veterans (n=116) with PTSD. Mindfulness-based stress reduction therapy included eight weekly 2.5 hour group sessions and a retreat lasting one day (Polusny et al., 2015). The treatment's focus was on teaching patients to deal with the present moment nonjudgmentally. Present-centered group therapy consisted of nine weekly 1.5-hour group sessions focusing on current life problems. Patients in the mindfulness-based stress reduction therapy group showed greater (although modest) self-reported improvement in PTSD symptom severity during treatment than those in the present-centered group therapy.

Pharmacotherapy Treatments

In a recent systematic review and meta-analysis of pharmacotherapy for PTSD, researchers discussed how previous meta-analyses have not been consistent regarding pharmacological treatment of PTSD (Hoskins et al., 2015). Only paroxetine, mirtazapine, amitriptyline and phenelzine were noted as significantly superior to placebo in the National Institute for Health and Care Excellence (NICE) guidelines, while all were recommended only as second-line treatment after trauma-focused psychological treatment. The recommendation that pharmacological interventions should not be preferred to trauma-focused psychological treatment came also from the guidelines of the Australian Centre for Posttraumatic Mental Health (ACPMH). The APA guidelines as well as the guidelines from the International Society for Traumatic Stress Studies have been more positive about pharmacological treatment, while the Institute of Medicine was unable to find evidence determining the efficacy of pharmacological treatment for PTSD. Comparisons are difficult due to the difference in methodological quality between the studies. The World Health Organization (WHO) commissioned the update of the

results of published systematic reviews (NICE, ACPMH, and Cochrane Collaboration) which are presented in this recent systematic review and meta-analysis (Hoskins et al., 2015).

Studies (n=51) selected for the Hoskins review referred to above included those with "no restriction on the basis of onset, duration or severity of PTSD symptoms, or on the presence of comorbid disorders, trauma type, age or gender of participants" (Hoskins, p. 93). Outcome measures included clinician-administered continuous measures of symptom severity, e.g., Clinician Administered PTSD Scale. Considered separately were self-rated PTSD symptom scales. Included in this review were 51 studies, of which 31 assessed serotonergic agents - SSRIs (sertraline, fluoxetine, paroxetine, citalopram, escitalopram, and fluvoxamine). In the meta-analysis of reduction in severity of any PTSD symptom for SSRIs (when grouped together) versus placebo, there was a small positive effect with SSRIs. Comparison of individual SSRIs to placebo found that two drugs were significantly superior to placebo in the reduction in severity of PTSD symptoms: paroxetine and fluoxetine. A serotonergic-noradrenergic agent (SNRI), venlafaxine, was also superior to placebo in reducing the severity of PTSD symptoms. The meta-analysis found no evidence for the following drugs versus placebo: brofaromine, olanzapine, sertraline or topiramate. In single randomized controlled trials, four drugs showed superiority over placebo: amitriptyline, GR205171 (neurokinin- 1 antagonist),mirtazapine, and phenelzine, while the following agents did not: alprazolam, citalopram, desipramine, escitalopram, imipramine, lamotrigine, nefazadone, risperidone, tiagabine, and valproate semisodium. Authors noted that evidence from the review does not consider drug or placebo combined with psychological treatment, as the review considers only drug monotherapy (Hoskins et al., 2015).

Authors in the above study (Hoskins et al., 2015) noted that when comparing pharmacological treatments for PTSD with placebo, the effect sizes were low and inferior to those reported for psychological treatments with a trauma focus over treatment as usual controls. They cited a WHO development group that recommended antidepressants as a second line of treatment of PTSD after unsuccessful psychological treatment. Authors also reported that the most recent Australian guidelines "concluded that pharmacological interventions should not be preferentially used as a routine first treatment of PTSD over trauma-focused psychological treatments" (Hoskins et al., p. 96).

The World Health Organization's guidelines recommend that selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) should not be offered as the first choice of treatment for PTSD in adults. They indicated that SSRIs and TCAs be considered when stress management, CBT with a trauma focus, and EMDR have either failed or are not available. They also indicated their use in the presence of co-morbid moderate – severe depression (WHO, 2013).

The FDA has approved two medications, sertraline and paroxetine, for treating adults with PTSD. In four large FDA trials, these two drugs showed only moderate effect sizes (NIMH, 2015).

Sympatholytics / alpha-adrenergic antagonists / beta-adrenergic blockers - A review of seven studies (n=210 subjects) examined the impact of prazosin therapy as an augmenting agent to traditional antidepressant interventions on predominately combat-related PTSD nightmare as a primary outcome. Results showed that prazosin is an "effective off-label option for combat-related PTSD nightmares" (Writer et al., 2014, p. 24). Authors **suggested** future randomized, controlled examination of prazosin.

Stellate Ganglion Block (SGB), a common and minimally invasive anesthetic procedure widely used for treating chronic pain, has been reviewed as a new technique in the treatment of PTSD (Lipov, 2015). Lipov cited a study of the first time SGB was performed for PTSD and published (2008), and reported that more than 2000 SGBs have been performed at military hospitals for PTSD, with a published success rate of more than 70%. Clinical changes after the procedure included not only improved sleep, but also

reduction of hypervigilance and reduced reactivity to stimuli. However, SGB is not available to patients with PTSD, as it is an unproven approach and is considered off-label. The author suggests that it is "time to look at the available data and apply SGB to the population most affected by PTSD, the military men and women who service this country so valiantly" (Lipov, 2015).

Individually Based Precision Biotherapies for PTSD and PTSD-Related Conditions - Rasmusson et al. noted a "failure to address individual variability in the complex interacting biological processes that converge on the otherwise relatively uniform PTSD phenotype or that define PTSD endophenotypes or particular PTSD-related medical, psychiatric, and substance abuse comorbidity patterns" (Rasmusson et al., p.8). They **suggested** that new multimodal study designs incorporating rapidly evolving molecular, neuroimaging, psychophysiology, and data analytic strategies aid the development of individually based precision biotherapies for PTSD. Further they noted that the impact of trauma must be understood at three levels: organic, cellular and molecular (Rasmusson et al., 2015).

Combined Treatments

In a double-blind, placebo-controlled clinical trial including Iraq and Afghanistan veterans (n=156), researchers examined the effectiveness of virtual reality exposure augmented with D-cycloserine (50 mg) or alprazolam (0.25 mg), compared with placebo, in reducing PTSD (Rothbaum et al., 2014). This study found no significant difference between D-cycloserine and placebo on the Clinician-Administered PTSD Scale (CAPS) at three, six and 12 months, whereas participants in the alprazolam cohort showed a higher rate of PTSD at post-treatment and three months post-treatment. Finding a significant interaction between learning and treatment condition, researchers **suggested** an association between extinction learning (when operant behavior previously reinforced no longer results in reinforcing consequences) and outcomes only in the D-cycloserine condition. Significant findings included the following: lack of overall support of D-cycloserine enhancement treatment for PTSD symptoms; patients with more between session learning who received D-cycloserine treatment had enhanced virtual reality outcomes; use of alprazolam during treatment was associated with decreased efficacy of exposure therapy; and D-cycloserine demonstrated benefits on salivary cortisol level and startle response which were sensitive to treatment gains. Researchers concluded that this group of veterans has familiarity with video games, finding virtual reality exposure therapy easier than talk therapy and assisting emotional engagement. **They also cautioned using benzodiazepines in patients with PTSD as "they seemed to have attenuated overall response in the long term**" (Rothbaum et al, p. 7).

Acute Stress Disorder (ASD) in Adults

General/Assessment

All of the conditions included in the diagnostic criteria require exposure to a traumatic or stressful event, i.e., actual or threatened death, serious injury, or sexual violence. The traumatic event(s) may be experienced directly, witnessed in person as it occurs to others, or experienced indirectly as it occurred to a close family member or close friend. The exposure may also include "experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse) (APA, 2013). Diagnostic criteria for ASD are met when individuals meet nine or more of listed symptoms in five categories: intrusion symptoms, negative mood, dissociative symptoms, avoidance symptoms, and arousal symptoms beginning or worsening after occurrence of the traumatic event(s). The symptoms usually begin immediately following the trauma, but must persist for at least three days and up to a month (APA, 2013).

Psychotherapy Treatments

According to the World Health Organization (WHO), although psychological treatments are used to manage people experiencing the symptoms of acute distress, there is no consensus on the effectiveness of such interventions for acute traumatic stress symptoms. WHO guidelines for the management of conditions specifically related to stress recommend, "Cognitive-behavioral therapy (CBT) with a trauma focus should be considered in adults with acute traumatic stress symptoms associated with significant impairment in daily functioning" (WHO, 2013). They also note, "On the basis of available evidence, no specific recommendations can be made about stand-alone problem-solving counseling, eye movement desensitization and reprocessing (EMDR), relaxation or psycho-education in the first month for adults with acute traumatic stress symptoms associated with significant impairment in daily functioning after a potentially traumatic event" (WHO, 2013).

Pharmacological Treatments

According to WHO guidelines, clinicians must rule out concurrent disorders warranting treatment with either antidepressants or benzodiazepines. The guidelines recommend that "Benzodiazepines and antidepressants should not be offered to adults to reduce acute traumatic stress symptoms associated with significant impairment in daily functioning in the first month after a potentially traumatic event" (WHO, 2013). **The guidelines further indicate that pharmacological treatments, especially benzodiazepines, are often prescribed for treating symptoms of acute distress, noting the lack of consensus on the effectiveness of pharmacological treatments**.

Posttraumatic Stress Disorder in Adults

Table of Recommendations Based on Guideline and Recent Literature Review

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS General/Assessment	
Recommendations	**Recommended Resources**
❖ The American Psychiatric Association (APA) Guideline Watch (March 2009) indicated that factors predicting the development of Acute Stress Disorder (ASD) or Posttraumatic Stress Disorder (PTSD) have still not been established and reported that research results found that ASD was a poorer predictor of getting PTSD than just having PTSD criteria alone in the acute stage (APA, 2009). A review of 22 studies **suggested** that at least half of trauma survivors with ASD meet criteria for subsequent PTSD whereas most individuals with PTSD do not initially have ASD (Bryant, 2013). ASD is a transient stress response sometimes remitting within one month of trauma exposure or it may progress to PTSD after one month. The DSM-5 reported that approximately 50 percent of individuals who eventually develop PTSD initially present with ASD (APA, 2013). ❖ PTSD is no longer included in the class of anxiety disorders but is instead included in a new class of trauma- and stressor-related disorders. All of the conditions included in the diagnostic criteria require exposure to a traumatic or stressful event, i.e., actual or threatened death, serious injury or sexual violence. The first diagnostic criterion in	Diagnostic criteria for ASD and PTSD in *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, DSM-5* (APA, 2013)

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS

General/Assessment

Recommendations	Recommended Resources
DSM-5 provides clarity in how a traumatic event may be experienced, e.g., police officers repeatedly exposed to details of child abuse and first responders collecting human remains. Instead of three clusters of DSM-IV symptoms, DSM-5 includes four clusters: intrusion symptoms associated with traumatic event(s); persistent avoidance of stimuli associated with the traumatic event(s); marked alterations in arousal and reactivity associated with the traumatic event(s); and negative alterations in cognitions and mood associated with the traumatic event(s). While criteria in DSM-IV required fear, helplessness or horror happening right after the trauma, these are no longer included in DSM-5. A new subtype, "with dissociative symptoms," is now included when the individual's symptoms meet the criteria for PTSD and persistent or recurrent symptoms of depersonalization or de-realization are experienced. A subtype in DSM-IV, "delayed onset," is now "delayed expression" as some symptoms appear immediately and the delay is in meeting full criteria (APA, 2013).	
❖ In the DSM-5, a new subtype is PTSD for children six years and younger and includes separate diagnostic criteria (APA, 2013).	
❖ Children exposed to traumatic events respond differently than adults yet have the potential to develop serious psychological/developmental consequences depending on maturational factors, i.e., child's knowledge base, appraisal of emotion, response to memory. An estimated 64 percent of children exposed to trauma do not develop PTSD (Alisic et al., 2011). According to statistics from the U.S. Department of Veterans Affairs National Center for PTSD, about 15-43 percent of girls and 14-43 percent of boys experience at least one trauma, and 3-15 percent of those girls and 1-6 percent of those boys who have experienced a trauma develop PTSD (U.S. Dept. of Veterans Affairs). Research contributions to child trauma theory from meta-analytic findings showed that important predictors of long-term posttraumatic stress in children were: ○ symptoms of acute and short-term posttraumatic stress ○ depression ○ anxiety and ○ parental posttraumatic stress (Alisic et al., 2011). The National Center for PTSD indicates that factors increasing the chances children will get PTSD include: severity of trauma, parents' reactions to the trauma, and how close or far away the child is from the trauma. It also points out that such events as rape and assault are more likely to result in PTSD than other traumas, and the greater number of traumas experienced results in a higher risk of PTSD (U.S. Dept. of Veterans Affairs). Female gender, injury severity, duration of hospitalization and heart rate shortly after admission to the hospital accounted for small effects. However, age, minority status and socio-economic status were not significantly associated with long-term posttraumatic stress reactions in children (Alisic et al., 2011).	Practice Parameter for the Assessment and Treatment of Children and Adolescents with Posttraumatic Stress Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, Volume 49, Number 4, April 2010
❖ Meta-analytic review of current evidence has shown that a history of sexual abuse is associated with an increased risk of a lifetime diagnosis of PTSD (Chen et al., 2010). Other analyses of epidemiological survey data have shown that reported torture has the strongest association with PTSD in the post-conflict/refugee population. Psychiatric morbidity (particularly PTSD and depressive symptoms) is common in adult and	

Recommendations	Recommended Resources
pediatric burn, traumatic injury and other critical illness survivors experiencing Intensive Care Unit (ICU) stays (Steel et al., 2009; Davydow et al., 2009). A review of seven studies assessing the prevalence of PTSD after an awareness episode occurring during anesthesia found prevalence of PTSD ranging from 0 to 71 percent (Aceto et al.,2013). ❖ A recent prospective longitudinal study of U.S. Marines investigated whether reduced heart rate variability (HRV) before combat deployment may be a contributing risk factor for PTSD after deployment (Minassian et al., 2015). Researchers defined HRV as the "quantitative assessment of variation in heartbeat intervals," an index of autonomic nervous system function (Minassian et al., p. 980). This study assessed active duty Marines (n=2160) both one month before deployment as well as 3-6 months after their return from active service. Researchers found a modest association between lower HRV prior to deployment and increased risk of PTSD upon return. They concluded that reduced HRV "may contribute to vulnerability and resilience to PTSD along with known risk factors, such as combat exposure and preexisting stress and trauma symptoms" (Minassian et al., p. 985). They further noted that if supported in future studies, this association "sheds light on the interplay between complex biological systems and the psychological and functional consequence of trauma and may provide new opportunities for prevention" (Minassian et al., p. 985). ❖ According to research, the prevalence rate of PTSD among individuals actively serving in wars, e.g., Afghanistan and Iraq, is approximately 8%, and veterans may suffer from PTSD symptoms for years after their war experience (Stecker et al., 2014). According to researchers, only about 25% seek treatment despite extensive outreach by various government agencies. ❖ A prospective study of the World Trade Center disaster (WTCD) in New York City found that current PTSD in these victims after one year following the catastrophic event was associated with females, younger adults, those with lower self-esteem, lower social support, higher WTCD exposure, more lifetime traumatic events and a history of pre-WTCD depression. The second follow-up (a year later) showed that current PTSD was associated with 1) Latinos, 2) non-native born persons, 3) those with lower self-esteem, 4) more negative life events, 5) more lifetime traumatic events and 6) mixed handedness (Boscarino et al., 2009). A later longitudinal assessment of gender differences in the development of PTSD among U.S. military personnel deployed in support of the operations in Iraq and Afghanistan **suggested** that women have no significantly different risk for developing PTSD than men after experiencing combat (Jacobson et al., 2015). ❖ In a review of literature considering recommendations and guidelines of medical societies from Germany and abroad, authors noted higher risk of PTSD when trauma is inflicted deliberately rather than as the results of natural catastrophes and accidents (Frommberger et al., 2014). ❖ A recent study analyzing information obtained from 1987 to 2011 on Vietnam veterans	

Recommendations	Recommended Resources
(n=2400) found that "Male Vietnam war theater veterans who had PTSD were about 87% more likely to die between 1987 and 2011 than those without PTSD – even after adjusting for demographic, social and economic factors" (Medscape, 2015). Authors found that PTSD was associated with a greater risk of death from cancer, traffic accidents, suicide, murder and accidental factors. Noting that Vietnam veterans are the majority of living veterans in the U.S., they emphasized the importance of studying the long-term mental and physical health effects of their war experiences to provide better care for veterans (Medscape, 2015). ❖ According to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5),* PTSD with delayed expression must be diagnosed if the full diagnostic criteria are not met until at least six months after the event (the onset and expression of some symptoms may be immediate) (APA, 2013). Prevalence estimates have varied widely in the literature but results of a large meta-analysis of prospective studies showed that delayed PTSD was found in about a quarter of PTSD cases representing exacerbation of prior symptoms (Smid et al., 2009). ❖ Determine symptoms occurring in response to exposure to actual or threatened death, serious injury or sexual violence in at least one of the following: traumatic event(s) experienced directly; traumatic event(s) witnessed others; awareness that the traumatic event (violent or accidental) happened to a close family member/close friend; and repeated/extreme exposure to aversive details of the traumatic event(s) (APA, 2013). ❖ Identify signs and symptoms of and/or PTSD, falling into four major symptom clusters: o Intrusion symptoms associated with traumatic event(s) o Avoidance (persistent) symptoms of traumatic event(s) stimuli o Symptoms of marked alterations in arousal and reactivity associated with the traumatic event(s) o Symptoms of negative alterations in cognitions and mood associated with the traumatic event(s) (APA, 2013). ❖ Determine time of most recent traumatic event and duration of symptoms: o If symptoms persist from three days up to one month after the trauma, consider diagnosis of ASD. If symptoms were present prior to event, determine presence of prior traumatic event and consider PTSD or other disorder. o If duration of the disturbance (including symptoms above) is more than one month, consider diagnosis of PTSD (APA, 2013). ❖ Determine presence or absence of exposure to prior traumatic event(s) increasing risk or severity of PTSD. Differentiate between "simple PTSD" in which trauma consists of one or more isolated episodes (e.g., calamitous event, transportation accident, crime / assault), and "complex PTSD" in which trauma occurs repeatedly and escalates through the duration, e.g., childhood abuse, prisoner of war or refugee status, human trafficking (APA, 2004; Courtois, 2004). A recent study analyzing data from two community samples revealed that emotional numbing occurred primarily in the presence of	

Recommendations	Recommended Resources
pervasive disturbance and rarely in trauma-exposed subjects with intermediate disturbance (Breslau et al., 2005). ❖ Consider military deployment status and history in the assessment process: ○ Data from a recent study showed that witnessing atrocities had the strongest association with mental disorders and service use. A close-response relationship between exposure to traumatic events and PTSD suggests that the exposure to traumatic experiences during deployment – rather than deployment per se, increases the risk of mental health problems after deployment (Sareen et al., 2007). ○ After adjusting for exposure to combat and witnessing atrocities, participation in peacekeeping operations was not associated with increased likelihood of mental health problems. Peacekeeping operations can have a variety of negative and positive aspects (Sareen et al., 2007). ○ Ill treatment during captivity, e.g., psychological manipulations, humiliating treatment, etc., does not seem to be substantially different from physical torture in terms of the severity of the mental suffering they cause, the underlying mechanism of traumatic stress and the long-term psychological outcome (Basoğlu et al;, 2007). ❖ Exclude other disorders that could account for symptoms: ○ Substance use disorders, e.g., substance intoxication or withdrawal ○ Anxiety disorder ○ Psychotic disorder, mood disorder with psychotic features, or delirium (APA, 2004). ❖ Assess for co-morbid conditions. High rates of co-morbid psychiatric and medical disorders occur in those with PTSD: (APA, 2004). ○ Mood disorders ○ Eating disorders ○ Sleep disorders ○ Somatoform disorders ○ Personality disorders ○ Psychiatric disorders ○ Physical conditions, e.g., trauma- or stress-related injury or illness (especially traumatic brain injury), chronic pain, infectious disease, including HIV and other sexually-transmitted disease (APA, 2004). ❖ Consider the effect of assessment interview procedures on the patient's mental status, distress level and avoidance motivation. Adapt interview procedures accordingly and emphasize a sense of trust and safety regarding the therapeutic environment and relationship. The interviewer may defer discussion of intense anxiety-producing aspects of trauma until stabilization, unless there is a legal or other reason why specifics require immediate assessment. ❖ Normalize the distress-producing aspects of assessment and treatment (APA, 2004).	Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Substance Use Disorders* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Panic Disorder* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Assessment and Treatment of Patients with Generalized Anxiety Disorder* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Treatment of Bipolar Disorder* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Assessment and*

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS

General/Assessment

Recommendations	Recommended Resources
❖ Assess present risk status (Magellan Healthcare, 2010; APA, 2004): ○ Suicidal thought or behavior, (if present, perform suicide risk assessment). Meta-analytic findings revealed no evidence of a link between PTSD and subsequent completed suicide, but showed that PTSD was moderately associated with prior attempted suicide and suicidal ideation (Magellan Healthcare, 2010; Krysinska and Lester, 2010). Various studies have found evidence that PTSD is a risk factor for suicidal behaviors (Gradus et al., 2013). ○ Self-injurious behavior such as self-mutilation, not related to suicidal thought or intent. ○ Aggressive behavior, including thoughts, plans, or intentions of harm and access to means. ○ Environmental safety, i.e., risk of further exposure to trauma or danger, e.g., military duty, domestic violence, gang-related violence. ○ Nicotine dependence (Analysis of data on members of the Vietnam Era Twin Registry revealed that pre-existing nicotine dependence is associated with a two-fold increased risk of PTSD when exposed to traumatic events such as combat) (Koenen et al., 2005). ○ Past studies have linked PTSD to cardiovascular disease without conclusively linking PTSD and atherosclerosis (Medscape, 2015). A recent study, presented by Dr. Ahmadi at the American Psychiatric Association's 2015 annual meeting, included participants (n=246) with and without PTSD who underwent clinically indicated computed tomography (CT) angiography and assessment of the coronary distensibility index (CDI).Researchers **suggested** further studies investigating early diagnosis of PTSD and related coronary atherosclerosis.	*Treatment of Patients with Major Depressive Disorder* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Assessment and Treatment of Patients with Eating Disorders* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Schizophrenia* www.MagellanHealth.com/provider Magellan Healthcare *Clinical Practice Guideline for Assessing and Managing the Suicidal Patient* www.MagellanHealth.com/provider
❖ Assess current stressors, e.g., loss of loved ones, loss of property or livelihood, loss of physical functioning, legal system involvement (VA/DOD, 2010). A recent study found that Iraq and Afghanistan veterans present with higher levels of anger-related problems, suggesting that extended tours, multiple deployments and increased likelihood of redeployment affect symptom presentation and treatment needs (Seal et al., 2012). ❖ Assess use of opioid regimens, especially in veterans with PTSD and other mental disorders, e.g., substance use disorder, traumatic brain injury. A retrospective cohort study including Iraq and Afghanistan veterans (n=141,029) investigated the effect of mental health disorders, especially PTSD, on risks as well as adverse clinical outcomes associated with prescription opioid use. This study found that veterans with substance use disorder or traumatic brain injury received more prescriptions of opioids when PTSD was a co-morbid diagnosis and the use of opioids was associated with increased risk of adverse clinical outcomes, e.g., alcohol-, drug-, and opioid-related overdose and self-inflicted injuries (Seal et al., 2012). ❖ Use structured clinician interview tools, such as the Clinician-Administered PTSD Scale, the Structured Interview for PTSD, the Primary Care PTSD Screen (PCPS), the Short Screening Scale for PTSD (SSSP) and the New York PTSD Risk Score; and self-report instruments, such as the PTSD Checklist (Koenen et al., 2005). These documents are available for civilian and for military personnel, are in the public domain and may be of	VA/DOD Clinical Practice Guideline for the Management of Post-Traumatic stress Guideline Summary 2010

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS General/Assessment	
Recommendations	**Recommended Resources**
benefit in eliciting information that patients might hesitate to share verbally (APA, 2004; VA/DOD, 2010; Boscarino et al., 2009). ❖ Assess patient resiliency, strengths, family/social supports and adaptive coping strategies (APA, 2004; VA/DOD, 2010). ❖ Assess psychosocial needs, e.g., housing, employment and other factors that, if destabilized, will reduce likelihood of treatment success (VA/DOD, 2010).	

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS Patient and Family Education	
Recommendations	**Recommended Resources**
❖ Consider adding education and motivation enhancement components to early PTSD treatment to improve outcomes, since studies have found that patients become more motivated to change some symptoms, such as anger (Murphy et al., 2004), and have more satisfaction and optimism about treatment (Gray et al., 2004). ❖ Target education to both the patient and the family whenever possible, and should address the disorder, common symptoms, and the range of available and effective treatments, both pharmacologic and non-pharmacologic. ❖ Education also should address any co-morbid medical or psychiatric disorders; how co-morbid symptoms may affect core PTSD symptoms; and how the treatment plan will be adapted to address co-morbidity (VA/DOD, 2010). ❖ Education includes normalizing patient experiences, reducing anxiety about them, and offering hope that with time and treatment symptoms can be overcome (VA/DOD, 2010). ❖ When medications are prescribed, education should address the regimen, effects and side effects, and the importance of adherence even when symptoms begin to abate (APA, 2004). ❖ The tension between motivation for treatment and the symptoms of avoidance must be discussed early, as some psychotherapies can temporarily increase subjective in-session and between-session distress, which can lead to early dropout (APA, 2004). ❖ Education about the positive impact of reducing social isolation and identifying family and/or other social supports are important early in treatment. Provide assistance to identify appropriate self-help or treatment groups in which peer-to-peer assistance is	

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS **Patient and Family Education**	
Recommendations	**Recommended Resources**
obtained, and to identify strategies for overcoming avoidance in family or other close relationships (Jovanovic et al., 2004). ❖ Outcomes of mental health treatment after the World Trade Center attack indicated that early brief interventions at the worksite were the most effective post-disaster treatment followed by informal support seeking from friends, neighbors and from spiritual communities (Boscarino et al., 2009).	

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS **Psychotherapy Treatments**	
Recommendations	**Recommended Resources**
❖ The European Network for Traumatic Stress (TENTS) noted in their guidelines for psychosocial care following disasters that there was a strong consensus against early application of formal intervention universally for all individuals involved in traumatic events (Bisson et al., 2010). Similarly, in terms of PTSD prevention following traumatic events, meta-analytic findings **suggested** no recommendation for psychological intervention (single or multiple sessions) for *routine* use as it may have an adverse effect on some people (Roberts et al., 2009). Another study stressed the importance of making sure that the normal potent recovery process does not interfere with any intervention and of addressing basic needs, e.g., restoring physiological needs, providing information and orientation, and helping the individual find a source of support (Zohar et al., 2011). ❖ Initial interventions should include education about the disorder, common symptoms, and the range of available and effective treatments, including pharmacologic and non-pharmacologic. Initial choice of pharmacological, psychotherapeutic or combined treatment depends upon clinician and patient preference in light of the manifesting symptoms and any co-occurring disorders, since research does not favor any one modality as first-line treatment (APA, 2004; VA/DOD, 2010). ❖ Selection of a psychotherapeutic approach should be guided by the clinical circumstances, including co-occurring disorders, patient needs and preferences, and clinician skill level, guide the election of a psychotherapeutic approach. While all therapy has supportive elements, psychotherapeutic approaches for PTSD represent a continuum from supportive-only to trauma-focused. Supportive therapy has less reliance on structured techniques, and more emphasis on addressing current life issues, increasing coping and fostering a sense of interpersonal comfort. Trauma-focused therapies directly address the patient's traumatic experiences, memories and PTSD symptoms (VA/DOD, 2010). ❖ Although techniques and approaches may differ, overarching goals of treatment for PTSD are to: o Reduce frequency and intensity of distressing and intrusive symptoms o Reduce symptoms of co-occurring disorders	Bisson JI, Tavakoly B, Witteveen AB, Ajdukovic D, Hehel L, Johansen VJ, Nordanger D, Garcia FO, Punamaki RL, Schnyder U, Sezgin A, Wittmann L, Olff M. *TENTS guidelines: development of post-disaster psychosocial care guidelines through a Delphi process*. The British Journal of Psychiatry (2010)

Psychotherapy Treatments

Recommendations	Recommended Resources
○ Improve functioning in daily life ○ Protect against relapse ○ Integrate the effects of the trauma into the patient's construct of risk, safety, prevention and protection (VA/DOD, 2010). ❖ A recent systematic review and meta-analysis assessed the efficacy, comparative effectiveness and adverse effects of psychological treatment for adults with PTSD (Cusack et al., 2015). This study included 64 trials including patients with severe PTSD. Evidence supported efficacy of the following: exposure therapy including manualized prolonged exposure (PE); cognitive therapy (CT); cognitive processing therapy; cognitive behavioral therapy (CBT)-mixed therapies; eye movement desensitization and reprocessing (EMDR); and narrative exposure therapy. To determine whether evidence supported the efficacy of specific types of interventions, authors first examined studies with inactive comparison groups, e.g., usual care, followed by examination of studies with active comparison groups. Information about specific therapies obtained from this study is included in the sections below. ○ In most instances, head-to-head evidence from this meta-analysis was insufficient in determining whether the different psychotherapies differ in effectiveness. Moderate strength of evidence **suggested** the following: that exposure therapy was superior in reducing PTSD symptoms when compared to relaxation therapy; and that exposure therapy and cognitive therapy were similar in loss of PTSD diagnosis. ❖ APA Guideline Watch (March 2009) emphasized that research published since 2004 supports exposure-based cognitive-behavioral therapies such as cognitive processing therapy and prolonged exposure therapy as effective treatments for PTSD when delivered in individual formats (APA, 2009). ❖ World Health Organization guidelines recommend the following for treatment of adults with PTSD: individual or group cognitive behavioral therapy (CBT) with a trauma focus; eye movement desensitization and reprocessing (EMDR); stress management; and psychoeducation. The guideline noted moderate quality of evidence for individual CBT and EMDR and low quality of evidence for group CBT and stress management (WHO, 2013). ❖ Brief Phone-Based CBT Intervention to Improve PTSD Treatment Utilization by Returning Service Members ○ A recent study tested the effectiveness of a brief, telephone-based, cognitive-behavioral intervention in the treatment of service members returning from Afghanistan and Iraq who screened positive for PTSD but had not engaged in PTSD treatment. Service members (n=300) were randomized to one of two conditions: intervention or control. Participants in the intervention condition received a brief telephone-based, cognitive behavioral therapy intervention administered by a psychologist that lasted 45-60 minutes while those in the control condition did not receive this intervention session. All participants received follow-up phone calls at one, three and six months to assess	

Recommendations	Recommended Resources

symptoms and utilization of treatment services. Participants who received the intervention attended twice as many PTSD treatment sessions as those in the control condition at one-month follow-up. Earlier engagement in treatment led to immediate symptom reduction. No differences were found at longer-term follow-up, suggesting additional intervention may be necessary to build upon the initial gains (Stecker et al., 2014).

- Cognitive Therapy (CT)
  - CT has been shown in random, controlled trials to reduce distressing, trauma-related thoughts, which when modified, can ameliorate symptoms and improve mood and functioning. CT may be especially helpful in cases with co-occurring depression and/or anxiety disorders (APA, 2004; VA/DOD, 2010).
  - A meta-analytic review of cognitive behavioral treatments (CBT) for anxiety in adults found that cognitive therapy and exposure therapy alone, in combination or combined with relaxation training, were efficacious across the anxiety disorders with no differential efficacy for any treatment components for any specific diagnoses. When comparing across diagnoses, outcomes for generalized anxiety disorder and PTSD were superior to those for social anxiety disorder (Norton et al., 2007).
  - A clinical trial showed that brief early CBT accelerated recovery of acute PTSD, but did not influence long-term results (Sijbrandij et al., 2007).
  - CT targets trauma-related thoughts and beliefs, e.g., survivor guilt, self-blame, worries about functioning and/or the future (Seal et al., 2012).
  - CT emphasizes patient education about the effect of thoughts on mood and functioning, and includes techniques such as recording and systematically challenging distress-producing thoughts, modifying non-adaptive core beliefs that may maintain symptoms or poor functioning, stopping dysfunctional thoughts and learning positive self-talk (Seal et al., 2012).
  - Contraindications for CT include psychosis, severe brain injury and severe intellectual impairment.
  - A recent systematic review and meta-analysis found evidence supporting the efficacy of cognitive therapy, including cognitive processing therapy, to improve the symptoms of PTSD, improve depression and anxiety symptoms, and reduce disability for adults with PTSD. For loss of diagnosis, 50% more participants treated with cognitive therapy achieved this outcome compared with control groups. The strength of the evidence in these studies was moderate (Cusack et al., 2015).

- Intensive Cognitive Therapy
  - A recent randomized controlled trial comparing 7-day intensive and three months of standard weekly cognitive therapy with three months of emotion-focused supportive therapy in the treatment of patients (n=121) with chronic PTSD found that intensive cognitive therapy was as effective as standard weekly cognitive therapy and both were superior to emotion-focused supportive therapy (Ehlers et al., 2014). Researchers noted advantages, e.g., faster symptom reduction with the intensive version of cognitive therapy. As

Recommendations	Recommended Resources
patients with PTSD often have problems with concentration and memory, the intensive version "may help keep the therapeutic material fresh in patients' minds until the next session" (Ehlers et al., p. 303). ❖ Cognitive Processing Therapy (CPT) o CPT demonstrated feasibility and effectiveness in settings that have limited mental health resources, e.g., Democratic Republic of Congo. A recent study that randomized sexual assault survivors (n=405) from villages in the Democratic Republic of Congo to receive individual support or group CPT (1 individual session and 11 group sessions) found that the CPT group had greater improvements in PTSD symptoms after treatment as well as at six-month follow-up when compared with the individual support group. The group CPT used the cognitive model only, without a trauma narrative. Researchers **suggested** that CPT and other manualized treatment can be both feasible and effective outside of specialized PTSD programs (Bass et al., 2013). ❖ Exposure Therapy (ET) o ET has been shown in random, controlled trials to reduce fear associated with traumatic experiences and has been recommended as a quick-acting treatment for intrusive thoughts, flashbacks, trauma-related fears, panic attacks, avoidance and generalized anxiety in patients with PTSD (VA/DOD, 2010). o ET has been compared with Cognitive Behavioral Therapy (CBT), which adds a behavioral component to CT. ET has performed as well or better than CBT, with some reviews finding ET superior to CBT for PTSD. ET is frequently combined with CT with good effect (VA/DOD, 2010; Bisson et al., 2010). o Meta-analytic results of 13 studies (total n=675) showed no significant difference in treatment efficacy between prolonged exposure (PE) consisting of 9-12 sessions/90 minutes in length and other active treatments, i.e., CT, Eye Movement Desensitization and Reprocessing (EMDR), Stress Inoculation Training (SIT) and Cognitive Processing Therapy (CPT). The average PE treated patient fared better than 86 percent of control patients (Powers et al., 2010). o ET consists of therapist-guided repeated exposure, either imagined or actual, to feared stimuli, including traumatic memories, activities, objects and places (VA/DOD, 2010). o Because ET temporarily increases distress and may aggravate symptoms in the short-term, clinicians must screen patients carefully and present a clear rationale for using ET, explore patient concerns and build realistic expectations (VA/DOD, 2010). o Contraindications for ET include current unsafe life circumstances, health problems that could be aggravated by physiological arousal, current suicidal ideation, active substance use disorder, co-morbid psychosis or lack of motivation (VA/DOD, 2010). o In treating female active duty and veterans for PTSD, prolonged exposure was more effective in reducing symptoms than present-centered therapy (Schnurr et al., 2007). o APA Guideline Watch (March 2009) noted that Virtual Reality Exposure Therapy (VRET) shows promise in the treatment of disaster workers with PTSD but that	

Psychotherapy Treatments

Recommendations	Recommended Resources
larger randomized controlled trials are needed (APA, 2009). ○ A recent systematic review and meta-analysis of the comparative effectiveness and harms of psychological and pharmacological interventions or adults with PTSD found the strongest evidence of efficacy for improving PTSD symptoms were exposure-based therapy when compared with cognitive processing therapy, cognitive therapy, cognitive behavioral therapy mixed therapies, eye movement desensitization and reprocessing (EMDR) and narrative exposure therapy (AHRQ, 2013). ○ A later systematic review and meta-analysis found high strength of evidence for exposure therapy, including prolonged exposure, for improving PTSD symptoms. Compared with those in waitlist control groups, 66% more subjects treated with exposure therapy achieved loss of PTSD (Cusack et al., 2015). ○ Cusack et al. acknowledged that the high benefits and strength of evidence for exposure therapy supports its use as a first-line treatment for PTSD. However, they cautioned that factors, e.g., patient preference, access to treatment, and clinical judgment, be considered when selecting a treatment. They noted that both exposure therapy and CPT are not likely to be available in community-based mental health centers. Most of the studies included in the meta-analysis excluded patients with substance dependence or suicidality, affecting the choice of first treatment (Cusack et al., 2015). ❖ Interpersonal Psychotherapy for PTSD ○ Interpersonal psychotherapy (IPT), a non-exposure-based, non-cognitive behavioral treatment, has demonstrated antidepressant efficacy and promise in PTSD research (Markowitz et al., 2015). ○ In a randomized, 14-week trial comparing IPT, prolonged exposure, and relaxation therapy in the treatment of patients (n=110) with severe, chronic PTSD, researchers found that IPT demonstrated that it was not inferior to exposure therapy, the "gold standard" PTSD treatment. Finding that ITP had higher response rates than prolonged exposure, researchers **suggested** that "PTSD treatment may not require cognitive behavioral exposure to trauma reminders" and "patients with comorbid major depression may fare better in Interpersonal Psychotherapy than Prolonged Exposure" (Markowitz et al., 2015, p. 2). ○ Roy-Byrne noted, "The results of this trial add a new, non-CBT treatment armamentarium, showing that there is not 'one royal road to PTSD response' " (Roy-Byrne, 2015, p.404). He pointed out a distinct advantage of IPT: how it focuses on and addresses a patient's emotional and interpersonal life. ❖ Eye Movement Desensitization and Reprocessing (EMDR) ○ EMDR has been found to be about as effective as other modalities for reducing symptoms of PTSD, although various studies have concluded that EMDR is more effective, less effective, and about the same as no treatment and as other treatments for PTSD. ○ APA Guideline Watch (March 2009) reported the results of small studies of EMDR and indicated that brief EMDR in sexual assault victims and witnesses to vehicular accidents may be efficacious for these groups but that these findings	Agency for Healthcare Research and Quality (AHRQ) 2013. Psychological and pharmacological treatments for adults with posttraumatic stress disorder (PTSD).

Psychotherapy Treatments

Recommendations	Recommended Resources
cannot be generalized to combat veterans (APA, 2009). o EMDR may provide relief earlier than other modalities, and may be tolerated better than ET by some patients. A contribution by the eye or other physical movements to the treatment effect has not been proven (VA/DOD, 2010). o EMDR is used with caution in patients with a history of dissociative disorder. It can be very helpful for the treatment of PTSD with dissociation symptoms by providers well trained in both EMDR and the treatment of dissociative disorder and using especially modified protocols for EMDR (International Society for the Study of Trauma and Dissociation, 2011). o A recent study explored the impact of avoidant coping on treatment response in women with rape-related PTSD (n=62), finding that higher levels of avoidance coping before treatment was associated with less severe PTSD following EMDR and prolonged exposure treatment (Leiner et al., 2012). o A recent systematic review and meta-analysis found low strength of evidence of EMDR for reducing PTSD symptoms due to some inconsistency and imprecision. However, moderate evidence in achieving loss of PTSD diagnosis as well as for improving depression symptoms was found for EMDR. Compared with subjects in wait-list control groups, 64% more subjects treated with EMDR experienced this outcome (Cusack et al., 2015). ❖ Stress Inoculation Training (SIT) o SIT is a form of CBT that has been shown to be effective in treating PTSD related to sexual assault, but has been less successful in treating combat veterans. o Trials comparing SIT with a form of ET showed that ET was superior to SIT in the long-term, although they were equally effective in the short-term. o SIT is a set of techniques that emphasizes adopting skills to reduce fear and anxiety through progressive muscle relaxation, deep abdominal breathing, positive self-talk, assertiveness and role playing (VA/DOD, 2010). ❖ Imagery Rehearsal Therapy (IRT) o IRT has been shown to reduce chronic nightmares associated with PTSD, improve sleep quality and decrease PTSD symptom severity in victims of crime and sexual assault, and in combat veterans, although no randomized controlled trials have been done (VA/DOD, 2011). o In IRT, patients use imagery to master the threatening content of nightmares to change the meaning, importance and effect of the nightmare. It deemphasizes exposure by minimizing direct discussion of the trauma-related content in favor of nightmare content (VA/DOD, 2011. ❖ Psychodynamic Therapies (PT) o PT may be especially useful for treatment of PTSD in patients who experienced childhood sexual abuse (VA/DOD, 2011. o Few controlled studies on the use of PT for PTSD exist, with most data coming from case reports (VA/DOD, 2011. o APA Guideline Watch (March 2009) argued that although controlled studies of psychodynamic psychotherapy are lacking, clinical consensus reflects the idea that a psychodynamic approach is useful in helping the patient integrate past	

Recommendations	Recommended Resources
traumatic experience(s) into a more adaptive or constructive schema of risk, safety, prevention and protection; thereby, reducing core symptoms of PTSD (APA, 2009). ○ In one randomized controlled trial, psychodynamic psychotherapy was compared with hypnotherapy, desensitization and wait list control; patients in all three treatment groups improved compared with controls with comparable reduction in intrusive symptoms and avoidance, and PT group patients showed improved coping ability and greater self-esteem (VA/DOD, 2010). ○ One form of PT for PTSD emphasizes the effect of the traumatic experience on the patient's experiences, self-esteem, experiences of safety and loss of self-cohesiveness. Another form of PT for PTSD emphasizes coping skills and defenses, and explores the meaning of the trauma in the context of existing psychological conflicts and developmental factors (APA, 2004). ❖ Other Psychotherapies ○ APA Guideline Watch (March 2009) reported published studies of other types of psychotherapy including group therapy, coping skills therapy, eclectic psychotherapy, psychodynamic psychotherapy, cognitive restructuring and brainwave neurofeedback. The Guideline Watch noted that the utility and generalizability of conclusions are limited by methodological issues (APA, 2009). ❖ Virtual Reality Exposure Therapy (VRET) ○ Magellan Healthcare Technology Assessment Report: ***Virtual Reality Exposure Therapy (VRE or VRET) for the Treatment of Post-traumatic stress disorder (PTSD), Specific Phobia, Social Phobia and Panic Disorder with Agoraphobia*** reviewed various published studies that examined the effects of VRE on active duty service members and veterans suffering from war-related PTSD. One small study (n=20) showed that patients receiving virtual reality-graded exposure therapy had greater improvement in PTSD symptoms after 10 weeks of treatment than those receiving treatment as usual. Two other studies found that relative to their pretreatment self-reported symptoms of PTSD, patients treated with VRE reported a significant reduction at posttreatment. Magellan determined that VRE is an investigational procedure showing potential in the treatment of PTSD for war combat veterans, but it remains an investigational procedure until the results of large randomized clinical trials are published. It also remains investigational as treatment for PTSD rape victims (Magellan Healthcare Technology Assessment, 2013). ❖ Psychological First Aid (A Preventative Approach) ○ APA Guideline Watch (March 2009) acknowledged that this modality is supported by considerable empirical evidence, but notes that questions remain regarding how this public health intervention should be delivered, i.e., type of format and responder. The Guideline Watch categorized this modality as *evidence-informed* rather than *evidence-based* (APA, 2009). A framework for implementing psychological first aid within high-risk organizational settings, e.g., hospital trauma centers, was proposed in a recent article that **suggested** that randomized controlled trials in these settings can be used to establish the	

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS **Psychotherapy Treatments**	
Recommendations	**Recommended Resources**
value of the components of psychological first aid (Forbes et al., 2011). ❖ Staged Approach to Treatment of Complex PTSD ○ The DSM-5 does not include a new diagnostic category for complex PTSD, which usually results from repetitive and chronic interpersonal trauma over the lifetime, most often, but not limited, to developmental trauma beginning in childhood. Complex PTSD is viewed as a subset of PTSD, not a separate disorder; some cases of the "with dissociative symptoms" subtype of PTSD fall in this subset. Severe recurrent trauma may be experienced by victims of ongoing childhood abuse and by victims of genocide campaigns. Treatment for patients with complex PTSD usually requires a somewhat different approach to be addressed in forthcoming guidelines. Treatment for these patients tends to be quite challenging, and usually requires a staged approach to treatment, with an early emphasis on developing the grounding, safety and internal containment skills necessary to tolerate re-experiencing the trauma. It is important for the clinician to understand the nature of the posttraumatic disorders with which individuals present and to ensure that the clinician has the proper training and experience to provide appropriate treatment (American Psychological Association and International Society for the Study of Trauma and Dissociation, 2014).	

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS **Complementary and Alternative Treatment**	
Recommendations	**Recommended Resources**
Complementary and Alternative Medicine (CAM) in VA PTSD programs is widespread; CAM treatments include progressive muscle relaxation therapy, stress management relaxation therapy, art therapy, tai chi, biofeedback, music therapy, yoga, meditation, mindfulness-based stress reduction, and guided imagery. Researchers **suggested** the widespread use of CAM treatment in VA PTSD programs provides an excellent opportunity to determine the impact of the treatments on their efficacy as well as to develop ways to tailor treatments to veterans with PTSD (Libby et al., 2012). ❖ Acupuncture ○ A recent pilot trial indicated that acupuncture provided similar treatment effects as CBT in reducing symptoms of PTSD, anxiety and impairment in people diagnosed with DSM-IV PTSD. Effects of both treatments were maintained for three months. Study researchers note that interpretations from their findings be viewed with cautious optimism and that acupuncture should not be recommended as a treatment of PTSD unless further corroborative and more definitive data become available (Hollifield et al., 2007). ❖ Yoga ○ A major initiative of the Department of Veterans Affairs strategic plan is to	

Recommendations	Recommended Resources
explore innovative treatment approaches for the treatment of PTSD. In a study using a yoga intervention, the feasibility of this intervention in an outpatient VA PTSD population was tested along with the acceptability of this therapy to this population of veterans. Results showed that the yoga program may be effective in improving hyperarousal symptoms of PTSD as well as some elements of sleep quality (Staples et al., 2013). ❖ Targeted Sleep Treatments ○ Literature suggests that sleep disturbances, i.e., disturbed REM or non-REM sleep, can contribute to trauma responses leading to poor psychiatric outcomes following trauma exposure. Reviewing the literature, researchers **suggested** that effective pharmacological and behavioral treatments which enhance sleep consolidation in the early aftermath following trauma exposure may affect the efficacy of first-line PTSD treatments, accelerating recovery from trauma exposure and PTSD (Germain, 2013). ❖ Mindfulness-Based Stress Reduction for Posttraumatic Stress Disorder Among Veterans ○ A randomized clinical trial compared mindfulness-based stress reduction therapy with present-centered group therapy in veterans (n=116) with PTSD. Mindfulness-based stress reduction therapy included eight weekly 2.5-hour group sessions and a retreat lasting one day (Polusny et al., 2015). The treatment's focus was on teaching patients to deal with the present moment nonjudgmentally. Present-centered group therapy consisted of nine weekly 1.5-hour group sessions focusing on current life problems. Patients in the mindfulness-based stress reduction therapy group showed greater (although modest) self-reported improvement in PTSD symptom severity during treatment than those in the present-centered group therapy.	

Pharmacotherapy Treatments

Recommendations	Recommended Resources
When beginning treatment of PTSD, initial interventions should include education about the disorder, common symptoms, and the range of available and effective treatments, both pharmacologic and non-pharmacologic, and elicitation of patient preferences. Initial choice of pharmacological, psychotherapeutic or combined treatment depends on clinician and patient choice in light of the manifesting symptoms of PTSD and any other disorders. , since research does not favor any one modality as first-line treatment (APA, 2004; VA/DOD, 2010). Further, there is little definitive evidence to guide the clinician in choosing polypharmacy over monotherapy for amelioration of PTSD symptoms; the choice of polypharmacy can be made in light of clinical presentation and symptoms of co-occurring psychiatric disorders (VA/DOD, 2010). In a recent systematic review and meta-analysis of pharmacotherapy for PTSD, researchers discussed how previous meta-analyses have not been consistent regarding pharmacological treatment of PTSD (Hoskins et al., 2015). Only paroxetine, mirtazapine, amitriptyline and phenelzine were noted as significantly superior to placebo in the National Institute for Health and Care Excellence (NICE) guidelines, while all were recommended only as second-line treatment after trauma-focused psychological treatment. The recommendation that pharmacological interventions should not be preferred to trauma-focused psychological treatment came also from the guidelines of the Australian Centre for Posttraumatic Mental Health (ACPMH). The APA guidelines as well as the guidelines from the International Society for Traumatic Stress Studies have been more positive about pharmacological treatment while the Institute of Medicine was unable to find evidence determining the efficacy of pharmacological treatment for PTSD. Comparisons are difficult due to the difference in methodological quality between the studies. The World Health Organization (WHO) commissioned the update of the results of published systematic reviews (NICE, ACPMH, and Cochrane Collaboration) which are presented in this recent systematic review and meta-analysis (Hoskins et al., 2015). Studies (n=51) selected for the Hoskins review referred to above included those with “no restriction on the basis on onset, duration or severity of PTSD symptoms, or on the presence of comorbid disorders, trauma type, age or gender of participants” (Hoskins, p. 93). Outcome measures included clinician-administered continuous measures of symptom severity, e.g., Clinician Administered PTSD Scale. Considered separately were self-rated PTSD symptom scales. Included in this review were 51 studies, of which 31 assessed serotonergic agents - SSRIs (sertraline, fluoxetine, paroxetine, citalopram, escitalopram, and fluvoxamine). In the meta-analysis of reduction in severity of any PTSD symptom for SSRIs (when grouped together) versus placebo, there was a small positive effect with SSRIs. Comparison of individual SSRIs to placebo found two drugs were significantly superior to placebo in the reduction in severity of PTSD symptoms: paroxetine and fluoxetine. A serotonergic-noradrenergic agent (SNRI), venlafaxine, was also superior to placebo in reducing the severity of PTSD symptoms. The meta-analysis found no evidence for the following drugs versus placebo: brofaromine, olanzapine, sertraline or topiramate. In single randomized controlled trials, four drugs showed superiority over placebo: amitriptyline, GR205171 (neurokinin- 1 antagonist), mirtazapine, and phenelzine, while the following agents did not: alprazolam, citalopram, desipramine, escitalopram, imipramine, lamotrigine, nefazadone, risperidone, tiagabine, and valproate semisodium. Authors noted that evidence from the review does not consider drug or placebo combined with	VA/DoD *Clinical Practice for Management of Post-Traumatic Stress Guideline Summary 2010*

Recommendations	Recommended Resources
psychological treatment, as the review considers only drug monotherapy (Hoskins et al., 2015). Authors in the study above (Hoskins et al., 2015) noted that when comparing pharmacological treatments for PTSD with placebo, the effect sizes were low and inferior to those reported for psychological treatments with a trauma focus over treatment as usual controls. They cited a WHO development group that recommended antidepressants as a second line of treatment of PTSD after unsuccessful psychological treatment. Authors also reported that the most recent Australian guidelines "concluded that pharmacological interventions should not be preferentially used as a routine first treatment of PTSD over trauma-focused psychological treatments" (Hoskins et al., p. 96). The World Health Organization's guidelines recommend that selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) should not be offered as the first choice of treatment for PTSD in adults. They indicated that SSRIs and TCAs be considered when stress management, CBT with a trauma focus, and EMDR have either failed or are not available. They also indicated their use in the presence of co-morbid moderate – severe depression (WHO, 2013).	World Health Organization. Guidelines for the management of conditions specifically related to stress 2013
First Tier ❖ **Serotonergic Agents (SSRIs):** o The FDA has approved two medications, sertraline and paroxetine, for treating adults with PTSD. In four large FDA trials, these two drugs showed only moderate effect sizes (NIMH, 2015). o SSRIs have been widely recommended as first-line agents with clearly demonstrated efficacy in reducing PTSD global symptoms, as well as re-experiencing, avoidance/numbing and hyperarousal (APA, 2004; VA/DOD, 2010). o APA Guideline Watch (March 2009) indicated that more recent research suggests that SSRIs may no longer be recommended with the same level of confidence for veterans with combat-related PTSD as for patients with non-combat related PTSD (APA,2009). APA Guideline Watch (March 2009) noted that further research is needed to answer why combat-related vs. non-combat-related populations have been shown to have differential responses to SSRI treatment (APA, 2009). There are limited data supporting the use of SSRIs in the treatment of children and adolescents with PTSD. Two studies on the use of sertraline alone or adjunctively with trauma-focused CBT compared to placebo did not show resultant differences in primary outcomes (Strawn et al., 2010). o Patients with PTSD may have delayed response, with some not responding to an adequate trial until after the initial 12 weeks, so at least 12 weeks are recommended before changing the regimen (VA/DOD, 2010). o Meta-analytic findings also indicate that continuation of SSRI treatment has a substantial and consistent effect on PTSD and other anxiety disorders in preventing relapse and demonstrated value for use in long term management of PTSD (VA/DOD, 2010; Donavan et al., 2010).	VA/DoD *Clinical Practice for Management of Post-Traumatic Stress Guideline Summary 2010*

Pharmacotherapy Treatments

Recommendations	Recommended Resources

- Meta-analysis of dropout due to side effects among patients treated with SSRIs, TCAs and MAOIs show no differences among groups (VA/DOD, 2010).
- Medication compliance checks are recommended for each contact with the patient:
  - Sertraline 50-200mg/d
  - Paroxetine 20-60mg/d
  - Fluoxetine 20-60mg/d
  - Fluvoxamine 50-150mg/d
  - Citalopram 20-60mg/d
  - Escitalopram 10-29 mg/d (VA/DOD, 2010)
- In a systematic review and meta-analysis of the comparative effectiveness and harms of pharmacological interventions for PTSD, researchers found evidence of moderate strength supporting the efficacy of fluoxetine, paroxetine and sertraline for improving the symptoms of PTSD. There was moderate strength of evidence of the achievement of remission at week 12 in patients treated with paroxetine compared with insufficient evidence from the use of fluoxetine and sertraline (AHRQ, 2013).
- A recent research article examined the occurrence of sudden gains (rapid improvements in symptoms) in sertraline for chronic PTSD in a study where individuals with PTSD (n=200) were randomized to sertraline or 10 weekly sessions of prolonged exposure (PE) treatment. In sertraline and PE the number of patients experiencing sudden gains was similar, i.e., 37.5 percent of individuals and better treatment outcomes were associated with sudden gains. Patients treated with sertraline had larger gains in the first two to four weeks on treatment, whereas those on PE made more gains in the last two weeks of treatment. Patients receiving sertraline exhibited an early, sharp drop in symptoms but a significant minority had a reversal of the gains. Researchers highlighted the need to research prominent within-treatment factors associated with the sudden gains in order to identify how to personalize and enhance treatment (Jun et al., 2013).

❖ **Serotonergic-Noradrenergic Agents (SNRIs)**

- One randomized controlled trial found patients treated with venlafaxine ER (mean maximum daily dose was 221.5 mg/day) showed significantly more improvement in PTSD than placebo for the symptoms of re-experiencing and avoidance/numbing, but not for hyperarousal (Davidson et al., 2006). Another randomized controlled trial found that remission rates were significantly greater with venlafaxine ER (37.5 – 300 mg/d) than with sertraline (25-200 mg/d) at weeks four and six of a 12-week course (Davidson et al., 2006).
- In a trial comparing the efficacy of venlafaxine extended release (ER), sertraline and placebo in patients with PTSD, no significant difference was found between venlafaxine ER (37.5-300 mg/d) and sertraline (25-200 mg/d) in effectiveness for improvements of PTSD symptoms (AHRQ, 2013).

Second Tier

❖ **Tricyclic Antidepressants (TCAs)**

Pharmacotherapy Treatments

Recommendations	Recommended Resources

- Among TCAs, nortriptyline (VA/DOD, 2010), amitriptyline (APA, 2004) and imipramine (APA, 2004) have published evidence that supports efficacy for PTSD, but also other TCAs are used. Therapeutic blood levels have not been established in the treatment of PTSD (VA/DOD, 2010).
- Meta-analysis of dropout due to side effects among patients treated with SSRIs, TCAs and MAOIs show no differences among groups (VA/DOD, 2010).
- Medication compliance checks are recommended (per Veterans Administration / Department of Defense dose guidelines (Sareen et al., 2007) for each contact with the patient:
  - Nortriptyline 50-150mg/d
  - Amitriptyline 150-300mg/d
  - Imipramine 150-300mg/d
  - Desipramine 100-300mg/d
  - Protriptyline 30-60mg/d
  - Clomipramine 150-250mg/d (VA/DOD, 2010).

❖ **Monoamine Oxidase Inhibitors (MAOIs)**

- Among MAOIs, there are data to suggest efficacy of phenelzine, moclobemide and brofaromine (the latter two are not approved for use in the United States) (APA,2004).
- In one study (n=60) on male combat veterans, phenelzine was found to be superior to the TCA Imipramine in reducing symptoms as measured on a self-report instrument (APA, 2004).
- Meta-analyses of dropout due to side effects among patients treated with SSRIs, TCAs and MAOIs show no differences among groups (VA/DOD, 2010).
- Medication compliance checks are recommended for each contact with the patient:
  - Phenelzine 45-75 mg/d in divided doses
  - Tranylcypromine 10-60 mg/d
  - Moclobemide (not currently available in the U.S.) (VA/DOD, 2010; (APA, 2004.

❖ APA Guideline Watch (March 2009) summarized findings from studies that have been published since the 2004 APA Guideline, i.e., comparing nefazodone and sertraline, venlafaxine and sertraline, the SNRI reboxetine and fluvoxamine, and fluoxetine, moclobemide and tianeptine. The Guideline Watch concluded that these studies have generally demonstrated the superiority of antidepressants to placebo, but have done little to clarify the relative utility of these different antidepressants (APA, 2009). The VA/DoD guideline considers both mirtazapine and nefazodone as second tier agents (along with TCAs and MAOIs) that may be used as monotherapy in PTSD (VA/DOD, 2010).

❖ **Sympatholytics / alpha-adrenergic antagonists / beta-adrenergic blockers**

- The APA Guideline Watch (March 2009) noted that use of the alpha-adrenergic antagonist, prazosin, for the treatment of trauma-related nightmares and sleep disruption is among the most promising advances in the pharmacological treatment of PTSD as demonstrated in placebo-controlled augmentation trials

Recommendations	Recommended Resources
(APA, 2009). ○ The APA Guideline Watch (March 2009) also indicated that prazosin trials allowed patients to continue maintenance medication, including SSRIs, since the primary outcome variables were related to sleep disturbance rather than daytime PTSD symptoms and recommends the following effective dosage range: prazosin 6-10 mg at night (APA, 2009). Further investigation may clarify an optimal dosage and titration for prazosin (VA/DOD, 2010). ○ APA Guideline Watch (March 2009) specified that long-term efficacy of prazosin for this indication has not been established (APA, 2009). ○ A recent randomized controlled pharmacologic trial found that prazosin was effective and significantly superior to placebo for three outcome measures: overall PTSD symptoms, global functions and sleep quality. Trial participants (n=67) were active-duty soldiers and recently discharged Army veterans who had served in the Iraq or Afghanistan conflicts and met the diagnostic criteria for PTSD. They had also been screened and met criteria for the presence of at least two nights per week distressing combat-related nightmares. Although results of this 15-week randomized controlled trial showed that prazosin is effective for combat-related PTSD with trauma-related nightmares, most of the soldiers continued to experience PTSD symptoms, leading the researchers to suggest further studies combining prazosin with effective psychotherapies (Petrie et al., 2013). ○ A later review of seven studies (n=210 subjects) examined the impact of prazosin therapy as an augmenting agent to traditional antidepressant interventions on predominately combat-related PTSD nightmare as a primary outcome. Results showed that prazosin is an "effective off-label option for combat-related PTSD nightmares" (Writer et al., 2014, p. 24). Authors **suggested** future randomized, controlled examination of prazosin. ○ A recent randomized controlled trial that compared guanfacine to placebo in veterans with chronic PTSD showed that the drug had no effect on PTSD symptoms, subjective sleep quality or general mood disturbances. The VA/DoD guideline specifically recommends against the use of guanfacine as monotherapy in the management of PTSD (VA/DOD, 2010; Neylan et al., 2006). ○ APA Guideline Watch (2009) acknowledged the potential role for propranolol from earlier studies but reports new research findings where propranolol compared with gabapentin compared with placebo failed to demonstrate the superiority of either medication over placebo (APA, 2009). Propranolol has been used to reduce stress and levels of recall of distressing memories, which can be intrusive in PTSD. Dosage range: Propranolol10-40mg/d (VA/DOD, 2010). ○ The VA/DoD guideline indicates there is insufficient evidence to recommend a sympatholytic as an adjunctive therapy for PTSD (VA/DOD, 2010). ○ Stellate Ganglion Block (SGB), a common and minimally invasive anesthetic procedure widely used for treating chronic pain, has been reviewed as a new technique in the treatment of PTSD (Lipov, 2015). Lipov cited a study of the first time SGB was performed for PTSD and published (2008), and reported that more than 2000 SGBs have been performed at military hospitals for PTSD, with a published success rate of more than 70%. Clinical changes after the procedure	

Recommendations	Recommended Resources
included not only improved sleep, but also reduction of hypervigilance and reduced reactivity to stimuli. However, SGB is not available to patients with PTSD, as it is an unproven approach and is considered off-label. The author suggests that it is "time to look at the available data and apply SGB to the population most affected by PTSD, the military men and women who service this country so valiantly" (Lipov, 2015). ❖ **Benzodiazepines** ○ Benzodiazepines are not recommended for monotherapy or adjunctive therapy for PTSD/ASD as their utility has not been adequately evaluated and risks may outweigh potential benefits (VA/DOD, 2010). ○ The existing evidence does not support reduction in core symptoms, e.g., syndromal symptoms of avoidance or dissociation, and their usage may actually potentiate the acquisition of fear responses and worsen recovery from trauma (APA, 2004; VA/DOD, 2010). ○ The VA/DoD guideline indicated that benzodiazepine use should be considered relatively contraindicated in combat veterans with PTSD because of the very high co-morbidity of combat-related PTSD with alcohol misuse and substance use disorders and potential problems with tolerance and dependence (APA, 2004; VA/DOD, 2010). ○ Rebound anxiety after five weeks, and exacerbation of PTSD symptoms after discontinuation, have been observed in studies of alprazolam: ➢ Alprazolam 1.5-6mg/d ➢ Clonazepam start 0.25mg *bid,* increase by 0.25mg *q*1-2 days ➢ maximum 20mg/d ➢ Lorazepam 2-4mg/d ➢ Diazepam 10-40mg/d (APA, 2004; VA/DOD, 2010). ❖ **Anticonvulsants** ○ Mood stabilizers/anticonvulsants have shown some ability to treat hyper-arousal, re-experiencing and avoidance/numbing, but the quality of available evidence is not strong enough to support routine use of this class (APA, 2004): ➢ Valproate target 10-15mg/kg/d ➢ Carbamazepine target 400-1600mg ➢ Lamotrigine start 25mg/d x 2 weeks, then 50 mg/*d* x 2 weeks, then 100mg/d x1 week for a maximum dose of 200mg/d ➢ Gabapentin target 300-3600 mg/d ➢ Topiramate target 200-400 mg/d: start with 25-50 mg/d and increase by 15-50 mg/week to a maximum dose or as tolerated (APA, 2004; VA/DOD, 2010). ❖ A Food and Drug Administration (FDA) Alert was issued on 5/6/2013 notifying healthcare professionals and women that the anti-seizure medication valproate and related products, valproic acid and divalproex sodium, are contraindicated and should not be taken by pregnant women as they can cause decreased IQ scores in children whose mothers take them while pregnant (FDA, 2013). ❖ APA Guideline Watch (March 2009) summarized recent clinical trials, i.e., topiramate,	

Recommendations	Recommended Resources

tiagabine and divalproex, compared with placebo, and noted limited efficacy of anticonvulsants despite some promising results in open label studies. The Guideline Watch noted these finding preclude any recommendations for change in practice (APA, 2009).

- The VA/DoD guideline indicates that current existing evidence does not support use of anticonvulsants (tiagabine, topiramate or valproate) as monotherapy or adjunctive therapy for the management of PTSD core symptoms (VA/DOD, 2010).

- **Second generation / atypical antipsychotics**
  - Atypical antipsychotics have not shown robust efficacy as monotherapy and there is insufficient evidence to recommend their routine use (APA, 2004; VA/DOD, 2010).
  - Olanzapine used to augment sertraline reduced PTSD, depressive and sleep-related symptoms in one study (APA, 2004).
  - For patients with co-morbid psychosis, risperidone was used successfully in one small sample (Sareen et al, 2007), but does not appear to affect core PTSD symptoms (APA, 2004).
    - Olanzapine 5-20mg/d
    - Quetiapine 300-800mg/d
    - Risperidone 1-6mg/d (VA/DOD, 2010).
  - APA Guideline Watch (March 2009) summarized more recent research studies and reported encouraging findings for adjunctive treatment with second-generation antipsychotic in patients who have partially responded to an SSRI or an SNRI. The Guideline Watch emphasized monitoring of patients for side effects including weight gain and metabolic changes when using these agents (APA, 2009).
  - The VA/DoD guideline recommends the usage of risperidone, olanzapine or quetiapine as adjunctive treatment to antidepressants, due to their demonstrated efficacy in clinical trials composed primarily of veterans (VA/DoD, 2010).

- **First generation / typical antipsychotics**
  - Chlorpromazine and thioridazine each have one case report of use in PTSD (VA/DOD, 2010). There is insufficient evidence to recommend its routine use.
  - Since publication of the adopted APA guideline, a Food and Drug Administration (FDA) Alert was issued on 6/16/08 notifying healthcare professionals that both conventional and atypical (SGA) antipsychotics are associated with an increased risk of mortality in elderly patients treated for dementia-related psychosis (FDA, 2008).

- **Experimental/Investigational Pharmacological Treatments for PTSD**
  - The effects of pairing reactivation of a trauma memory with an administration of sirolimus, a protein synthesis inhibitor, on the frequency and intensity of PTSD symptoms in male combat veterans (n=51) was examined in a double-blind, placebo-controlled study. Although positive effects did not persist at three months, veterans treated with sirolimus reported significantly fewer and

Recommendations	Recommended Resources
less intense PTSD symptoms at one month posttreatment. Researchers **suggested** further studies to explore whether more than a single administration of sirolimus would be more effective than a single administration (Suris et al., 2013). ○ Another investigational therapy for PTSD was tested in a follow-up study of patients (n=20) with treatment-resistant PTSD that were randomly assigned to psychotherapy combined with 3,4-methylenedioxymethamphetamine (MDMA) in an earlier study. Three and a half years after the earlier study's exit date, researchers reported long-term outcome results showing a sustained benefit over time including decreased PTSD symptoms. Researchers stressed the prominent psychoactive effects of MDMA as well as its effects on blood pressure and pulse rate and acknowledged the challenges in distinguishing the drug effects from the effects of psychotherapy with placebo. They suggest that if further research validates their findings, MDMA-assisted psychotherapy may become important in the treatment of PTSD. Researchers pointed out that none of the participants in the study developed a substance abuse problem with illicit drugs after MDMA-assisted psychotherapy (Mithoefer et al., 2013). ❖ **Individually Based Precision Biotherapies for PTSD and PTSD-Related Conditions** ○ Rasmusson et al. noted a "failure to address individual variability in the complex interacting biological processes that converge on the otherwise relatively uniform PTSD phenotype or that define PTSD endophenotypes or particular PTSD-related medical, psychiatric, and substance abuse comorbidity patterns" (Rasmusson et al., p.8). They **suggested** that new multimodal study designs incorporating rapidly evolving molecular, neuroimaging, psychophysiology, and data analytic strategies aid the development of individually based precision biotherapies for PTSD. Further, they noted that the impact of trauma must be understood at three levels: organic, cellular and molecular (Rasmusson et al., 2015).	

Combined Treatments

Recommendations	Recommended Resources
❖ Combination treatment does not yet have sufficient research evidence to support its use, but clinical consensus supports a combined approach (APA, 2004; VA/DOD, 2010; Hetrick et al., 2010). One rationale is that medication can address symptoms of PTSD that would otherwise reduce the effectiveness of psychotherapy or discourage the patient from continuing any therapy (APA, 2004). ❖ APA Guideline Watch (March 2009) revealed that pilot studies on the neurobiology of the traumatic stress response, emotional learning and impairment of extinction learning, suggest that psychotherapy may be facilitated by the pharmacological agent D-cycloserine (a partial agonist at the N-methyl-D-aspartate [NMDA] receptor). Published clinical trials using d-cycloserine and other pharmacological agents used to enhance psychotherapy in patients with PTSD are needed (APA, 2009). A recent study examining person-level variables affecting response to d-cycloserine augmentation of exposure therapy in patients with PTSD randomized patients (n=67) to exposure therapy augmented with either d-cycloserine or placebo. Results showed that highly conscientious patients and patients with low extraversion showed better outcome with d-cycloserine relative to placebo on symptoms of PTSD. Researchers concluded that since d-cycloserine augmented exposure outcome was related to personality traits, treatment-matching strategies may improve treatment efficacy of exposure therapy for PTSD (De Kleini et al., 2013). ❖ In a double-blind, placebo-controlled clinical trial including Iraq and Afghanistan veterans (n=156), researchers examined the effectiveness of virtual reality exposure augmented with D-cycloserine (50 mg) or alprazolam (0.25 mg), compared with placebo, in reducing PTSD (Rothbaum et al., 2014). This study found no significant difference between D-cycloserine and placebo on the Clinician-Administered PTSD Scale (CAPS) at 3, 6, and 12 months, whereas participants in the alprazolam cohort showed a higher rate of PTSD at post-treatment and three months post-treatment. Finding a significant interaction between learning and treatment condition, researchers **suggested** an association between extinction learning (when operant behavior previously reinforced no longer results in reinforcing consequences) and outcomes only in the D-cycloserine condition. Significant findings included the following: lack of overall support of D-cycloserine enhancement treatment for PTSD symptoms; patients with more between-session learning who received D-cycloserine treatment had enhanced virtual reality outcomes; use of alprazolam during treatment was associated with decreased efficacy of exposure therapy; and D-cycloserine demonstrated benefits on salivary cortisol level and startle response which were sensitive to treatment gains. Researchers concluded that this group of veterans has familiarity with video games, finding virtual reality exposure therapy easier than talk therapy and assisting emotional engagement. **They also cautioned using benzodiazepines in patients with PTSD, as "they seemed to have attenuated overall response in the long term" (Rothbaum et al, p. 7).** ❖ A randomized controlled trial compared prolonged exposure therapy combined with either paroxetine or placebo in the treatment of survivors of the World Trade Center	

Combined Treatments

Recommendations	Recommended Resources
attack (n=37) with terrorism-related PTSD. Improvement in PTSD symptoms, response rate and quality of life were significantly improved in patients receiving prolonged exposure therapy and paroxetine than in those receiving prolonged exposure therapy plus placebo over a 10-week treatment period. No differences were found in patients (n=26) who continued randomized treatment for 12 additional weeks. Researchers **suggested** further study of combined treatment medication and prolonged exposure therapy in larger samples (Schneier et al., 2012). ❖ In patients with co-occurring psychiatric conditions, such as suicidal ideation, depression or anxiety, combination treatment may be advisable for effective and timely improvement in clinical status (APA, 2004). ❖ Problematic patterns of substance use, whether or not meeting the threshold for a substance use disorder, should be addressed early and directly in the treatment plan, since substance use can exacerbate symptoms, complicate pharmacological treatment, reduce effectiveness of psychotherapy, and introduce new threats to well-being and recovery from PTSD. For patients with a substance use disorder, un-remitted PTSD symptoms can trigger relapse to substance use (APA, 2004). A recent study **suggested** that treatment should address both substance abuse and PTSD to reduce the risk of death from all causes, especially for young veterans. In an article exploring issues related to how to address both the trauma symptoms and the misuse of substances, authors referred to research indicating potential for using trauma processing models for some substance-misusing clients early in treatment. Authors **suggested** that when determining whether to treat substance misuse or trauma first, the answer is usually both. Authors discussed the stage-based approach for treating PTSD: 1) establishing safety, 2) remembrance and mourning, and 3) reconnection with ordinary life; they pointed out attention to this process helps establish stability and safety and they addressed substance use as a component of safety (Litt et al., 2013). ❖ Also, in a recent clinical trial, patients diagnosed with both PTSD and alcohol dependence were treated with CBT targeting the alcoholism and either sertraline or placebo for the PTSD symptoms. Results showed that improvements in PTSD had a greater impact on improvement in alcohol dependence than the reciprocal relationship. Improvement in hyperarousal PTSD symptoms, in particular, was related to substantially improved alcohol use severity (Back et al., 2006). ❖ A stepped-care approach, in which either psychotherapy or psychopharmacology is used initially and if, after sufficient trials, acceptable remission has not been achieved, the complimentary strategy is added. This is supported by clinical consensus, although it has not been studied for PTSD (VA/DOD, 2010).	

POSTTRAUMATIC STRESS DISORDER (PTSD) IN ADULTS **Monitor Progress and Address Sub-optimal Recovery**	
Recommendations	**Recommended Resources**
❖ **Treatment-Resistant Cases** ○ Because PTSD is a chronic disorder, patients may need to be on medication indefinitely and assessments for appropriateness of maintenance level treatment are required periodically (VA/DOD, 2010). ○ Treatment compliance may affect outcomes and should be discussed regularly with the patient, including medication side effects, reasons for non-adherence to medication and/or psychotherapy plan, and reasons for continuation of medication regimen (APA, 2009; VA/DOD, 2010). ○ In the natural course of treatment, there may be periods of symptom exacerbation that can discourage the patient and reduce coping and adaptation. Reassurance about the nature of recovery, assistance with symptom management and adjustments in the treatment plan, e.g., increase medication, switch from exposure modality to cognitive therapy, increase frequency of sessions, can be helpful at these points (VA/DOD, 2010). ○ PTSD frequently co-occurs with other psychiatric disorders; clinical outcomes can be negatively affected if the other disorders are un-diagnosed, un-treated or under-treated. Symptoms of co-occurring disorders may emerge and/or diminish, and new co-morbidities may develop during the course of PTSD treatment. Co-morbid symptoms should be reassessed regularly (APA, 2004; APA, 2009). Patients with PTSD may experience serious and/or chronic disruptions in social, occupational and other life domains during the course of treatment that can impact treatment outcomes. ○ Reassessment of psychosocial factors should be made periodically and at times of poor treatment response (VA/DOD, 2010). ❖ **Victims of Terror** ○ A study compared the rehabilitation outcomes of terror victims with multiple traumas to the outcomes of patients with non-terror-related multiple traumas treated in the same facility. Victims of terror spent longer periods in rehabilitation than the non-terror group; however, they regained most activity of daily living function, similar to the non-terror group. In addition, despite the higher rate of PTSD, terror victims succeeded in returning to their previous occupations at a similar rate to that of the non-terror group (Schwartz et al., 2007).	Refer to Magellan's Clinical Practice Guidelines noted in previous sections for clarification of conditions co-occurring with PTSD/ASD.

Acute Stress Disorder in Adults

Table of Recommendations Based on Guideline and Recent Literature Review

ACUTE STRESS DISORDER (ASD) IN ADULTS **General/Assessment**	
Recommendations	**Recommended Resources**
❖ The Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder reported that while early intervention studies for acute stress disorder (ASD) are currently in progress, no major research on the treatment of ASD has been completed since publication of the 2004 Guideline (APA, 2009).	
❖ The Guideline Watch (2009) indicated that factors predicting the development of ASD or posttraumatic stress disorder (PTSD) have still not been established and reported research results findings that ASD was a poorer predictor of getting PTSD than just having PTSD criteria alone in the acute stage (APA, 2009). A review of 22 studies **suggested** that at least half of trauma survivors with ASD meet criteria for subsequent PTSD whereas most individuals with PTSD do not initially have ASD (Bryant, 2003). ASD is a transient stress response sometimes remitting within one month of trauma exposure or it may progress to PTSD after one month. The DSM-5 reported that approximately 50 percent of individuals who eventually develop PTSD initially present with ASD (APA, 2013).	Diagnostic criteria for ASD and PTSD in American Psychiatric Association (2013) *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, DSM-5*[3]
❖ ASD and PTSD are no longer included in the class of anxiety disorders but are instead included in a new class of "trauma and stressor-related disorders." All of the conditions included in the diagnostic criteria require exposure to a traumatic or stressful event, i.e., actual or threatened death, serious injury, or sexual violence. The traumatic event(s) may be experienced directly, witnessed in person as it occurs to others, or learned as it occurred to a close family member or close friend. The exposure may also include "experiencing repeated or extreme exposure to aversive details of the traumatic event(s) (e.g., first responders collecting human remains, police officers repeatedly exposed to details of child abuse) (APA, 2014). Criteria in DSM-IV required fear, helplessness or horror happening right after the trauma; these were removed in DSM-5. Diagnostic criteria for ASD are met when individuals meet nine or more of listed symptoms in five categories: intrusion symptoms, negative mood, dissociative symptoms, avoidance symptoms, and arousal symptoms beginning or worsening after occurrence of the traumatic event(s). The symptoms usually begin immediately following the trauma, but must persist for at least three days and up to a month (APA, 2013).	
❖ The rate of ASD occurring after a small- or large-scale trauma, e.g., physical/sexual assault, accident/fire, combat, terrorism or disaster-related event, is much higher than the rate of PTSD; e.g., as many as 90 percent of individuals who experience sexual assault have symptoms of ASD in the weeks following the event (APA, 2004; VA/DOD, 2010).	
❖ According to the DSM-5, the prevalence of ASD varies in survivors of trauma. ASD is	

Recommendations	Recommended Resources
identified in less than 20 percent of cases following traumatic events without interpersonal assault; 13-21 percent of cases following motor vehicle accidents; 14 percent of cases following mild trauma injury; 19 percent of cases following assault; 10 percent of cases following severe burns; 6-12 percent of cases following industrial accidents; and 20-50 percent of cases following interpersonal trauma events, e.g., assault, rape and witnessing mass shootings (APA, 2013). ❖ Adolescent trauma survivors have high rates of ASD. The Trauma Recovery Project in Adolescents presented findings from a prospective epidemiological study and reported a 40 percent ASD rate in adolescent survivors of serious injuries, e.g., motor vehicle crash, recreational accident: all-terrain vehicle/ skateboard/team sport, bicycle, intentional injuries, falls and pedestrian struck. Rates of ASD were higher in adolescent female patients versus male patients. Perceived threat to life and intentional or violence-related injury were significantly associated with ASD onset (Holbrook et al., 2005). ❖ Research contributions to child trauma theory from meta-analytic findings showed that important predictors of long-term posttraumatic stress in children were: 1) symptoms of acute and short-term posttraumatic stress, 2) depression, 3) anxiety and 4) parental posttraumatic stress. Female gender, injury severity, duration of hospitalization and heart rate shortly after admission to the hospital accounted for small effects. However, age, minority status and socioeconomic status were not significantly related to long-term posttraumatic stress reactions in children (Alisic et al., 2011). ❖ If the traumatic event was very recent, evaluation for Acute Stress Reaction (ASR) may be appropriate. Identification of a patient with ASR is based on observation of behavior and function. There is no evidence to support any specific screening tool (VA/DOD, 2010). ❖ ASR features are considered normal in the sense of affecting most traumatized persons, being socially acceptable, psychologically effective and self-limited. At this stage (less than four days after the trauma exposure), it is important not to portray these reactions as symptoms indicative of a mental disorder (VA/DOD, 2010): o Physical: exhaustion, hyper-arousal, somatic complaints (gastrointestinal, genitourinary, musculoskeletal, cardiovascular, respiratory, nervous system), conversion disorder symptoms, such as the involuntary loss of one or more bodily functions, e.g., blindness, paralysis or the inability to speak, in the absence of a physical cause (Medicine Plus, 2004) o Emotional: anxiety, depression, guilt/hopelessness o Behavioral: avoidance, problematic substance use o Cognitive/mental: amnesic or dissociative symptoms, hyper-vigilance, paranoia, intrusive re-experiencing. ❖ Manifestations of ASR vary. Some want and feel a need to discuss the event, and some have no such need. Respect individual and cultural preferences in the attempt to meet their needs as much as possible. Allow normal recovery and monitor (VA/DoD, 2010).	

ACUTE STRESS DISORDER (ASD) IN ADULTS General/Assessment	
Recommendations	**Recommended Resources**
❖ In the absence of ASR, the assessment for ASD is identical to the assessment for PTSD; see the Magellan adopted guidelines for PTSD.	

ACUTE STRESS DISORDER (ASD) IN ADULTS Patient and Family Education	
Recommendations	**Recommended Resources**
❖ Education should be targeted to both the patient and the family whenever possible, and should address the disorder, common symptoms, and the range of available and effective treatments, both pharmacologic and non-pharmacologic. ❖ Education also should address any co-morbid medical or psychiatric disorders, how co-morbid symptoms may affect core ASD symptoms or be affected by them, and how the treatment plan will be adapted to address comorbidity (VA/DOD, 2010.) ❖ Education includes normalizing patient experiences, reducing anxiety and offering hope that with time and treatment, symptoms can be overcome (VA/DOD, 2010). ❖ If medications are prescribed, education should address the regimen, the effects and side effects, and the importance of adherence even when symptoms begin to abate (APA, 2004). ❖ Education about the positive impact of reducing social isolation and identifying family and/or other social supports is important early in treatment. Assistance also should be provided in identifying appropriate self-help or treatment groups in which peer-to-peer assistance can be obtained, and in identifying strategies for overcoming avoidance in family or other close relationships (Jovanovic et al., 2004).	

ACUTE STRESS DISORDER (ASD) IN ADULTS Supportive Interventions	
Recommendations	**Recommended Resources**
❖ If evidence of ASR is found, the patient may benefit most from supportive interventions (VA/DOD, 2010): o Review / link to support services for basic survival needs and comfort, e.g., liquids, food, shelter, clothing, heat/cooling o Help patients achieve restful and restorative sleep o Preserve an interpersonal safety zone protecting basic personal space, e.g., privacy, quiet, personal effects o Provide non-intrusive ordinary social contact, e.g., a "sounding board,"	

ACUTE STRESS DISORDER (ASD) IN ADULTS **Supportive Interventions**	
Recommendations	**Recommended Resources**
judicious use of humor, small talk about current events, silent companionship ○ Address immediate physical health problems or exacerbations of prior illnesses ○ Assist in locating and verifying the personal safety of separated loved ones or friends; reconnect patients with loved ones, friends, trusted other persons, e.g., work mentors, health care, clergy ○ Help patients take practical steps to resume ordinary day-to-day life. e.g., daily routines or rituals ○ Help patients take practical steps to resolve pressing immediate problems caused by the traumatic event, e.g., loss of a functional vehicle, finance, housing ○ Facilitate resumption of normal family, community, school and work roles ○ Provide opportunities for grieving for losses ○ Help patients reduce problematic tension or anxiety to manageable levels ○ Support patients' helpers through consultation and training about common stress management techniques.	

ACUTE STRESS DISORDER (ASD) IN ADULTS **Psychotherapy Treatments**	
Recommendations	**Recommended Resources**
❖ According to the World Health Organization (WHO), although psychological treatments are used to manage people experiencing the symptoms of acute distress, there is no consensus on the effectiveness of such interventions for acute traumatic stress symptoms (WHO), 2013). ❖ WHO guidelines for the management of conditions specifically related to stress recommend, "Cognitive-behavioral therapy (CBT) with a trauma focus should be considered in adults with acute traumatic stress symptoms associated with significant impairment in daily functioning" (WHO, 2013). ❖ WHO guidelines also note, "On the basis of available evidence, no specific recommendations can be made about stand-alone problem-solving counseling, eye movement desensitization and reprocessing (EMDR), relaxation or psycho-education in the first month for adults with acute traumatic stress symptoms associated with significant impairment in daily functioning after a potentially traumatic event" (WHO, 2013). ❖ Supportive interventions including education of the patient and family, identification of strengths and resources, and use of existing support networks, may be effective in reducing the need for further intervention (APA, 2004). ❖ Cognitive-behavioral therapies, especially those that include exposure therapy components, have shown some effect in speeding recovery and reducing occurrence of	

ACUTE STRESS DISORDER (ASD) IN ADULTS **Psychotherapy Treatments**	
Recommendations	**Recommended Resources**
ASD when administered over a few sessions beginning two to three weeks post-trauma (APA,2004;VA/DOD, 2010). ❖ A meta-analysis of 15 randomized controlled trials of early psychological interventions starting within three months of a traumatic event was conducted. Patients included those with ASD, acute PTSD or sub threshold PTSD. The majority of studies evaluated trauma focused cognitive-behavioral therapy (TF-CBT) against either waiting list or a range of supportive interventions. i.e., supportive counseling, structured writing therapy, TF-CBT without exposure, relaxation) or other psychological modalities. i.e., TF-CBT plus anxiety management, TF-CBT plus hypnosis. Findings showed that TF-CBT had greater treatment effect than waiting list/usual care and supportive counseling at reducing traumatic stress symptoms especially for those who met full diagnosis for ASD and acute PTSD (VA/DOD, 2010). ❖ Single-session psychological debriefings are not recommended since they may increase symptoms and have not been shown effective in preventing subsequent PTSD (APA, 2004; VA/DOD, 2010). ❖ The European Network for Traumatic Stress (TENTS) noted in their guidelines for psychosocial care following disasters that there was a strong consensus against early application of formal intervention universally for all individuals involved in traumatic events (Bisson et al., 2010). Similarly, in terms of PTSD prevention following traumatic events, meta-analytic findings suggest that no psychological intervention (single or multiple sessions) can be recommended for *routine* use and may have an adverse effect on some people (Roberts et al., 2009).	Bisson JI et al. TENTS guideline development of post-disaster psychosocial care guidelines through a Delphi process. *The British Journal of Psychiatry* (2010)

ACUTE STRESS DISORDER (ASD) IN ADULTS **Pharmacological Treatments**	
Recommendations	**Recommended Resources**
❖ According to WHO guidelines, clinicians must rule out concurrent disorders warranting treatment with either antidepressants or benzodiazepines. ❖ The WHO guidelines recommend that "Benzodiazepines and antidepressants should not be offered to adults to reduce acute traumatic stress symptoms associated with significant impairment in daily functioning in the first month after a potentially traumatic event" (WHO, 2013). The guidelines further indicate that pharmacological treatments, especially benzodiazepines, are often prescribed for treating symptoms of acute distress. **They note the lack of consensus on the effectiveness of pharmacological treatments.** ❖ For patients with ASD, there are few studies of pharmacological interventions to guide clinical decision-making, and very limited evidence that any specific pharmacological intervention can reduce likelihood of development of PTSD (APA, 2004; VA/DOD, 2010).	VA/DoD *Clinical Practice for Management of Post-Traumatic Stress Guideline Summary 2010*

ACUTE STRESS DISORDER (ASD) IN ADULTS **Pharmacological Treatments**	
Recommendations	**Recommended Resources**
❖ Pharmacological treatments for PTSD cannot be automatically recommended for use in ASD due to insufficient evidence. However, a trial of medication may be warranted in cases where patients are unable to participate in cognitive-behavioral therapies to relieve targeted specific symptoms associated with the event, e.g., pain, insomnia, depression (Kavan et al., 2012). ❖ Goals of pharmacological treatments are to reduce physical, psychological, and behavioral morbidity associated with acute stress reaction, hasten a return to full functioning, and diminish the likelihood of chronicity (VA/DOD, 2010). ❖ The use of medications for short-term treatment of targeted symptoms may be beneficial (e.g., insomnia) (APA, 2004; VA/DOD, 2010). **First Tier** o Selective Serotonin Reuptake Inhibitors (SSRIs) o Data supporting the use of SSRIs as a treatment for ASD do not exist, but clinical experience and consensus support their use (APA, 2004). o Tricyclic Antidepressants (TCAs) o A single prospective, randomized, double-blind study in pediatric burn patients **suggested** that imipramine was effective in improving symptoms: ➢ Imipramine (Tofranil) 150-300mg/d; up to seven days to target hyper-arousal/panic symptoms (APA, 2004; VA/DOD, 2010). **Second Tier** ❖ Sympatholytics / alpha-adrenergic agonists / beta-adrenergic blockers o A single randomized study using a very small sample demonstrated some benefit of propranolol administered within six hours of a traumatic event for post-event hyperarousal with some indication of reduced development of subsequent PTSD: ➢ Propranolol (Inderal) has been used in single dose for prevention of PTSD. ❖ Benzodiazepines o Benzodiazepines are not recommended for monotherapy or adjunctive therapy for PTSD/ASD as their utility has not been adequately evaluated and risks may outweigh potential benefits (Roberts et al., 2009). o The existing evidence does not support reduction in core symptoms, e.g., syndromal symptoms of avoidance or dissociation, and their usage may actually potentiate the acquisition of fear responses and worsen recovery from trauma (APA, 2004; Roberts et al., 2009). o The VA/DoD guideline indicated that benzodiazepine use should be considered relatively contraindicated in combat veterans with PTSD because of the very high co-morbidity of combat-related PTSD with alcohol misuse and substance use disorders and potential problems with tolerance and dependence (APA, 2004; VA/DOD, 2010).	VA/DoD *Clinical Practice for Management of Post-Traumatic Stress Guideline Summary 2010* VA/DoD *Clinical Practice for Management of Post-Traumatic Stress Guideline Summary 2010*

ACUTE STRESS DISORDER (ASD) IN ADULTS **Combined Treatments**	
Recommendations	**Recommended Resources**
❖ Combination treatment does not have evidence to support its use, but clinical consensus supports the combined approach (APA, 2004). ❖ In patients with co-occurring psychiatric conditions, such as suicidal ideation, depression or anxiety, combination treatment may be advisable for effective and timely improvement in clinical status (APA, 2004; VA,DOD,2010). ❖ Problematic patterns of substance use, whether or not meeting threshold for a substance use disorder, should be addressed early and directly in the treatment plan, since substance use can exacerbate symptoms, complicate pharmacological treatment, reduce effectiveness of psychotherapy and introduce new threats to well-being and recovery from ASD (APA, 2004; VA,DOD,2010).	

ACUTE STRESS DISORDER (ASD) IN ADULTS **Monitor Progress and Address Sub-optimal Recovery**	
Recommendations	**Recommended Resources**
❖ Symptoms of ASD may remit or may persist. If they persist, a diagnosis of PTSD is appropriate, and treatment strategies targeting PTSD core symptoms should be initiated (APA, 2004; VA,DOD,2010). ❖ If symptoms of ASD remit, any associated co-morbidities may persist, and the treatment plan should be adapted accordingly (APA, 2004; VA,DOD,2010).	

Recommended Resources

Magellan Healthcare *Clinical Practice Guideline for Assessing and Managing the Suicidal Patient*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Treatment of Bipolar Disorder*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Major Depressive Disorder*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Obsessive-Compulsive Disorder*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Treatment of Patients with Panic Disorder*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Treatment of Schizophrenia*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Assessment and Treatment of Patients with Substance Use Disorders*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Assessment and Treatment of Patients with Eating Disorders*. www.MagellanHealth.com/provider.

Magellan Healthcare *Clinical Practice Guideline for the Assessment and Treatment of Patients with Generalized Anxiety Disorder*. www.MagellanHealth.com/provider.

Practice Parameter for the Assessment and Treatment of Children and Adolescents with Posttraumatic Stress Disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, Volume 49, Number 4, April 2010.

VA/DoD *Clinical Practice Guideline for Management of Post-Traumatic Stress Guideline Summary 2010.* Online at http://www.healthquality.va.gov/PTSD-full-2010c.pdf.

World Health Organization guidelines for the management of conditions specifically related to stress. Geneva: WHO, 2013.

References

1. Aceto P, Perilli V, Lai C. Sacco T, Ancona P, Gasperin E. Sollazzi L. Update on post-traumatic stress syndrome after anesthesia. *Eur Rev Med Pharmacol Sci* 2013;7:1730-1737.

2. Agency for Healthcare Research and Quality (AHRQ) 2013. Psychological and pharmacological treatments for adults with posttraumatic stress disorder (PTSD). Accessed online on Nov. 4, 2013 at http://www.ncbi.nlm.nih.gov/books/NBK137702/.

3. Alisic E, Jongmans MJ, van Wesel F, Kleber RJ. Building child trauma theory from longitudinal studies: A meta-analysis. *Clinical Psychology Review* 2011; 31:736-747.

4. American Psychiatric Association (2004) Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder. *Am J Psychiatry* 161(11 Supple):3-31.

5. American Psychiatric Association Guideline Watch (March 2009): Practice Guideline for the Treatment of Patients with Acute Stress Disorder and Posttraumatic Stress Disorder.

6. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).

7. American Psychiatric Association. Syllabus and Scientific Proceedings from the 168th Annual Meeting of the American Psychiatric Association 2015; Toronto, Canada.

8. American Psychological Association Division 56 (Trauma Psychology) and the International Society for the Study of Trauma and Dissociation (ISSTD). Treatment of Complex Posttraumatic Stress Disorder in Adults. Executive Summary 2014.

9. Back SE, Brady KT, Sonne SC, Verduin ML. Symptom improvement in co-occurring PTSD and alcohol dependence. *J Nerv Ment Dis* 2006; 194(9):690-6.

10. Başoğlu M, Livanou M, Crnobarić C. Torture vs. other cruel, inhuman, and degrading treatment: is the distinction real or apparent? *Arch Gen Psychiatry* 2007; 64(3):277-85.

11. Bass JK, Annan J, Murray M, Griffiths S, Kaysen D, Griffiths S, Cetinoglu T, Bolton PA. Controlled trial of psychotherapy for Congolese survivors of sexual violence. *New England Journal of Medicine* 2013; 368:2182-2191.

12. Bisson JI, Tavakoly B, Witteveen AB, Ajdukovic D, Hehel L, Johansen VJ, Nordanger D, Garcia FO, Punamaki RL, Schnyder U, Sezgin A, Wittmann L, Olff M. TENTS guidelines: development of post-disaster psychosocial care guidelines through a Delphi process. *The British Journal of Psychiatry* 2010.

13. Boscarino JA, Adams RE. PTSD onset and course following the World Trade Center disaster: findings and Implications for future research. *Soc Psychiatry Psychiatr Epidemiol* 2009; 44(10):887-898.

14. Breslau N, Reboussin BA, Anthony JC, Storr CL. The structure of posttraumatic stress disorder: latent class analysis in 2 community samples. *Arch Gen Psychiatry*. 2005;62(12):1343-51.

15. Bryant RA. Acute stress disorder as a predictor of posttraumatic stress disorder: a systematic review. *J. Clin Psychiatry* 2011; 72(2):233-239.

16. Bryant RA. An update of acute stress disorder. *PTSD Research Quarterly* 2013; 24(1):1050-1835.

17. Chen LP, Murad MH, Paras ML, Colbenson KM, Sattler AL, Goranson EN, Elamin MB, Seime RJ, Shinozaki G, Prokop LJ, Zirakzadeh A. Sexual Abuse and Lifetime Diagnosis of Psychiatric Disorder: Systematic Review and Meta-Analysis. *Mayo Clini Proc*.July 2010; 85(7):618-629.

18. Courtois C. Complex trauma, complex reactions: assessment and treatment. *Psychotherapy: Theory, Research, Practice, Training* 2004; 41(4):412-425.

19. Cusack K, Jonas DE, Forneris CA, Wines C, Sonis J, Middleton JC, Feltner C, Brorwnley KA, Olmsted KR, Greenbelt A, Weil A, Gaynes BN. Psychological treatments for adults with posttraumatic stress disorder: a systematic review and meta-analysis. *Clin Psychol Rev* 2015.

20. Davidson J, Baldwin D, Stein DJ, Kuper E, Benattia I, Ahmed S, Pedersen R, Musgnung J. Treatment of posttraumatic stress disorder with venlafaxine extended release: a 6-month randomized controlled trial. *Arch Gen Psychiatry* 2006; 63(10):1158-65.

21. Davidson J, Rothbaum BO, Tucker P, Asnis G, Benattia I, Musgnung JJ. Venlafaxine extended release in posttraumatic stress disorder: a sertraline- and placebo-controlled study. *J Clin Psychopharmacol* 2006; 26(5):473.

22. Davydow DS, Katon WJ, Zatzick DF. Psychiatric Morbidity and Functional Impairments in Survivors of Burns, Traumatic Injuries, and ICU Stays for Other Critical Illnesses: A Review of the Literature. *Int Rev Psychiatry* 2009;6:531-539.

23. De Kleini RA, Hendriks GH, Smits JA, Broekman TG, van Minnen A. Prescriptive variables for d-dycloserine augmentation of exposure therapy for posttraumatic stress disorder. J Psychiatr Res 2013; pii: S0022-3956(13)00317-8.

24. Donovan MR, Glue P, Kolluri S, Emir B. Comparative efficacy of antidepressants in preventing relapse in anxiety disorder – A meta-analysis. *Journal of Affective Disorders* 2010; 123:9-16.

25. Ehlers A, Hackmann A, Grey N, Wild J, Liness S, Albert I, Deale A, Stott R, Clark DM. A randomized controlled trial of 7-day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. *Am J Psychiatry* 2014; 171:294-304.

26. Forbes D, Lewis V, Varker T, Phelps A, O'Donnell M, Wade DJ, Ruzek JI, Watson P, Bryant R, Creamer M. Psychological first aid following trauma: implementation and evaluation framework for high-risk organizations. *Psychiatry* 2011; 74(3).

27. Frommberger U, Angenendt J, Berger M. Post-traumatic stress disorder-a diagnostic and therapeutic challenge. *Dtsch Arztebi Int* 2014; 111(5): 59-65.

28. Germain A. Sleep disturbances as the hallmark of PTSD: where are we now? *Am J Psychiatry* 2013; 170(4):372-82.

29. Gradus JL, Suvak MK, Wisco BE, Marx BP, Resick PA. Treatment of posttraumatic stress disorder reduces suicidal ideation. Depress Anxiety 2013; 00:1-8.

30. Gray MJ, et al. Enhancing patient satisfaction and increasing treatment compliance: patient education as a fundamental component of PTSD treatment. *Psychiatric Quarterly* 2004; 75(4):32-332.

31. Hetrick SE, Purcell R, Garner B, Parslow R. Combined pharmacotherapy and psychological therapies for posttraumatic stress disorder (PTSD). Cochrane Database of Systematic Reviews 2010; Issue 7.

32. Holbrook TL, Hoyt DB, Coimbra R, Potenza B, Sise M, Anderson JP. High Rates of Acute Stress Disorder Impact Quality-of-Life Outcomes in Injured Adolescents: Mechanism and Gender Predict Acute Stress Disorder Risk. *J Trauma* 2005; 59:1126-1130.

33. Hollifield M, Sinclair-Lian N, Warner TD, Hammerschlag R. Acupuncture for posttraumatic stress disorder: a randomized controlled pilot trial. *J Nerv Ment Dis*. 2007;195(6):504-13.

34. Hoskins M, Pearce J, Bethell A, Dankova L, Barbui C, Toi WA, van Ommeren M, de Jong J, Seedat S, Chen H, Bisson JI. Pharmacotherapy for post-traumatic stress disorder: systematic review and meta-analysis. *Br J Psychiatry* 2015; 206(12): 93-100.

35. International Society for the Study of Trauma and Dissociation (2011): Guidelines for Treating Dissociative Identity Disorder in Adults, Third Revision. J Trauma Dissoc 12:2:115-187.

36. Jacobson IG, Donoho CJ, Crum-Cianflone NF, Maguen S. Longitudinal assessment of gender differences in the development of PTSD among US military personnel deployed in support of the operations in Iraq and Afghanistan. *J Psychiatr Res* 2015; 68: 30-36.

37. Jovanovic AA, et al. Family hardiness and social support as predictors of Post-traumatic Stress Disorder. *Psychiatry, Psychology and Law* 2004; 11(2):263-268.

38. Jun JJ, Zoellner LA, Feeny NC. Sudden gains in prolonged exposure and sertraline for chronic PTSD. *Depress Anxiety* 2013; 30:607-613.

39. Kavan MG, Elsasser GN, Barone EJ. The physician's role in managing acute stress disorder. *Am Fam Physician* 2012; 86(7):643-9.

40. Koenen KC, Hitsman B, Lyons MJ, Niaura R, McCaffery J, Goldberg J, Eisen SA, True W, Tsuang M. A twin registry study of the relationship between posttraumatic stress disorder and nicotine dependence in men. *Arch Gen Psychiatry* 2005; 62(11):1258-65.

41. Krysinska K, Lester D. Post-Traumatic Stress Disorder and Suicide Risk: A Systematic Review. *Archives of Suicide Research* 2010;14:1-23.

42. Leiner AS, Jackson JL, Astin MC, Rothbaum BO. Avoidant coping and treatment outcome in rape-related posttraumatic stress disorder. *J Consult Clin Psychol* 2012;80(2):317-321.

43. Libby DJ, Pilver CR, Desai R. Complementary and alternative medicine in VA specialized PTSD treatment programs. *Psychiatric Services* 2012; 63(11):1134-1136.

44. Lipov E. With war-related posttraumatic stress disorder being resistant to pharmaceuticals, is it time to give stellate ganglion block (SGB) a shot*? J Trauma Treat* 2015; Accessed online on Dec. 2, 2015 at http://www.omicsgroup.org/journals/with-warrelated-post-traumatic-stress-disorder-being-resistant-to-pharmaceuticals-is-it-time-to-give-stellate-ganglion-block-sgb-a-shot-2167-1222-S4-020.php?aid=61076.

45. Litt L. Clinical decision making in the treatment of complex PTSD and substance misuse. *J Clin Psychol* 2013; 69(5).

46. Magellan Healthcare (2014) Clinical Practice Guideline for Assessing and Managing the Suicidal Patient. www.MagellanHealth.com/provider.

47. Magellan Healthcare. Technology Assessment Report: Virtual Reality Exposure Therapy (VRE or VRET). 2013.

48. Markowitz JC, Petkova E, Neria Y, Van Meter PE, Ahao Y, Hembree E, Lovell K, Biyanova T, Marshall R. Is exposure necessary? A randomized clinical trial of interpersonal psychotherapy for PTSD. *Am J Psychiatry* 2015; 172:4330-440.

49. Medline Plus (2004) http://www.nlm.nih.gov/medlineplus/ency/article/000954.htm accessed 01/31/2006.

50. Medscape 2015. PTSD linked to endothelial dysfunction. Accessed online on Dec. 2, 2015 at http://www.medscape.com/viewarticle/846046_print.

51. Medscape , December 4, 2015. Risk of death nearly doubled for Vietnam veterans. Accessed online on Dec. 2, 2015 at http://www.medscape.com/viewarticle/855432?src=wnl_edit_tpal&uac=81928HN.

52. Minassian A, Haihofer AX, Baker DG, Nievergelt CM, Geyer MA, Risbrough VB. Association of predeployment heart rate variability with risk of postdeployment posttraumataic stress disorder in active-duty marines. *JAMA Psychiatry* 2015; 72(10): 979-86.

53. Mithoefer MC, Wagner MT, Mithoefer AT, Jerome L, Martin SF, Yazar-Klosinski B, Michel Y, Brewerton TD, Doblin R. Durability of improvement in post-traumatic stress disorder symptoms and absence of harmful effects or drug dependency after 3,4-methylenedioxymethamphetamine-assisted psychotherapy: a prospective long-term study. *J Psychopharmacol* 2013; 27(1):28-39.

54. Murphy, et al. Readiness to change PTSD symptoms and other problems among veterans participating in a motivation enhancement group. *Behavior Therapist* 2004; 27(2):33-36.

55. National Institute of Mental Health. Post-traumatic Stress Disorder (PTSD). Accessed online on Dec. 2, 2015 at http://www.nimh.nih.gov/health/publications/post-traumatic-stress-disorder-ptsd/index.shtml.

56. Neylan TC, Lenoci M, Samuelson KW, Metzler TJ, Henn-Haase C, Hierholzer RW, Lindley SE, Otte C, Schoenfeld FB, Yesavage JA, Marmar CR. No improvement of posttraumatic stress disorder symptoms with guanfacine treatment *Am J Psychiatry* 2006;163(12):2186-8.

57. Norton PJ, Price EC. Meta-analytic review of adult cognitive-behavioral treatment outcome across the anxiety disorders. *J Nerv Ment Dis* 2007;195(6):521-31.

58. Petrie EC, Gross C, Mayer CL, Freed MC, Engel C, Peskind ER. A trial of prazosin for combat trauma PTSD with nightmares in active-duty soldiers returned from Iraq and Afghanistan. *Am J Psychiatry* 2013; 170:1003-1010.

59. Polusny M, Erbes CR, Thuras P, Moran A, Lamberty GJ, Collins RC, Rodman JL, Lim KO. Mindfulness-based stress reduction for posttraumatic stress disorder among veterans: a randomized clinical trial. *JAMA* 2015; 314(5): 456-465.

60. Powers MB, Halpern JM, Ferenschak MP, Gillihan SJ, Foa EB. A meta-analytic review of prolonged exposure for posttraumatic stress disorder. *Clinical Psychology Review* 2010; 30:625-641.

61. *Psychiatric Times* 2015. When the psychiatrist has PTSD. Accessed online on Dec. 2, 2015 at http://www.psychiatrictimes.com/ptsd/when-psychiatrist-has-ptsd.

62. Rasmusson AM, Abdallah CG. Biomarkers for treatment and diagnosis. *PTSD Research Quarterly* 2015; 26(1): 1050-1835.

63. Roberts NP, Kitchiner NJ, Kenardy J, Bisson J. Multiple session early psychological interventions for the prevention of post-traumatic stress disorder. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art No.: CD006869.

64. Rothbaum BO, Price M, Jovanoic T, Norrholm SD, Dunlop B, Bradley DM, Duncan EJ, Ressler RA. A randomized, double-blind evaluation of D-cycloserine or alprazolam combined with virtual reality exposure therapy for posttraumatic stress disorder in Iraq and Afghanistan war veterans. *Am J Psychiatry* 2014; 171:640=648.

65. Roy-Byrne P. Improving relationships in trauma victims: the case for interpersonal psychotherapy and

PTSD. *AM J Psychiatry* 2015; 172: 403-405.

66. Sareen J, Cox BJ, Afifi TO, Stein MB, Belik SL, Meadows G, Asmundson GJ. Combat and peacekeeping operations in relation to prevalence of mental disorders and perceived need for mental health care: findings from a large representative sample of military personnel. *Arch Gen Psychiatry* 2007; 64(7):843-52.

67. Schneier FR, Neria Y, Pavlicova M, Hembree E, Suh EJ, Amsel L, Marshall RD. Combined prolonged exposure therapy and paroxetine for PTSD related to the World Trade Center attack: a randomized controlled trial. *Am J Psychiatry* 2012;169:80-88.

68. Schnurr PP, Friedman MJ, Engel CC, Foa EB, Shea MT, Chow BK, Resick PA, Thurston V, Orsillo SM, Haug R, Turner C, Bernardy N. Cognitive behavioral therapy for posttraumatic stress disorder in women: a randomized controlled trial. *JAMA* 2007; 297(8):820-30.

69. Schwartz I, Tsenter J, Shochina M, Shiri S, Kedary M, Katz-Leurer M, Meiner Z. Rehabilitation outcomes of terror victims with multiple traumas. *Arch Phys Med Rehab.* 2007; 88(4):440-8.

70. Seal KH, Shi Y, Cohen G, Cohen BE, Maguen S, Krebs EE, Neylan TC. Association of mental health disorders with prescription opioids and high-risk opioid use in US veterans of Iraq and Afghanistan. *JAMA* 2012; 307(9):940-947.

71. Sijbrandij M, Olff M, Reitsma JB, Carlier IV, de Vries MH, Gersons BP. Treatment of acute posttraumatic stress disorder with brief cognitive behavioral therapy: a randomized controlled trial. *Am J Psychiatry;* 164(1):82-90.

72. Smid GE, Mooren TTM, van der Mast RC, Gersons BPR, Kleber RJ. Delayed Posttraumatic Stress Disorder: Systematic Review, Meta-Analysis, and Meta-Regression Analysis of Prospective Studies. J *Clin Psychiatry* 2009; 70:11.

73. Staples JK, Hamilton MF, Uddo M. A yoga program for the symptoms of post-traumatic stress disorder in veterans. *Mil Med* 2013; 178(8):854-60.

74. Stecker T, McHugo G, Xie H, Whyman K, Jones M. RCT of a brief phone-based CBT intervention to improve PTSD treatment utilization by returning service members.

75. Steel Z, Chey T, Silove D, Marnane C, Bryant RA, van Ommeren M. Association of Torture and Other Potentially Traumatic Events With Mental Health Outcomes among Populations Exposed to Mass Conflict and Displacement. *JAMA* 2009; 302(5).

76. Strawn JR, Keeshin BR, DelBello MP, Geracioti TD, Putnam FW. Psychopharmacologic Treatment of Posttraumatic Stress Disorder in Children and Adolescents: A Review. *J Clin Psychiatry* 2010; 71:7.

77. Suris A, Powell C, North CS. Interfering with the reconsolidation of traumatic memory: Sirolimus as a novel agent for treating veterans with posttraumatic stress disorder. *Ann Clin Psychiatry* 2013; 25(1):33-40.

78. U.S. Department of Veterans Affairs: National Center for PTSD. PTSD in children and teens. Accessed online on Nov.18, 2013 at http://www.ptsd.va.gov/professional/newsletters/research-quarterly/v24n1.pdf.

79. VA/DoD Clinical Practice Guideline for Management of Post-Traumatic Stress Guideline Summary 2010.

80. World Health Organization. Guidelines for the management of conditions specifically related to stress. Geneva: WHO, 2013.

81. Writer BW, Meyer EG, Schillerstrom JE. Prazosin for military combat-related PTSD nightmares: a critical review. J Neuropsychiatry Clin Neurosci 2014; 26(1): 24-33.

82. Zohar J, Juven-Wetzler A, Sonnino R, Hamzany SC, Balaban E, Cohen H. New insights into secondary prevention in post-traumatic stress disorder. Dialogues *Clin Neurosci* 2011; 13(3):301-9.