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Literature on *DSM-5* and *ICD-11*

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Although it's been more than a year since the fifth edition of the American Psychiatric Association's (APA) *Diagnostic and Statistical Manual (DSM-5)* has been published, articles regarding the new criteria have been appearing since 2011. This is because, any revisions of the *DSM-IV* criteria for PTSD (whether removal, addition or modification of specific symptoms) had to be supported by strong empirical evidence. As a result, review articles and position papers were undertaken to synthesize all relevant empirical findings in order to guide final decisions regarding the diagnostic criteria. This process was true for all *DSM-5* diagnoses, not just for PTSD (Kupfer, Kuhl, & Regier, 2013) Given the strong empirical approach and the high burden of proof required for changing any diagnostic criterion, the *DSM-5* process was essentially conservative. Therefore, it should come as no surprise, that except for Criterion A2 (which was removed), all 17 *DSM-IV* PTSD criteria were retained although, in some cases, greatly modified. In addition three new symptoms were added. Other major changes in *DSM-5* were: 1) establishing a new *DSM-5* diagnostic category, "Trauma and Stressor-Related Disorders" for PTSD (and acute stress disorder, adjustment disorders, and others) so that PTSD is no longer classified as an anxiety disorder, 2) reconceptualizing PTSD broadly to include posttraumatic anhedonic/dysphoric, externalizing and dissociative clinical presentations along with the original fear-based anxiety disorder, and 3) establishment of preschool and dissociative subtypes.

Temporally overlapping the *DSM-5* process, the World Health Organization has been developing the eleventh edition of its *International Classification of Diseases (ICD-11)*. Although publication of *ICD-11* won't occur until 2015, it looks like the PTSD criteria will be very different than in *DSM-5*. There are a number of reasons for this: 1) *ICD-11* has endorsed a narrow approach that will focus exclusively on PTSD as a stress-induced fear-based anxiety disorder, 2) *ICD-11* has taken a much less conservative approach so that *DSM-5*'s requirement for a large burden of scientific proof to change any *DSM-IV* criterion has not been a guiding principle. As a result, the *ICD-11* revision looks much more drastic than *DSM-5*, and 3) *ICD-11* will include Complex PTSD as a separate diagnosis, whereas *DSM-5* will not.

With this as a background, I believe the best way to structure this guide to the literature is by identifying four different types of articles: 1) literature reviews and position papers that provide the rationale and scientific basis for *DSM-5* criteria, 2) position papers and reviews supporting proposed *ICD-11* revisions, 3) criticisms of *DSM-5*, and 4) research on *DSM-5* and/or *ICD-11* criteria.

Literature Reviews and Position Papers Regarding *DSM-5* Criteria

The following literature reviews are really position papers that were written by members of the *DSM-5* work group as they developed the *DSM-5* criteria. Most were published before *DSM-5* was finalized in 2013, therefore some recommendations in the position papers were not accepted by APA when the *DSM-5* criteria were finalized. The articles are particularly useful for providing the empirical evidence underlying the rationale for proposed revisions to *DSM-IV* criteria. Friedman et al. (2011a) provided the rationale for creating the new trauma and stressor-related disorders category in *DSM-5* (which will also be the case in *ICD-11*). At the time the article was written, there was serious consideration of expanding that category to include dissociative disorders. Because the research is mixed on whether all dissociative disorders are preceded by exposure to an aversive/traumatic event and because there was room within the *DSM-5* metastructure for two separate diagnostic categories, dissociative disorders were eventually classified separately.

Continued on page 2

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Continued from cover

Several articles (Friedman, et al., 2011b; Kilpatrick, 2013) described the empirical data and rationale for the current *DSM-5* PTSD diagnostic criteria with a four factor model replacing *DSM-IV*'s three factor model. Scheeringa and colleagues (2012) provided the empirical data and rationale for the new PTSD preschool subtype for traumatized children six and younger; the diagnostic symptom thresholds have been lowered and subjective symptoms eliminated. Lanius and colleagues (2012) shared the evidence and rationale for inclusion of the new PTSD dissociative subtype that is based on latent class analyses, brain imaging data and a different pattern of treatment responses to current cognitive-behavioral treatments. Initially, it did not appear likely that a dissociative subtype would be accepted for *DSM-5* (See Friedman et al., 2011a). However, newer evidence changed that including findings from 25,018 respondents from 16 countries enrolled in the World Mental Health Survey showing that 14% of PTSD cases met criteria for the dissociative subtype throughout the world and that dissociation was associated with greater symptom severity, role impairment and suicidality (Stein et al., 2013). Readers who are especially interested in the Dissociative Subtype should read the special issue of the *PTSD Research Quarterly* (Volume 24/No. 4) that is devoted entirely to this topic. Finally, Hinton and Lewis-Fernandez (2011) reviewed the cross-cultural applicability and validity of PTSD. In this regard, there was a genuine effort to incorporate cross-cultural symptom expression within all *DSM-5* diagnostic categories, rather than relegating such symptoms to an appendix, as in *DSM-IV*. Friedman (2013) discussed how and why decisions were made that resulted in the final *DSM-5* PTSD criteria.

ICD-11

Because the *ICD-11* process is at least two years behind *DSM-5*, with a projected publication date in 2015, there are only a few available articles to give us a glimpse of what is to come. Three articles lay out the rationale for the narrow approach to PTSD and restriction to six symptoms (Brewin, 2013; Maerker et al., 2013; Maerker & Perkonigg, 2013). This approach can be traced back to an important article by Brewin and colleagues (2009) that clearly influenced the *ICD-11* work group. Another key position paper is that providing the rationale and supporting data from latent profile analysis for inclusion of Complex PTSD in *ICD-11* (Cloitre et al., 2013).

Critiques

A number of critiques exist of *DSM-5*. Galatzer-Levy and Bryant (2013) argued that "one consequence of (the *DSM-5* PTSD symptom) expansion is that it increases the amorphous nature of the classification so that there are now "636,120 ways to have" PTSD. Young and colleagues (2014) took this one step further and argued that when the most common conditions that are comorbid with PTSD are considered (e.g., major depressive disorder, chronic pain, neurocognitive disorder due to traumatic brain injury, alcohol use disorder, somatic symptom disorder and borderline personality disorder) there are "one quintillion ways to have PTSD comorbidity." The *DSM-5* response to this is that PTSD ranked among the three psychiatric disorders with the highest inter-rater reliability in the *DSM-5* field trials, with major depressive disorder showing very low inter-rater reliability (Regier et al., 2013).

Other critiques concerned the stressor criterion, Criterion A. Roberts et al. (2012), using data from 3,013 women enrolled in The Nurses' Health Study, reprised the important question (Brewin et al., 2009) about the utility of Criterion A. Although *DSM-5* attempted to reduce ambiguity about the distinction between "traumatic" and "non-traumatic" events, these articles suggest that what really matters is whether individuals exhibit PTSD symptoms whether or not they were exposed to Criterion A events. Bensimon and colleagues (2013) argued that both *DSM-5* and *ICD-11* suffer from a Euro-American bias that makes Criterion A refer, mostly, to single traumatic incidents rather than to chronic national traumatic stress "where exposure to terror is persistent, constant and of national proportions." Zoellner and colleagues (2011) criticized the removal of PTSD from the anxiety disorders category arguing that there was insufficient evidence to do so and that there is "a compelling evidence base arguing that PTSD is an anxiety disorder." Zoellner et al. (2013) reviewed the forensic implications of the *DSM-5* revisions and argued that by increasing the heterogeneity of individuals receiving the PTSD diagnosis, there will be "continued confusion about what constitutes a traumatic stressor, difficulties with differential diagnosis, increased ease in malingering, and improper linking of symptoms to causes of behavior." Finally, Young (2014) reviewed the research domain criteria (RDoC) as an alternative approach to diagnosis with a specific emphasis on genetic-linked neurobiological endophenotypes underlying phenomenologically-based diagnostic classification schemes such as *DSM-5* and *ICD-11*. Perhaps there will be sufficient evidence to incorporate the RDoC approach into *DSM-6* or *ICD-12*, but we are not at that stage at present. There are other articles criticizing the *DSM-5* approach, in general that are beyond the scope of this review. The *Journal of Traumatic Stress* devoted a lively special section to the *DSM-5* criteria with an initial discussion (Friedman, 2013a) followed by three commentaries (Brewin, 2013; Kilpatrick, 2013; Maerker & Perkonigg, 2013) and a final rebuttal (Friedman, 2013b).

Research on *DSM-5* and/or *ICD-11* Criteria

A big question has been how changes in *DSM-IV* criteria would affect prevalence estimates in *DSM-5*. Kilpatrick and colleagues (2013) reported results from a national sample of almost 3,000 adults recruited from an online panel. Comparing results for different definitions of Criterion A, they found that prevalence estimates for *DSM-5* were slightly lower than *DSM-IV*. The major reasons for differences were tightening of Criterion A for indirect exposure in *DSM-5*; elimination of *DSM-IV*'s A2 Criterion, and the requirement of one avoidance symptom for *DSM-5*. Miller et al. (2013) reporting on the same online civilian sample as well as a convenience sample of U.S. military Veterans found the final *DSM-5* criteria and the *DSM-IV* criteria to yield similar estimates of 16.6% and 16.4%, respectively, for lifetime PTSD. Utilizing confirmatory factor analyses, these authors demonstrated the goodness-of-fit of the four factor *DSM-5* model of PTSD. Item-response theory analyses indicated that psychogenic amnesia (D1) and reckless/self-destructive behavior deviated from other symptoms in their respective symptom cluster. Elhai et al. (2012), reporting on data from college students, found small differences in prevalence estimates between *DSM-IV* and *DSM-5*. Their data also conformed well with the *DSM-5* four factor model.

Finally, correlations with depression were not enhanced, as expected, in *DSM-5*, despite addition of two symptoms in the Negative Mood and Cognitions category. Carmassi and colleagues (2013) found 87% overlap in PTSD diagnosis between *DSM-IV* and *DSM-5* among Armenian high school earthquake survivors. Major reasons for non-overlap were the requirement of at least one avoidance symptom.

Another set of published works have addressed PTSD trajectories, assessment, and its relationship to depression. Santiago et al. (2013) reviewed longitudinal studies published between 1988 and 2010 and found that PTSD due to intentional causes increased over time, whereas non-intentional trauma-related PTSD trajectories decreased over time. Koffel, Polusny, Arbisi & Erber (2012) utilizing pre/post- deployment data from National Guard servicemembers deployed to Iraq, observed that increased anger was most closely associated with PTSD whereas negative expectations and aggressive behaviors were less specific, showing equivalent correlations with depression and substance use.

Two articles have shown good correlations between PTSD's negative mood and cognitions factor and depressive symptoms, especially the non-somatic depression factor (Biehn et al., 2013; Contractor et al., 2014). This is consistent with Koffel et al. (2012) and the general concerns of the *ICD-11* work group regarding the nonspecificity of these symptoms. On the other hand, it is inconsistent with Elhai et al. (2012) who found a negligible change in depression co-morbidity in *DSM-5*.

With the change in diagnostic criteria, it is crucial that PTSD assessment instruments be revised accordingly. Weathers, Marx, Friedman & Schnurr (2014) provide a thoughtful review of how each *DSM-5* PTSD symptom has been translated in the new revision of the Clinician Administered PTSD Scale for *DSM-5* (CAPS-5). They conclude that published and future studies are likely to show "substantial diagnostic correspondence" between *DSM-IV* and *DSM-5* with the latter being "somewhat more conservative" and "restrictive."

Two important papers comparing *DSM-5* with ICD-11 have appeared although others are in various stages of preparation. O'Donnell et al. (2014) compared PTSD prevalence according to *DSM-IV*, *DSM-5*, *ICD-10* and *ICD-11* criteria respectively among 510 randomly selected injury patients assessed 72 months post-trauma. *ICD-11* prevalence, co-morbidity with depression and disability rates were lower than with the other three systems. Although there was great overlap between individuals who met both *DSM-5* and *ICD-11* criteria, a substantial number met criteria for one but not for the other. Similar findings were reported by Stein et al. (2014) from 23,936 respondents from 13 countries included in the World Mental Health Survey. Only one-third of broadly defined cases met criteria in all four classification schemes (e.g., *DSM-IV/5* and *ICD-10/11*) and another third met PTSD criteria in only one of the four systems. The authors concluded that "all four definitions (of PTSD) are providing information on unique clinically significant cases that are omitted from the other systems" so that "any one diagnostic system will overlook many individuals who suffer from clinically significant symptoms including distress and impairment" (page 502).

The controversy about whether complex PTSD is a unique, empirically based diagnosis in its own right has raged for decades. Resick and colleagues (2012) concluded that "available evidence does not support a new diagnostic category at this time. (See also Friedman et al., 2011a; Friedman, 2013a). Based on such reviews of the literature, complex PTSD was not included in *DSM-5* although Sar (2011) provided a thoughtful argument for its adoption as a subtype of *DSM-5* PTSD. On the other hand, *ICD-11* came to a very different conclusion and decided to include Complex PTSD as a unique diagnosis, with the condition that such individuals must first meet PTSD diagnostic criteria (Maerker et al., 2013). Cloitre et al., (2013) utilizing latent profile analysis on 302 treatment seeking individuals, concluded that there is a valid distinction between PTSD and complex PTSD. Wolf et al., (2014) disagreed on the basis of data collected from 2,695 community participants and 323 Veterans. They not only concluded that their results do not support a distinction between PTSD and complex PTSD but that Cloitre and associates would have come to the same conclusion had they utilized a factor mixed model analysis. Finally, Knefel and Lueger-Schuster (2013) reported PTSD prevalence among 229 Austrian adult survivors of childhood abuse with regard to *ICD-10* (53%) and *ICD-11* (17%). When individuals with complex PTSD are included, *ICD-11* prevalence is increased to 38%, indicating that it is "highly relevant for individuals with a complex trauma history."

Final Remarks

It is apparent from this brief review of the new literature on *DSM-5* and *ICD-11* that we have just begun to investigate the scientific and clinical implications of these very different sets of diagnostic criteria which are based on very different conceptualizations of PTSD. These controversies will definitely result in important new research that will advance our scientific understanding of PTSD in order to develop the best treatments for PTSD.

FEATURED ARTICLES

Biehn, T.L., Elhai, J.D., Seligman, L.D., Tamburrino, M., Armour, C., and Forbes, D. (2013). **Underlying dimensions of DSM-5 posttraumatic stress disorder and major depressive disorder symptoms.** *Psychological Injury and Law, 6*, 290-298. doi:10.1007/s12207-013-9177-4 This study examined the relationship between the underlying latent factors of major depression symptoms and *DSM-5* PTSD symptoms (American Psychiatric Association, 2013). A nonclinical sample of 266 participants with a trauma history participated in the study. Confirmatory factor analyses were conducted to evaluate the fit of the *DSM-5* PTSD model and dysphoria model, as well as a depression model comprised of somatic and nonsomatic factors. The *DSM-5* PTSD model demonstrated somewhat better fit over the dysphoria model. Wald tests indicated that PTSD's negative alterations in cognitions and mood factor was more strongly related to depression's nonsomatic factor than its somatic factor. This study furthers a nascent line of research examining the relationship between PTSD and depression factors in order to better understand the nature of the high comorbidity rates between the two disorders. Moreover, this study provides an initial analysis of the new *DSM-5* diagnostic criteria for PTSD.

Brewin, C.R., Lanius, R.A., Novac, A., Schnyder, U., and Galea, S. (2009). **Reformulating PTSD for DSM-V: Life after Criterion A.** *Journal of Traumatic Stress, 22*, 366-373. doi:10.1002/jts.20443 The diagnosis of PTSD has been criticized on numerous grounds, but principally for three reasons (a) the alleged pathologizing of normal events, (b) the inadequacy of Criterion A, and (c) symptom overlap with other disorders. The authors review these problems along with arguments why the diagnosis is nevertheless worth retaining in an amended form. A proposal for *DSM-V* is put forward that involves abolishing Criterion A, narrowing the B criteria to focus on the core phenomena of flashbacks and nightmares, and narrowing the C and D criteria to reduce overlap with other disorders. The potential advantages and disadvantages of this formulation are discussed.

Carmassi, C., Akiskal, H.S., Yong, S.S., Stratta, P., Calderani, E. Massimetti, E., et al. (2013). **Post-traumatic stress disorder in DSM-5: Estimates of prevalence and criteria comparison versus DSM-IV-TR in a non-clinical sample of earthquake survivors.** *Journal of Affective Disorders, 151*, 843-848. doi:10.1016/j.jad.2013.07.020 *Background:* The latest edition of *DSM (DSM-5)* introduced important revisions to PTSD symptomatological criteria, such as a four-factor model and the inclusion of new symptoms. To date, only a few studies have investigated the impact that the proposed *DSM-5* criteria will have on prevalence rates of PTSD. *Methods:* An overall sample of 512 adolescents who survived the L'Aquila 2009 earthquake and were previously investigated for the presence of full and partial PTSD, using *DSM-IV-TR* criteria, were reassessed according to *DSM-5* criteria. All subjects completed the Trauma and Loss Spectrum-Self Report (TALS-SR). *Results:* A *DSM-5* PTSD diagnosis emerged in 39.8% of subjects, with a significant difference between the two sexes ($p<0.001$), and an overall 87.1% consistency with *DSM-IV-TR*. Most of the inconsistent diagnoses that fulfilled *DSM-IV-TR* criteria but not *DSM-5* criteria can be attributed to the subjects not fulfilling the new criterion C (active avoidance). Each *DSM-5* symptom was more highly correlated with its corresponding symptom cluster than with other symptom clusters, but two of the new symptoms showed moderate to weak item-cluster correlations. Among *DSM-5* PTSD cases: 7 (3.4%) endorsed symptom D3; 151 (74%) D4; 28 (13.7%) both D3 and D4; 75 (36.8%) E2. *Limitations:* The use of a self-report instrument; no information on comorbidity; homogeneity of study sample; lack of assessment on functional impairment; the rates of DSM-IV-TR qualified PTSD in the sample was only 37.5%. *Conclusions:* This study provides an inside look at the empirical performance of the *DSM-5* PTSD criteria in a population exposed to a natural disaster, which suggests the need for replication in larger epidemiological samples.

Cloitre, M., Garvert, D.W., Brewin, C.R., Bryant, R.A., and Maercker, A. (2013). **Evidence for proposed ICD-11 PTSD and complex PTSD: A latent profile analysis.** *European Journal of Psychotraumatology, 4,* 1-12. doi:10.3402/ejpt.v4i0.20706 *Background:* The WHO International Classification of Diseases, 11th version (*ICD-11*), has proposed two related diagnoses, PTSD and complex PTSD within the spectrum of trauma and stress-related disorders. *Objective:* To use latent profile analysis (LPA) to determine whether there are classes of individuals that are distinguishable according to the PTSD and complex PTSD symptom profiles and to identify potential differences in the type of stressor and severity of impairment associated with each profile. *Method:* An LPA and related analyses were conducted on 302 individuals who had sought treatment for interpersonal traumas ranging from chronic trauma (e.g., childhood abuse) to single-incident events (e.g., exposure to 9/11 attacks). *Results:* The LPA revealed three classes of individuals: (1) a complex PTSD class defined by elevated PTSD symptoms as well as disturbances in three domains of self-organization: affective dysregulation, negative self-concept, and interpersonal problems; (2) a PTSD class defined by elevated PTSD symptoms but low scores on the three self-organization symptom domains, and (3) a low symptom class defined by low scores on all symptoms and problems. Chronic trauma was more strongly predictive of complex PTSD than PTSD and, conversely, single-event trauma was more strongly predictive of PTSD. In addition, complex PTSD was associated with greater impairment than PTSD. The LPA analysis was completed both with and without individuals with borderline personality disorder (BPD) yielding identical results, suggesting the stability of these classes regardless of BPD comorbidity. *Conclusion:* Preliminary data support the proposed *ICD-11* distinction between PTSD and complex PTSD and support the value of testing the clinical utility of this distinction in field trials. Replication of results is necessary.

Contractor, A.A., Durham, T.A., Brennan, J.A., Armour, C., Wutrick, H.R., Frueh, B.C., et al. (2014). **DSM-5 PTSD's symptom dimensions and relations with major depression's symptom dimensions in a primary care sample.** *Psychiatry Research, 215*, 146-153. doi:10.1016/j.psychres.2013.10.015 Existing literature indicates significant comorbidity between PTSD and major depression. We examined whether PTSD's dysphoria and mood/cognitions factors, conceptualized by the empirically supported four-factor *DSM-5* PTSD models, account for PTSD's inherent relationship with depression. We hypothesized that depression's somatic and non-somatic factors would be more related to PTSD's dysphoria and mood/cognitions factors than other PTSD model factors. Further, we hypothesized that PTSD's arousal would significantly mediate relations between PTSD's dysphoria and somatic/non-somatic depression. Using 181 trauma-exposed primary care patients, confirmatory factor analyses (CFA) indicated a well-fitting *DSM-5* PTSD dysphoria model, *DSM-5* numbing model and two-factor depression model. Both somatic and non-somatic depression factors were more related to PTSD's dysphoria and mood/cognitions factors than to re-experiencing and avoidance factors; non-somatic depression was more related to PTSD's dysphoria than PTSD's arousal factor. PTSD's arousal did not mediate the relationship between PTSD's dysphoria and somatic/non-somatic depression. Implications are discussed.

Elhai, J.D., Miller, M.E., Ford, J.D., Biehn, T.L., Palmieri, P.A., and Frueh, B.C. (2012). **Posttraumatic stress disorder in DSM-5: Estimates of prevalence and symptom structure in a nonclinical sample of college students.** *Journal of Anxiety Disorder, 26*, 58-64. doi:10.1016/j.janxdis.2011.08.013 We empirically investigated recent proposed changes to the PTSD diagnosis for *DSM-5* using a non-clinical sample. A web survey was administered to 585 college students using the Stressful Life Events Screening Questionnaire to assess for trauma exposure but with additions for the proposed traumatic stressor changes in *DSM-5* PTSD.

For the 216 subjects endorsing previous trauma exposure and nominating a worst traumatic event, we administered the original PTSD Symptom Scale based on *DSM-IV* PTSD symptom criteria and an adapted version for *DSM-5* symptoms, and the Center for Epidemiological Studies-Depression Scale. While 67% of participants endorsed at least one traumatic event based on *DSM-IV* PTSD's trauma classification, 59% of participants would meet *DSM-5* PTSD's proposed trauma classification. Estimates of current PTSD prevalence were .4-1.8% points higher for the *DSM-5* (vs. the *DSM-IV*) diagnostic algorithm. The *DSM-5* symptom set fit the data very well based on confirmatory factor analysis, and neither symptom set's factors were more correlated with depression.

Friedman, M.J. (2013a). **Finalizing PTSD in DSM-5: Getting here from there and where to go next.** *Journal of Traumatic Stress, 26*, 548-556. doi:10.1002/jts.21840 The process that resulted in the diagnostic criteria for PTSD in the Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM-5; American Psychiatric Association) was empirically based and rigorous. There was a high threshold for any changes in any *DSM-IV* diagnostic criterion. The process is described in this article. The rationale is presented that led to the creation of the new chapter, "Trauma- and Stressor-Related Disorders," within the *DSM-5* metastructure. Specific issues discussed about the *DSM-5* PTSD criteria themselves include a broad versus narrow PTSD construct, the decisions regarding Criterion A, the evidence supporting other PTSD symptom clusters and specifiers, the addition of the dissociative and preschool subtypes, research on the new criteria from both Internet surveys and the *DSM-5* field trials, the addition of PTSD subtypes, the non-inclusion of complex PTSD, and comparisons between *DSM-5* versus the World Health Association's forthcoming International Classification of Diseases (*ICD-11*) criteria for PTSD. The PTSD construct continues to evolve. In *DSM-5*, it has moved beyond a narrow fear-based anxiety disorder to include dysphoric/anhedonic and externalizing PTSD phenotypes. The dissociative subtype may open the way to a fresh approach to complex PTSD. The preschool subtype incorporates important developmental factors affecting the expression of PTSD in young children. Finally, the very different approaches taken by *DSM-5* and *ICD-11* should have a profound effect on future research and practice.

Friedman, M.J., Resick, P.A., Bryant, R.A., Strain, J., Horowitz, M., and Spiegel, D. (2011a). **Classification of trauma and stressor-related disorders in DSM-5.** *Depression and Anxiety, 28*, 737-749. doi:10.1002/da.20845 This review examines the question of whether there should be a cluster of disorders, including the adjustment disorders (ADs), acute stress disorder (ASD), PTSD, and the dissociative disorders (DDs), in a section devoted to abnormal responses to stress and trauma in the *DSM-5*. Environmental risk factors, including the individual's developmental experience, would thus become a major diagnostic consideration. The relationship of these disorders to one another is examined and also their relationship to other anxiety disorders to determine whether they are better grouped with anxiety disorders or a new specific grouping of trauma and stressor-related disorders. First how stress responses have been classified since *DSM-III* is reviewed. The major focus is on PTSD because it has received the most attention, regarding its proper placement among the psychiatric diagnoses. It is discussed whether PTSD should be considered an anxiety disorder, a stress-induced fear circuitry disorder, an internalizing disorder, or a trauma and stressor-related disorder. Then, ASD, AD, and DD are considered from a similar perspective. Evidence is examined pro and con, and a conclusion is offered recommending inclusion of this cluster of disorders in a section entitled "Trauma and Stressor-Related Disorders." The recommendation to shift ASD and PTSD out of the anxiety disorders section reflects increased recognition of trauma as a precipitant, emphasizing common etiology over common phenomenology. Similar considerations are addressed with regard to AD and DD.

Friedman, M.J., Resick, P.A., Bryant, R.A., and Brewin, C.R. (2011b). **Considering PTSD for DSM-5.** *Depression and Anxiety, 28*, 750-769. doi:10.1002/da.20767 This is a review of the relevant empirical literature concerning the *DSM-IV-TR* diagnostic criteria for PTSD. Most of this work has focused on Criteria A1 and A2, the two components of the A (Stressor) Criterion. With regard to A1, the review considers: (a) whether A1 is etiologically or temporally related to the PTSD symptoms; (b) whether it is possible to distinguish "traumatic" from "non-traumatic" stressors, and (c) whether A1 should be eliminated from *DSM-5*. Empirical literature regarding the utility of the A2 criterion indicates that there is little support for keeping the A2 criterion in *DSM-5*. The B (reexperiencing), C (avoidance/numbing) and D (hyperarousal) criteria are also reviewed. Confirmatory factor analyses suggest that the latent structure of PTSD appears to consist of four distinct symptom clusters rather than the three-cluster structure found in *DSM-IV*. It has also been shown that in addition to the fear-based symptoms emphasized in *DSM-IV*, traumatic exposure is also followed by dysphoric, anhedonic symptoms, aggressive/externalizing symptoms, guilt/shame symptoms, dissociative symptoms, and negative appraisals about oneself and the world. A new set of diagnostic criteria is proposed for *DSM-5* that: (a) attempts to sharpen the A1 criterion, (b) eliminates the A2 criterion, (c) proposes four rather than three symptom clusters, and (d) expands the scope of the B-E criteria beyond a fear-based context. The final sections of this review consider: (a) partial/subsyndromal PTSD, (b) disorders of extreme stress not otherwise specified (DESNOS)/complex PTSD, (c) cross- cultural factors, (d) developmental factors, and (e) subtypes of PTSD.

Hinton, D.E., and Lewis-Fernández, R. (2011). **The cross-cultural validity of posttraumatic stress disorder: Implications for DSM-5.** *Depression and Anxiety, 28*, 783-801. doi:10.1002/da.20753 *Background:* There is considerable debate about the cross-cultural applicability of the PTSD category as currently specified. Concerns include the possible status of PTSD as a Western culture-bound disorder and the validity of individual items and criteria thresholds. This review examines various types of cross-cultural validity of the PTSD criteria as defined in *DSM-IV-TR*, and presents options and preliminary recommendations to be considered for *DSM-5*. *Methods:* Searches were conducted of the mental health literature, particularly since 1994, regarding cultural-, race-, or ethnicity-related factors that might limit the universal applicability of the diagnostic criteria of PTSD in DSM-IV-TR and the possible criteria

for *DSM-5*. *Results:* Substantial evidence of the cross-cultural validity of PTSD was found. However, evidence of cross-cultural variability in certain areas suggests the need for further research: the relative salience of avoidance/numbing symptoms, the role of the interpretation of trauma-caused symptoms in shaping symptomatology, and the prevalence of somatic symptoms. This review also indicates the need to modify certain criteria, such as the items on distressing dreams and on foreshortened future, to increase their cross-cultural applicability. Text additions are suggested to increase the applicability of the manual across cultural contexts: specifying that cultural syndromes-such as those indicated in the *DSM-IV-TR* Glossary-may be a prominent part of the trauma response in certain cultures, and that those syndromes may influence PTSD symptom salience and comorbidity. *Conclusions:* The *DSM-IV-TR* PTSD category demonstrates various types of validity. Criteria modification and textual clarifications are suggested to further improve its cross-cultural applicability.

Kilpatrick, D.G., Resnick, H.S., Milanak, M.E., Miller, M.W., Keyes, K.M., and Friedman, M.J. (2013). **National estimates of exposure to traumatic events and PTSD prevalence using DSM-IV and DSM-5 criteria.** *Journal of Traumatic Stress, 26*, 537-547. doi:10.1002/jts.21848 Prevalence of PTSD defined according to *DSM-5* (2013) and *DSM-IV* (1994) was compared in a national sample of U.S. adults (*N* = 2,953) recruited from an online panel. Exposure to traumatic events, PTSD symptoms, and functional impairment were assessed online using a highly structured, self-administered survey. Traumatic event exposure using *DSM-5* criteria was high (89.7%), and exposure to multiple traumatic event types was the norm. PTSD caseness was determined using Same Event (i.e., all symptom criteria met to the same event type) and Composite Event (i.e., symptom criteria met to a combination of event types) definitions. Lifetime, past-12-month, and past 6-month PTSD prevalence using the Same Event definition for *DSM-5* was 8.3%, 4.7%, and 3.8% respectively. All 6 *DSM-5* prevalence estimates were slightly lower than their *DSM-IV* counterparts, although only 2 of these differences were statistically significant. *DSM-5* PTSD prevalence was higher among women than among men, and prevalence increased with greater traumatic event exposure. Major reasons individuals met *DSM-IV* criteria, but not *DSM-5* criteria were the exclusion of nonaccidental, nonviolent deaths from Criterion A, and the new requirement of at least 1 active avoidance symptom.

Koffel, E., Polusny, M.A., Arbisi, P.A., and Erbes, C.R. (2012). **A preliminary investigation of the new and revised symptoms of posttraumatic stress disorder in DSM-5.** *Depression and Anxiety, 29*, 731-738. doi:10.1002/da.21965 *Background:* Research has shown that PTSD is highly comorbid with other mental disorders. The *DSM-5* marks an opportunity to increase the differential diagnosis of PTSD by emphasizing symptoms that are specific to PTSD and deemphasizing symptoms that are common to many mental disorders. This study analyzes the new and revised PTSD symptom criteria proposed for *DSM-5* by examining their relations with diagnoses and measures of PTSD. In addition, we report the specificity of *DSM-5* symptoms with PTSD compared to depressive disorders and substance use. *Methods:* This study utilized pre- and postdeployment data collected from a sample of 213 National Guard Brigade Combat Team soldiers who were deployed to Iraq. Questionnaire data were collected pre- and postdeployment and interview data were collected postdeployment. Scales to measure the *DSM-5* symptoms were created using structural analyses and were correlated with interview and self-report measures of PTSD, depression, and substance use. *Results:* The *DSM-5* symptom of anger shows the most increase from pre- to postdeployment in participants diagnosed with PTSD. In addition, this scale showed the strongest relation to PTSD and showed some evidence of specificity. Other symptom scales, including those measuring negative expectations and aggressive behaviors, showed equivalent correlations with PTSD, depression, and substance use. *Conclusions:* It will be important to continue studying the specificity of anger with PTSD. Several of the other new and revised *DSM-5* symptoms appear to be nonspecific, and it is unlikely that their inclusion in the diagnostic criteria for PTSD will improve differential diagnosis.

Lanius, R.A., Brand, B., Vermetten, E., Frewen, P.A., and Spiegel, D. (2012). **The dissociative subtype of posttraumatic stress disorder: Rationale, clinical and neurobiological evidence, and implications.** *Depression and Anxiety, 29*, 701-708. doi:10.1002/da.21889 *Background:* Clinical and neurobiological evidence for a dissociative subtype of PTSD has recently been documented. A dissociative subtype of PTSD is being considered for inclusion in the forthcoming *DSM-5* to address the symptoms of depersonalization and derealization found among a subset of patients with PTSD. This article reviews research related to the dissociative subtype including antecedent, concurrent, and predictive validators as well as the rationale for recommending the dissociative subtype. *Methods:* The relevant literature pertaining to the dissociative subtype of PTSD was reviewed. *Results:* Latent class analyses point toward a specific subtype of PTSD consisting of symptoms of depersonalization and derealization in both Veteran and civilian samples of PTSD. Compared to individuals with PTSD, those with the dissociative subtype of PTSD also exhibit a different pattern of neurobiological response to symptom provocation as well as a differential response to current cognitive behavioral treatment designed for PTSD. *Conclusions:* We recommend that consideration be given to adding a dissociative subtype of PTSD in the revision of the *DSM*. This facilitates more accurate analysis of different phenotypes of PTSD, assist in treatment planning that is informed by considering the degree of patients' dissociativity, will improve treatment outcome, and will lead to much-needed research about the prevalence, symptomatology, neurobiology, and treatment of individuals with the dissociative subtype of PTSD.

Miller, M.W., Wolf, E.J., Kilpatrick, D., Resnick, H., Marx, B.P., Holowka, D.W., et al. (2013). **The prevalence and latent structure of proposed DSM-5 posttraumatic stress disorder symptoms in U.S. national and Veteran samples.** *Psychological Trauma: Theory, Research, Practice, and Policy, 5*, 501-512. doi:10.1037/a0029730 The Diagnostic and Statistical Manual, Fourth Edition (*DSM–IV*) is currently undergoing revisions in advance of the next edition, *DSM-5*. The *DSM-5* posttraumatic stress disorder workgroup has proposed numerous changes to the PTSD diagnosis. These include the addition of new symptoms, revision of existing ones, and a new four-cluster organization (Friedman, Resick, Bryant, & Brewin, 2011). We conducted two Internet-based surveys to provide preliminary information about how proposed changes

might impact PTSD prevalence and clarify the latent structure of the new symptom set. We used a newly developed instrument to assess event exposure and lifetime and current *DSM-5* PTSD symptoms among a nationally representative sample of American adults (*N* = 2,953) and a clinical convenience sample of U.S. military Veterans (*N* = 345). Results from both samples indicated that the originally proposed DSM-5 symptom criteria (i.e., requiring 1 B, 1 C, 3 D, and 3 E symptoms) yielded considerably lower PTSD prevalence estimates compared with *DSM–IV* estimates. These estimates were more comparable when the *DSM-5* D and E criteria were relaxed to 2 symptoms each (i.e., the revised proposal). Confirmatory factor analyses (CFA) indicated that the factor structure implied by the four-symptom criteria provided adequate fit to the data in both samples, and a *DSM-5* version of a dysphoria model (Simms, Watson, & Doebbeling, 2002) yielded modest improvement in fit. Item-response theory and CFA analyses indicated that the psychogenic amnesia and new reckless/self-destructive behavior symptom deviated from the others in their respective symptom clusters. Implications for final formulations of *DSM-5* PTSD criteria are discussed.

O'Donnell, M.L., Alkemade, N., Nickerson, A., Creamer, M., McFarlane, A.C., Silove, D., et al. [in press] **Impact of the diagnostic changes to post-traumatic stress disorder for DSM-5 and the proposed changes to ICD-11.** *British Journal of Psychiatry. Background:* There have been changes to the criteria for diagnosing PTSD in *DSM-5* and changes are proposed for *ICD-11*. *Aims:* To investigate the impact of the changes to diagnostic criteria for PTSD in *DSM-5* and the proposed changes in *ICD-11* using a large multisite trauma-exposed sample and structured clinical interviews. *Method:* Randomly selected injury patients admitted to four hospitals were assessed 72 months post trauma (*n* = 510). Structured clinical interviews for PTSD and major depressive episode, as well as self-report measures of disability and quality of life were administered. *Results:* Current prevalence of PTSD under *DSM-5* scoring was not significantly different from *DSM-IV* (6.7% v. 5.9%, z = 0.53, *p* = 0.59). However, the *ICD-11* prevalence was significantly lower than *ICD-10* (3.3% v. 9.0%, *z* = -3.8, *p*<0.001). The PTSD current prevalence was significantly higher for *DSM-5* than *ICD-11* (6.7% v. 3.3%, *z* = 2.5, *p* = 0.01). Using *ICD-11* tended to show lower rates of comorbidity with depression and a slightly lower association with disability. *Conclusions:* The diagnostic systems performed in different ways in terms of current prevalence rates and levels of comorbidity with depression, but on other broad key indicators they were relatively similar. There was overlap between those with PTSD diagnosed by *ICD-11* and *DSM-5* but a substantial portion met one but not the other set of criteria. This represents a challenge for research because the phenotype that is studied may be markedly different according to the diagnostic system used.

Regier, D.A., Narrow, W.E., Clarke, D.E., Kraemer, H.C., Kuramoto, S.J., Kuhl, E.A., et al. (2013). **DSM-5 field trials in the United States and Canada, Part II: Test-retest reliability of selected categorical diagnoses.** *American Journal of Psychiatry, 170*, 59-70. doi:10.1176/appi.ajp.2012.12070999 *Objective:* The *DSM-5* Field Trials were designed to obtain precise (standard error <0.1) estimates of the intraclass kappa as a measure of the degree to which two clinicians could independently agree on the presence or absence of selected *DSM-5* diagnoses when the same patient was interviewed on separate occasions, in clinical settings, and evaluated with usual clinical interview methods. *Method:* Eleven academic centers in the United States and Canada were selected, and each was assigned several target diagnoses frequently treated in that setting. Consecutive patients visiting a site during the study were screened and stratified on the basis of *DSM-IV* diagnoses or symptomatic presentations. Patients were randomly assigned to two clinicians for a diagnostic interview; clinicians were blind to any previous diagnosis. All data were entered directly via an Internet-based software system to a secure central server. Detailed research design and statistical methods are presented in an accompanying article. *Results:* There were a total of 15 adult and eight child/adolescent diagnoses for which adequate sample sizes were obtained to report adequately precise estimates of the intraclass kappa. Overall, five diagnoses were in the very good range (kappa=0.60–0.79), nine in the good range (kappa=0.40–0.59), six in the questionable range (kappa=0.20–0.39), and three in the unacceptable range (kappa values <0.20). Eight diagnoses had insufficient sample sizes to generate precise kappa estimates at any site. *Conclusions:* Most diagnoses adequately tested had good to very good reliability with these representative clinical populations assessed with usual clinical interview methods. Some diagnoses that were revised to encompass a broader spectrum of symptom expression or had a more dimensional approach tested in the good to very good range.

Resick, P.A., Bovin, M.J., Calloway, A.L., Dick, A.M., King, M.W., Mitchell, K.S., et al. (2012). **A critical evaluation of the complex PTSD literature: Implications for DSM-5.** *Journal of Traumatic Stress, 25*, 241-251. doi:10.1002/jts.21699 Complex PTSD has been proposed as a diagnosis for capturing the diverse clusters of symptoms observed in survivors of prolonged trauma that are outside the current definition of PTSD. Introducing a new diagnosis requires a high standard of evidence, including a clear definition of the disorder, reliable and valid assessment measures, support for convergent and discriminant validity, and incremental validity with respect to implications for treatment planning and outcome. In this article, the extant literature on complex PTSD is reviewed within the framework of construct validity to evaluate the proposed diagnosis on these criteria. Although the efforts in support of complex PTSD have brought much needed attention to limitations in the trauma literature, we conclude that available evidence does not support a new diagnostic category at this time. Some directions for future research are suggested.

Scheeringa, M.S., Myers, L., Putnam, F.W., and Zeanah, C.H. (2012). **Diagnosing PTSD in early childhood: An empirical assessment of four approaches.** *Journal of Traumatic Stress, 25*, 359-367. doi:10.1002/jts.21723 Prior studies have argued that *DSM-IV* criteria were insensitive for diagnosing PTSD in young children. Four diagnostic criteria sets were examined in 284 3- to 6-year-old trauma-exposed children. The *DSM-IV* criteria resulted in significantly fewer cases (13%) compared to an alternative algorithm for young children (PTSD-AA, 45%), the proposed *DSM-5* posttraumatic stress in preschool children (44%), and the *DSM-5* criteria with 2 symptoms that are under consideration by the committee (*DSM-5-UC*, 49%). Using *DSM-IV* as the standard, the misclassification rate was 32% for PTSD-AA, 32% for *DSM-5*, and 37% for *DSM-5-UC*. The proposed criteria sets showed high agreement on the presence

(100%), but low agreement on the absence (58-64%) of diagnoses. The misclassified cases were highly symptomatic, *M* = 7 or more symptoms, and functionally impaired, median = 2 domains impaired. The additional symptoms had little impact. Evidence for convergent validation for the proposed diagnoses was shown with elevations on comorbid disorders and Child Behavior Checklist Total scores compared to a control group (*n* = 46). When stratified by age (3-4 years and 5-6 years), diagnoses were still significantly elevated compared to controls. These findings lend support to a developmental subtype for PTSD.

Stein, D.J., Koenen, K.C., Friedman, M.J., Hill, E., McLaughlin, K.A., Petukhova, M., et al. (2012). **Dissociation in posttraumatic stress disorder: Evidence from the world mental health surveys.** *Biological Psychiatry, 73*, 302–312. doi:10.1016/j.biopsych.2012.08.022 *Background:* Although the proposal for a dissociative subtype of PTSD in *DSM-5* is supported by considerable clinical and neurobiological evidence, this evidence comes mostly from referred samples in Western countries. Cross-national population epidemiologic surveys were analyzed to evaluate generalizability of the subtype in more diverse samples. *Methods:* Interviews were administered to 25,018 respondents in 16 countries in the World Health Organization World Mental Health Surveys. The Composite International Diagnostic Interview was used to assess 12-month *DSM-IV* PTSD and other common *DSM-IV* disorders. Items from a checklist of past-month nonspecific psychological distress were used to assess dissociative symptoms of depersonalization and derealization. Differences between PTSD with and without these dissociative symptoms were examined across a variety of domains, including index trauma characteristics, prior trauma history, childhood adversity, sociodemographic characteristics, psychiatric comorbidity, functional impairment, and treatment seeking. *Results:* Dissociative symptoms were present in 14.4% of respondents with 12-month *DSM-IV*/Composite International Diagnostic Interview PTSD and did not differ between high and low/middle income countries. Symptoms of dissociation in PTSD were associated with high counts of re-experiencing symptoms and net of these symptom counts with male sex, childhood onset of PTSD, high exposure to prior (to the onset of PTSD) traumatic events and childhood adversities, prior histories of separation anxiety disorder and specific phobia, severe role impairment, and suicidality. *Conclusion:* These results provide community epidemiologic data documenting the value of the dissociative subtype in distinguishing a meaningful proportion of severe and impairing cases of PTSD that have distinct correlates across a diverse set of countries.

Stein, D.J., McLaughlin, K.A., Koenen, K.C., Atwoli, L., Friedman, M.J., Hill, E.D., et al. (2014). **DSM-5 and ICD-11 definitions of posttraumatic stress disorder: Investigating "narrow" and "broad" approaches.** *Depression and Anxiety, 31*, 494-505. doi:10.1002/da.22279 *Background:* The development of the *DSM-5* and *ICD-11* has led to reconsideration of diagnostic criteria for PTSD. The World Mental Health (WMH) surveys allow investigation of the implications of the changing criteria compared to *DSM-IV* and *ICD-10*. *Methods:* WMH surveys in 13 countries asked respondents to enumerate all their lifetime traumatic events (TEs) and randomly selected one TE per respondent for PTSD assessment. *DSM-IV* and *ICD-10* PTSD were assessed for the 23,936 respondents who reported lifetime TEs in these surveys with the fully structured Composite International Diagnostic Interview (CIDI). *DSM-5* and proposed *ICD-11* criteria were approximated. Associations of the different criteria sets with indicators of clinical severity (distress-impairment, suicidality, comorbid fear-distress disorders, PTSD symptom duration) were examined to investigate the implications of using the different systems. *Results:* A total of 5.6% of respondents met criteria for "broadly defined" PTSD (i.e., full criteria in at least one diagnostic system), with prevalence ranging from 3.0% with *DSM-5* to 4.4% with *ICD-10*. Only one-third of broadly defined cases met criteria in all four systems and another one-third in only one system (narrowly defined cases). Between-system differences in indicators of clinical severity suggest that *ICD-10* criteria are least strict and *DSM-IV* criteria most strict. The more striking result, though, is that significantly elevated indicators of clinical significance were found even for narrowly defined cases for each of the four diagnostic systems. *Conclusions:* These results argue for a broad definition of PTSD defined by any one of the different systems to capture all clinically significant cases of PTSD in future studies.

Weathers, F.W. Marx, B.P., Friedman, M.J., and Schnurr, P.P. (2014). **Posttraumatic stress disorder in DSM-5: New criteria, new measures, and implications for assessment.** *Psychological Injury and Law, 7*, 93-107. doi:10.1007/s12207-014-9191-1 The diagnostic criteria for PTSD were substantially revised for *DSM-5*. This in turn necessitated revision of *DSM*-correspondent assessment measures of PTSD. We describe the various changes to the PTSD diagnostic criteria and the corresponding changes to National Center for PTSD measures. We also discuss the implications of the new criteria for assessment of trauma exposure and PTSD. Although the *DSM-5* version of PTSD departs significantly in some respects from previous versions, we conclude that there is fundamental continuity with the original *DSM-III* conceptualization of PTSD as a chronic, debilitating mental disorder that develops in response to catastrophic life events.

Wolf. E.J., Miller, M.W., Kilpatrick, D., Resnick, H.S., Badour, C.L., Marx, B.P., et al. [in press]. **ICD-11 complex PTSD in US national and Veteran samples: Prevalence and structural associations with PTSD.** *Clinical Psychological Science*. The *ICD-11* is under development and current proposals include major changes to trauma-related psychiatric diagnoses, including a heavily restricted definition of PTSD and the addition of complex PTSD. We aimed to test the postulates of complex PTSD in samples of 2,695 community participants and 323 trauma-exposed military Veterans. Complex PTSD prevalence estimates were 0.6% and 13% in the community and Veteran samples, respectively; one-quarter to one-half of those with PTSD met criteria for complex PTSD. There were no differences in trauma exposure across diagnoses. A factor mixture model with two latent dimensional variables and four latent classes provided the best fit in both samples: classes differed by their level of symptom severity but did not differ as a function of the proposed PTSD vs. complex PTSD diagnoses. These findings should raise concerns about the distinctions between complex PTSD and PTSD proposed for *ICD-11*.

ADDITIONAL CITATIONS

Bensimon, M., Solomon, Z., and Horesh, D. (2013). **The utility of Criterion A under chronic national terror.** *Israeli Journal of Psychiatry and Related Sciences, 50*, 81-83. This is an editorial arguing that both *DSM* and *ICD* "appear to be larger products of the North American and European societies and therefore, may be culturally-biased." The authors argue that both diagnostic systems focus too much on events and fail to incorporate the everyday realities of individuals in nations such as Israel, Afghanistan, and Iraq who are chronically exposed to terrorist attacks and other traumatic events.

Brewin, C.R. (2013). **"I Wouldn't Start From Here"—An alternative perspective on PTSD from the ICD-11: Comment on Friedman.** *Journal of Traumatic Stress, 26*, 557-559. doi:10.1002/jts.21843 This is a commentary in response to Friedman (2013a) that eloquently criticizes the *DSM-5* approach while arguing forcefully for the *ICD-11's* "simple approach to diagnosis that can be used in minimally resourced, non-English-speaking-countries."

Friedman, M.J. (2013b). **PTSD in the DSM-5: Reply to Brewin (2013), Kilpatrick (2013), and Maercker and Perkonigg (2013).** *Journal of Traumatic Stress, 26*, 567–569. doi:10.1002/jts.21847 This is the final article in a special section of the Journal of Traumatic Stress (2013), 548-569. It begins with Friedman (2013a) and is followed by three commentaries, Brewin, 2013; Kilpatrick, 2013; and Maercker and Perkonigg, 2013 (all cited here). This is a reply to these commentaries.

Galatzer-Levy, I.R., and Bryant, R.A. (2013). **636,120 ways to have posttraumatic stress disorder.** *Perspectives on Psychological Science, 8*, 651-662. doi:10.1177/1745691613504115 Using a binomial equation to elucidate possible symptom combinations, the authors demonstrate *DSM-5*'s "high level of symptom profile heterogeneity." Whereas there were 79,794 ways to meet PTSD diagnostic criteria in *DSM-IV*, there are now 636,120 combinations in *DSM-5*. They further argue that this heterogeneity indicates "the limitations of *DSM*-based diagnostic entities for classification in research" and elucidates "inherent flaws that are either specific artifacts from the history of the *DSM* or intrinsic to the underlying logic of the *DSM*'s method of classification."

Kilpatrick, D.G. (2013). **The DSM-5 got PTSD right: Comment on Friedman (2013).** *Journal of Traumatic Stress, 26*, 563–566. doi:10.1002/jts.21844 This is another commentary in response to Friedman (2013a) that strongly argues in favor of the *DSM-5* revisions. Specifically, it states that: 1) placement of PTSD in the new Trauma and Stress-related Disorders category, 2) broadening the PTSD construct, and 3) utilizing the best empirical data, including recent surveys, are all major advances. The author raises concerns about the *ICD-11* approach and suggest that "substantial evidence be required before (its) proposed changes are made."

Knefel, M., and Lueger-Schuster, B. (2013). **An evaluation of ICD-11 PTSD and complex PTSD criteria in a sample of adult survivors of childhood institutional abuse.** *European Journal of Psychotraumatology, 4*, 22608. doi.10.3402/ejpt.v4i0.22608 This article compared "the appropriateness" of *ICD-10* and *ICD-11* with respect to 229 adult survivors of childhood institutional abuse. Prevalence was 52.8% for *ICD-10*; 17% for *ICD-11*; and 38.4% for *ICD-11* + complex PTSD. The prevalence of complex PTSD, alone, was 21.4% with 40.4% women and 15.8% men meeting criteria for complex PTSD. The authors argue that "(complex) PSTD is a highly relevant classification for individuals with complex trauma history."

Kupfer, D.J., Kuhl, E.A., and Regier, D.A. (2013). **DSM-5—The future arrived.** *JAMA, 309*, 1691-1692. doi:10.1001/jama.2013.2298 This brief editorial by the leaders of the DSM-5 process outlines how it differs from the DSM-IV. Among these, the focus on diagnosis and clinical care is emphasized along with special attention to the influence of development, gender and culture on the presentation of disorders.

Maercker, A., Brewin, C.R., Bryant, R.A., Cloitre, M., Reed, G.M., van Ommeren, M., et al. (2013). **Proposals for mental disorders specifically associated with stress in the International Classification of Diseases-11.** *Lancet, 381*, 1683-1685. doi:10.1016/S0140-6736 This brief editorial is written by *ICD-11*'s working group that addresses mental disorder specifically associated with stress. The article outlines major decisions regarding diagnoses included in this category, such as: 1) a separate diagnostic category for stress-related disorders, 2) attention to the distinction between PTSD and normal "adaptive fear reactions" to ongoing trauma (e.g., continuing conflict, forced migration, and natural disasters), 3) the narrow PTSD diagnostic criteria, restricted to two symptoms from each of three "core elements" (e.g., re-experiencing, avoidance, and arousal), 4) inclusion of complex PTSD, 5) inclusion of Prolonged Grief Disorder, 6) inclusion of Adjustment Disorder, 7) identifying Acute Stress Reaction as a normal reaction to an abnormal event, and 8) emphasizing the advantage of *ICD-11* over *DSM-5* because of greater simplicity, greater clinical utility and greater feasibility in "low resource and humanitarian settings."

Maercker, A., and Perkonigg, A. (2013). **Applying an international perspective in defining PTSD and related disorders: Comment on Friedman (2013).** *Journal of Traumatic Stress, 26*, 560-562. doi:10.1002/jts.21852 This is another commentary to Friedman (2013a) that appeared in the special section of the *Journal of Traumatic Stress*. It essentially reiterates the points make by Maecker, et al. (2013) mentioned previously.

Roberts, A.L., Dohrenwend, B.P., Aiello, A.E., Wright, R.J., Maercker, A., Galea, S., et al. (2012). **The stressor criterion for posttraumatic stress disorder does it matter?** *Journal of Clinical Psychiatry, 73*, e264-e270. doi:10.4088/JCP.11m07054 Used data from the 2009 PTSD diagnostic subsample (*n*=3013) of women from the Nurses' Health Study II to investigate the relative importance of traumatic events (as defined both in *DSM-III* and *DSM-IV*) as compared to non-traumatic events (e.g., miscarriage, financial problems, legal difficulties, etc.). The major comparison was between women who met all other PTSD diagnostic criteria whether or not they met Criterion A in either *DSM-III* or *DSM-IV*. The authors found that "sequelae of PTSD did not vary systematically with the type of stressful event that initiated PTSD symptoms" (whether it was traumatic or non-traumatic). The authors conclude, given their finding that events not considered traumatic produced PTSD as consequential as PTSD precipitated by a Criterion A event in either *DSM-III* or *DSM-IV*, that "PTSD may be an aberrantly severe but nonspecific stress response syndrome."

ADDITIONAL CITATIONS *continued*

Santiago, P.N., Ursano, R.J., Gray, C.L., Pynoos, R.S., Spiegel, D., Lewis-Fernandez, R. et al. (2013). **A systematic review of PTSD prevalence and trajectories in DSM-5 defined trauma exposed populations: Intentional and non-intentional traumatic events.** *PLOS One, 8*, e59236. doi:10.1371/journal.pone.0059236 The authors reviewed all longitudinal studies on PTSD published between 1998-2010 with regard to clinical trajectories. In general mean prevalence decreased across all studies from 28.8% (at 1 month) to 17.0% (at 12 months). When traumatic events were categorized as "intentional" (e.g., assault, war) or "non-intentional" (e.g., distress, accidents) the PTSD trajectories diverged with a 12 month increase in PTSD prevalence (11.8% to 23.3%) for intentional trauma as compared with a decrease for non-intentional trauma (30.1% to 14.0%). Among those with PTSD 34.8% remit after 3 months, 39.1% have a chronic course and a small fraction (3.5%) of new PTSD cases appear after three months.

Sar, V. (2011). **Developmental trauma, complex PTSD, and the current proposal of DSM-5.** *European Journal of Psychotraumatology, 2*, 5622. doi:10.3402/ejpt.v2i0.5622 This is a very thoughtful review by and international expert on Dissociative Disorders who participated in the *DSM-5* process. He commends *DSM-5* for setting aside a new category for trauma/stress disorders and argues for inclusion of Dissociative Disorders in that category. He recommends inclusion of a complex PTSD subtype of PTSD in *DSM-5* and expresses concerns that the new Dissociative Subtype may be too narrow because it excludes some of the mood and interpersonal symptoms of complex PTSD. "In fact a broader understanding of dissociation would not only support new empirical research and novel treatment modalities on trauma-related disorders, but it would also facilitate formulation of new theoretical paradigms necessary to provide integrated solutions for conceptual dilemmas of the field." Other topics considered are Borderline Personality Disorder and the clinical expression of developmental trauma.

Young, G. (2014). **PTSD, endophenotypes, the RDoC, and the DSM-5.** *Psychological Injury and Law, 7*, 75-91. doi:10.1007/s12207-014-9187-x This paper examines endophenotypes (e.g., measurable aspects in the pathway between genotype and disease) in relation to the NIMH RDoC and the *DSM-5*. The author proposes "a model for the study of endophenotypes that respects multiple influences on the etiology of psychiatric disorder, including psychosocial, without sacrificing the goal of finding causal links from genes to behavior." He concludes that it is currently premature to seek individual biomarkers for PTSD given the current state of the field, but that we should all keep up to date on the future breakthroughs since research is burgeoning.

Young, G., Lareau, C., and Pierre, B. (2014). **One quintillion ways to have PTSD comorbidity: Recommendations for the disordered DSM-5.** *Psychological Injury and Law, 7*, 61-74. doi:10.1007/s12207-014-9186-y This is an elaboration on Galatzer-Levy and Bryant (2013-see above) which considers the number of the ways to have PTSD and its most common comorbid conditions (e.g., major depressive disorder, chronic pain, neurocognitive disorder due to traumatic brain injury, alcohol use disorder and trauma-related/exacerbated premorbid personality disorder such as borderline personality disorder). They calculate that "over one quintillion combinations are possible." They recommend prioritizing PTSD and comorbidities as primary (e.g., unique marker), secondary (e.g., core essential) and tertiary (e.g., common cross-diagnostic). They assert that such prioritization "might help make the next version of the DSM more clinically useful both to clinicians and to court."

Zoellner, L.A., Bedard-Gilligan, M.A., Jun, J.J., Marks, L.H., and Garcia, N.M. (2013). **The evolving construct of posttraumatic stress disorder (PTSD): DMS-5 criteria changes and legal implications.** *Psychology Injury and the Law, 6*, 277-289. doi:10.1007/s12207-013-9175-6 This editorial considers the forensic implications of the DSM-5criteria. "The changes ... have the potential to increase the heterogeneity of individuals receiving a PTSD diagnosis by altering what qualifies as a traumatic event and by adding symptoms commonly occurring in other disorders ... Legal implications of these changes include continued confusion regarding what constitutes a traumatic stressor, difficulties with different diagnosis, increased ease in malingering, and improper linking of symptoms to causes of behavior."

Zoellner, L.A., Rothbaum, B.O., and Feeny, N.C. (2011). **PTSD not an anxiety disorder? DSM committee proposal turns back the hands of time.** *Depression and Anxiety, 28*, 853-856. doi:10.1002/da.20899 This editorial is strongly critical of the *DSM-5*'s removal of PTSD from the Anxiety Disorder category. Arguments are: 1) fear is a critical construct for the development of PTSD, 2) treating trauma-related fear and avoidance is central to PTSD, 3) a lack of evidence exists for a stressor meta-construct separate from the Anxiety Disorders, and 4) this shift ignores cumulative evidence and moves the field backward.

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Despite the rich history of group treatments for PTSD, there is a surprising lack of methodologically rigorous studies in this domain. We know that at one point, "rap groups" were seen to be the treatment of choice for Vietnam Veterans (Foy et al., 2000) and support groups still play a significant role in many agencies that serve trauma survivors, including Department of Veterans Affairs (VA) settings (Hundt, Robinson, Arney, Stanley, & Cully, 2015). Despite the popularity of support groups for trauma survivors, the group treatment research literature is characterized by open trial (e.g., Ready et al., 2008) or non-randomized designs (e.g., Resick & Schnicke, 1992), which are helpful in the beginning stages of treatment development. However, the number of randomized clinical trials (RCT) is limited. Consequently, there are currently no group treatments for PTSD recognized as evidence-based (e.g., VA & Department of Defense [DoD], 2010). In this article, we will summarize the current knowledge about group treatments for PTSD and highlight areas that deserve greater empirical focus.

Sloan, Feinstein, Gallagher, Beck, and Keane (2013) conducted a meta-analysis of RCTs of group treatment studies for PTSD. Studies were excluded if individual and group components were mixed within a protocol, resulting in 16 studies, with a total of 1,686 participants. Most of these treatments were cognitive behavioral, however, the content of these protocols varied considerably. Group treatment was found to have superior treatment outcome effects relative to wait list (WL). However, no significant differences were observed for cognitive behavioral group interventions relative to other active treatments (e.g., present centered treatment). Moderator analyses revealed smaller effect sizes for males relative to females and military-related and childhood trauma relative to mixed trauma samples. These findings should be interpreted with caution, given the small number of studies. Another important observation is that each of the 16 studies examined a different group treatment.

Since this meta-analysis was published, only a handful of additional RCT group trials for PTSD have been published (e.g., Bass et al., 2013; Castillo et al., 2016; Morland et al., 2014; Resick et al., 2015). Clearly, this is an area ripe for needed study.

Trauma-focused Group Treatment for PTSD

Although the advancement of group treatment for PTSD has been limited by the lack of RCTs, there are a number of protocols that have promise and deserve further investigation. Examining group formats of currently available first-line individual PTSD treatment approaches (VA & DoD, 2010), such as Cognitive Processing Therapy (CPT) and Prolonged Exposure (PE), is one obvious path to pursue. In fact, the first efficacy study of Cognitive Processing Therapy (CPT) used a group format of the treatment (Resick & Schnicke, 1992). Several additional studies have been conducted with CPT administered in group format, with variations including a cognitive only version of CPT, referred to as CPT-cognitive only (CPT-C; Morland et al., 2014; Resick et al., 2015), group CPT-C modified for cultural considerations (Bass et al., 2013), and a combined individual and group format of CPT (Chard, 2005). Most recently, Resick and colleagues investigated the CPT-C group format relative to group present centered therapy (PCT) with a cohort of active duty service men and women diagnosed with military-related PTSD. Both group treatments consisted of 12, 90 minute sessions. Findings indicated significant reductions in PTSD severity for both conditions. A significant reduction was also observed for depression in the CPT-C only. Without inclusion of a no-treatment comparison, it is unknown whether significant reductions in PTSD are the result of treatment or other factors such as the passage of time or nonspecific group support.

Continued on page 2

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Continued from cover

It should be noted that the group format of PCT has been found to be a moderately efficacious treatment in several group trial studies (Classen et al., 2011; Schnurr et al., 2003) and superior to a no treatment comparison condition (Classen et al., 2011). Thus, the limited number of studies using group formats of the first line PTSD treatments, combined with a lack of a no treatment comparison, limits interpretation of the Resick et al. (2015) findings.

Chard (2005) used a different approach to delivering CPT in a group format. In a study of women survivors of childhood sexual assault, Chard adapted the CPT protocol to include 27 sessions of group (17) and individual (9) sessions. Individual sessions were devoted to specifics of the individual event, including the trauma impact statement and trauma narratives. Group sessions were used to reinforce skills and concepts introduced in the individual sessions and to foster social bonds with other group members. Findings indicated significantly greater reductions of PTSD symptoms for the adapted CPT condition relative to a minimal attention (MA) comparison condition. Moreover, treatment gains for the adapted CPT condition were maintained at a one year follow-up. Given the various formats of group CPT that have been investigated, it is unclear at this time which format is the best to pursue for additional development.

Although there is a large literature demonstrating the efficacy and effectiveness of Prolonged Exposure (PE) therapy, there are no current studies investigating a group format of PE. Exposure is thought to be a critical component to effective PTSD treatment (e.g., Institute of Medicine, 2008), so inclusion of exposure within group treatment for PTSD is important. There is debate, however, about whether conducting trauma exposure within the group setting (rather than individually) is problematic, owing to vicarious traumatization of other members. There have been a number of group protocols that have used various approaches to conducting imaginal and/or *in vivo* exposures in the context of treatment. For example, Schnurr et al. (2003) examined the efficacy of a trauma-focused group treatment (TFGT) compared to group PCT for military-related PTSD. Both treatment conditions involved 30 weekly sessions lasting 90 minutes, although sessions that included exposure lasted two hours. Imaginal exposure was conducted within the group by Veterans taking turns recounting their trauma event while other members listened. Each Veteran had two sessions devoted to recounting their trauma event, with imaginal exposure sessions starting in session 9 through session 22. *In vivo* exposure was not included in the protocol. The time needed to conduct imaginal exposure within the group for each group member was extensive and may reduce the potential cost-effectiveness of the group format. Schnurr et al. attempted to make up for the limited time for in-session exposure through daily homework utilizing audiotapes. Findings indicated both groups had significant reductions in PTSD symptoms, with no between treatment differences. Significant between treatment differences were only observed for participants who completed treatment, with significantly greater reductions in TFGT relative to group PCT. Notably, treatment dropout was substantially higher in the TFGT (23%) relative to group PCT (9%). Although information was not collected regarding reasons for dropout, participants may have found exposures conducted in-session difficult to tolerate.

Ready and colleagues (2008) also conducted exposure in-session by adapting the approach used by Schnurr et al. (2003). In an open trial, these investigators examined the efficacy of group based exposure therapy (GBET) among 102 Veterans. The group protocol consisted of 3 hours of treatment twice a week for 16-18 weeks. A minimum of 60 hours of exposure was included (3 hours of within group exposure per Veteran, 30 hours of listening to recordings of imaginal exposure, and 27 hours of hearing other Veterans' trauma accounts). Significant reductions in PTSD severity were observed. Notably, only three people dropped out of the group prematurely suggesting that the in-session exposures were well tolerated. It should be stated that the protocol included group members having lunch together, which likely facilitated group cohesion.

Castillo et al. (2016) used a similar approach to conducting imaginal exposure. In this study, group treatment consisted of 90 minute, 16 weekly sessions with only three women Veterans per group. Participants first completed a trauma narrative as homework. Each Veteran received four sessions of imaginal exposure, in which they read their narrative out loud in the group session. The protocol also included cognitive and skills components. The group size was limited to three members to permit the increased dose of imaginal exposure conducted in session. Relative to a WL comparison, participants in the trauma-focused group had significant reductions in PTSD severity at post-treatment, with treatment gains maintained at 6 month follow-up. This protocol differs from Schnurr et al. (2003) and Ready et al. (2008) with a less time treatment protocol. Treatment dropout rate was 24%.

Beck, Coffey, Foy, Keane, and Blanchard (2009) used a different approach to conducting exposure treatment in the group context. Rather than have group members recount their trauma accounts out loud in-session, group members are instructed to write their trauma narrative during session. The trauma narratives are conducted in two sessions. This approach has the advantage of efficient use of time as all group members are conducting imaginal exposure simultaneously. The approach also reduces the risk of triggering responses among fellow group members. In addition, the protocol, referred to as group cognitive behavioral treatment (GCBT), includes *in vivo* exposures conducted between sessions as homework. The protocol consists of 14, 2-hour sessions. Beck et al. found significant reductions in PTSD severity for GCBT relative to WL with a sample of adults who had motor vehicle-related PTSD. Treatment dropout rate was 27%. A study is currently underway to investigate the efficacy of GCBT relative to group PCT in a sample of Veterans diagnosed with PTSD (Sloan, Unger, & Beck, 2016).

Taking a similar approach to Chard (2005), Beidel, Frueh, Uhde, Wong, and Mentrikoski (2011) used a combination of group and individual treatment. This protocol, referred to as Trauma Management Therapy (TMT), combines exposure therapy and social emotional rehabilitation. The exposure component is conducted in the individual sessions, whereas the social emotional rehabilitation is conducted using the group format. TMT is based on strong empirical evidence favoring exposure therapy delivered individually, which it combines with group treatment to address social functioning, thereby providing a more comprehensive approach. In a sample of 35 Veterans who were randomly assigned to TMT or exposure therapy without group treatment, both conditions displayed significant reductions in PTSD with no between-group differences. As anticipated, the TMT condition had greater improvements in social functioning relative to exposure only. Treatment dropout for TMT was 22% relative to 6% in exposure only.

The higher dropout rate in TMT may be due to the greater time commitment involved in this treatment relative to the exposure only condition. Although replication is needed, this approach may be particularly appealing to trauma survivors who have deficits in social functioning.

To summarize, protocols for group treatment for PTSD have used different approaches to conduct exposure thought to be critical to successful treatment. Two studies have used a combined group and individual format (Beidel et al., 2011; Chard, 2005), whereas most studies have incorporated exposure-based techniques in the group context. However, the format used for imaginal exposure has varied, with most protocols asking group members to recount their trauma memory out loud while other group members listen. In contrast, Beck and colleagues (2009) had group members write their trauma account during session. Beck et al. and Castillo et al. (2016) also had a lower treatment dose than other treatments (Ready et al., 2008; Schnurr et al., 2003). Despite the dose differences, large within-group effect sizes were observed for PTSD symptom reduction and similar treatment dropout rates were reported across the studies. Thus, no single protocol appears superior to another in terms of outcome effects. The protocols used by Schnurr et al. (2003) and Ready et al. (2008) are fairly time intensive. Similarly, the time required for protocols that use a combination of individual and group formats is greater than the protocols used by Castillo et al. and Beck et al. Given the data reported so far, it may be most cost effective to use a group treatment that involves less time.

Group Protocols that Address Comorbid Conditions

Comorbid psychiatric conditions are common in PTSD, thus a number of group treatments have been developed to target comorbid conditions. One such example is Dunn and colleagues (2007) who tested the efficacy of self-management group treatment among a sample of 101 male Veterans diagnosed with chronic PTSD and depression. Self-management group therapy is designed to target depression and includes self-monitoring of positive activities and daily mood, goal setting and self-reinforcement for gains. Relative to a psychoeducation group treatment, Veterans assigned to self-management therapy showed a small reduction in depression symptoms at post-treatment. However, this reduction was no longer observed at the follow-up assessment. Moreover, no between group treatment differences were observed for PTSD outcome. It should also be noted that 33% of participants assigned to self-management group dropped out prematurely compared with 12% in the psychoeducation group.

Another approach to treating comorbid depression among individuals with PTSD is interpersonal therapy, which has been found to be efficacious in the treatment of depression. In an open trial study, Ray and Webster (2010) found significant reductions in PTSD and depression symptoms as well as improvements in interpersonal functioning following an interpersonal group treatment among a small sample of Vietnam Veterans. The interpersonal group treatment involved assessing dysfunctional relationship patterns, developing new social contacts, and re-establishing lost relationships. The group consisted of eight, 2-hour sessions. Cloitre and Koenen (2001) also found significant improvements in PTSD and depression symptoms for women who completed a 12-week interpersonal process group. However, no treatment gains were observed when groups included one or more members who had a diagnosis of borderline personality disorder. Despite these promising findings for interpersonal therapy, there have been no additional studies of the efficacy of interpersonal group therapy for PTSD. Further investigation should be pursued in which a treatment comparison condition is included.

Seeking Safety (SS) is a well-known group treatment that targets a common comorbid condition in PTSD, substance use disorder. This treatment is a present-focused, coping skills approach that includes skills in distress tolerance and affect management. SS is frequently used in VA healthcare settings, yet efficacy findings for this treatment have been mixed. Early studies consisted of either an open trial design or a no treatment comparison condition. Findings from these studies demonstrated that SS reduces PTSD symptoms as well as substance use (for a review see, Najavits & Hein, 2013). However, more recent RCTs that have included an active treatment comparison condition (e.g., psychoeducation or treatment as usual), find significant within group effects for all treatment groups but no significant between group effects (Hien et al., 2009; Zlotnick, Johnson, & Najavits, 2009). It should also be noted that across studies, the effect sizes for PTSD symptom reduction tend to be larger than what has been observed for substance use, which may indicate that substance use is more difficult to treat (Najavits & Hien, 2013). Taken together, the findings to date do not indicate that SS is superior to other active group treatments, including psychoeducation. The continued popularity of SS may reflect the need for a treatment protocol that addresses PTSD and comorbid substance use combined as well as the limited availability of such protocols.

Human immunodeficiency virus (HIV) is another important comorbid condition among trauma survivors for which group treatment protocols have been developed. The rate of PTSD among individuals who are HIV positive is significantly higher than among the general population and those with PTSD tend to be less adherent to antiretroviral regimes, which can have fatal consequences (Beckerman & Auerbach, 2010). Thus, treatment of PTSD among HIV positive individuals is an important area to address. Sikkema et al. (2007) investigated the efficacy of a group treatment protocol designed to address trauma symptoms stemming from childhood sexual abuse among 202 HIV positive adults. The 15-session treatment uses a cognitive-behavioral model to address coping strategies for both sexual trauma and HIV infection. Significant reductions in PTSD symptoms were observed for the trauma and HIV coping treatment relative to a support group and a WL comparison conditions. No group differences were observed between the support group and the WL condition.

In light of considerable comorbidity, efforts to address PTSD in a group treatment setting are wise to incorporate therapeutic components that also focus on co-occurring psychiatric and physical health problems. As noted, the literature on group treatments targeting two conditions simultaneously is in its infancy. It is possible that as this literature grows, we will have a clearer idea of whether treatments that address comorbid conditions are more efficacious, relative to interventions that target PTSD alone. While efficacy may be equal between these two types of group treatments, one can wonder whether other dimensions of difference may appear. For instance, patients may prefer group treatments that target both PTSD and a co-occurring issue such as depression, as this type of approach may better address their concerns. Similarly, patients may be less likely to drop out of treatment that they believe is addressing their needs.

Limitations of the Literature and Future Directions

As noted, a number of limitations exist in the literature on group PTSD treatment. It is salient that many forms of group PTSD treatment have been developed, each with one, perhaps two, supportive studies. This diversity in treatment protocols and relative lack of supportive data from independent replications of these studies limits knowledge that can be gained and has led to the lack of an evidence-based group treatment approach for PTSD (Institute of Medicine, 2008; VA & DoD, 2010). Moreover, many extant studies are under-powered and fail to consider dependencies among participants. As discussed by Baldwin, Murray, and Shadish (2005), when treatments are conducted in a group, participants within each group share the specific group environment, leading to a lack of independence of observations. Analytic approaches need to account for the group clustering effect, a feature largely missing from the literature (Sloan et al., 2013). Exceptions are clearly present. For example, Schnurr et al. (2003) did their analyses by regarding the group as the unit rather than each patient as the unit. However, this methodological feature is unusual in this literature, at present. Clearly, the literature on group treatment of PTSD has room for growth, building on the most promising treatment approaches. As this literature evolves, greater attention is needed to methodological sophistication. Determination of cost-effectiveness and patient acceptability of group treatment would be a welcomed addition, particularly in comparison to individual approaches. With increased treatment demands and greater attention to patient-centered services, group treatments for PTSD need a more solid empirical foundation.

References

Department of Veterans Affairs & Department of Defense. (2010). *VA/DoD clinical practice guideline for management of post-traumatic stress.* Retrieved from http://www.healthquality.va.gov/guidelines/MH/ptsd/cpgPTSDFULL201011612c.pdf

Institute of Medicine. (2008). *Treatment of posttraumatic stress disorder: An assessment of the evidence.* Washington, DC: National Academies Press.

FEATURED ARTICLES

Baldwin, S. A., Murray, D. M., & Shadish, W. R. (2005). **Empirically supported treatments or Type I errors? Problems with the analysis of data from group-administered treatments.** *Journal of Consulting and Clinical Psychology, 73*, 924-935. doi:10.1037/0022-006X.73.5.924 When treatments are administered in groups, clients interact in ways that lead to violations of a key assumption of most statistical analyses-the assumption of independence of observations. The resulting dependencies, when not properly accounted for, can increase Type I errors dramatically. Of the 33 studies of group-administered treatment on the empirically supported treatments list, none appropriately analyzed their data. The current authors provide corrections that can be applied to improper analyses. After the corrections, only 12.4% to 68.2% of tests that were originally reported as significant remained significant, depending on what assumptions were made about how large the dependencies among observations really are.

FEATURED ARTICLES *continued*

Of the 33 studies, 6-19 studies no longer had any significant results after correction. The authors end by providing recommendations for researchers planning group-administered treatment research.

Bass, J. K., Annan, J., McIvor Murry, S., Kaysen, D., Griffiths, S., Cetinoglu, T., . . . Bolton, P. A. (2013). **Controlled trial of psychotherapy for Congolese survivors of sexual violence.** *New England Journal of Medicine, 368*, 2182-2191. doi:10.1056/NEJMoa1211853 *Background:* Survivors of sexual violence have high rates of depression, anxiety, and post-traumatic stress disorder (PTSD). Although treatment for symptoms related to sexual violence has been shown to be effective in high-income countries, evidence is lacking in low-income, conflict-affected countries. *Methods:* In this trial in the Democratic Republic of Congo, we randomly assigned 16 villages to provide cognitive processing therapy (1 individual session and 11 group sessions) or individual support to female sexual-violence survivors with high levels of PTSD symptoms and combined depression and anxiety symptoms. One village was excluded owing to concern about the competency of the psychosocial assistant, resulting in 7 villages that provided therapy (157 women) and 8 villages that provided individual support (248 women). Assessments of combined depression and anxiety symptoms (average score on the Hopkins Symptom Checklist [range, 0 to 3, with higher scores indicating worse symptoms]), PTSD symptoms (average score on the Harvard Trauma Questionnaire [range, 0 to 3, with higher scores indicating worse symptoms]), and functional impairment (average score across 20 tasks [range, 0 to 4, with higher scores indicating greater impairment]) were performed at baseline, at the end of treatment, and 6 months after treatment ended. *Results:* A total of 65% of participants in the therapy group and 52% of participants in the individual- support group completed all three assessments. Mean scores for combined depression and anxiety improved in the individual-support group (2.2 at baseline, 1.7 at the end of treatment, and 1.5 at 6 months after treatment), but improvements were significantly greater in the therapy group (2.0 at baseline, 0.8 at the end of treatment, and 0.7 at 6 months after treatment) ($P < 0.001$ for all comparisons). Similar patterns were observed for PTSD and functional impairment. At 6 months after treatment, 9% of participants in the therapy group and 42% of participants in the individual-support group met criteria for probable depression or anxiety ($P < 0.001$), with similar results for PTSD. *Conclusions:* In this study of sexual-violence survivors in a low-income, conflict-affected country, group psychotherapy reduced PTSD symptoms and combined depression and anxiety symptoms and improved functioning.

Beck, J. G., Coffey, S. F., Foy, D. W., Keane, T. M., & Blanchard, E. B. (2009). **Group cognitive behavior therapy for chronic posttraumatic stress disorder: An initial randomized pilot study.** *Behavior Therapy, 40*, 82-92. doi:10.1016/j.beth.2008.01.003 Individuals with posttraumatic stress disorder (PTSD) related to a serious motor vehicle accident were randomly assigned to either group cognitive behavioral treatment (GCBT) or a minimum contact comparison group (MCC). Compared to the MCC participants ($n = 16$), individuals who completed GCBT ($n = 17$) showed significant reductions in PTSD symptoms, whether assessed using clinical interview or a self-report measure. Among treatment completers, 88.3% of GCBT participants did not satisfy criteria for PTSD at posttreatment assessment, relative to 31.3% of the MCC participants. Examination of anxiety, depression, and pain measures did not show a unique advantage of GCBT. Treatment-related gains were maintained over a 3-month

follow-up interval. Patients reported satisfaction with GCBT, and attrition from this treatment was comparable with individually administered CBTs. Results are discussed in light of modifications necessitated by the group treatment format, with suggestions for future study of this group intervention.

Beckerman, N. L., & Auerbach, C. (2010). **Post-traumatic stress disorder and HIV: A snapshot of co-occurrence.** *Social Work in Health Care, 49*, 687-702. doi:10.1080/00981389.2010.485089 Although the medical advances in the area of human immunodeficiency virus (HIV)/acquired immune deficiency syndrome (AIDS) have undoubtedly improved the length and quality of life for those who are HIV-affected and medication adherent, there are still many psychosocial obstacles to effective HIV/AIDS medication adherence. Recent research has focused on one such obstacle. The significant link between post-traumatic stress disorder (PTSD) and HIV. This article reports on the nature of this relationship with a cross-sectional study of active clients (n = 186) who were receiving HIV services from community-based settings in the New York City area. With the use of the PTSD Checklist (PCL), this study determined that more than half of the sample tested positively for PTSD. Policy and clinical implications of this and other findings are discussed.

Beidel, D. C., Frueh, B. C., Uhde, T. W., Wong, N., & Mentrikoski, J. M. (2011). **Multicomponent behavioral treatment for chronic combat-related posttraumatic stress disorder: A randomized controlled trial.** *Journal of Anxiety Disorders, 25*, 224-231. doi:10.1016/j.janxdis.2010.09.006 This study examined the efficacy of a multicomponent cognitive-behavioral therapy, Trauma Management Therapy, which combines exposure therapy and social emotional rehabilitation, to exposure therapy only in a group of male combat veterans with chronic posttraumatic stress disorder (PTSD). Thirty-five male Vietnam veterans with PTSD were randomly assigned to receive either Trauma Management Therapy (TMT) or Exposure Therapy Only (EXP). Participants were assessed at pre-treatment, mid-treatment, and post-treatment. Primary clinical outcomes were reduction of PTSD symptoms and improved social emotional functioning. Results indicated that veterans in both conditions showed statistically significant and clinically meaningful reductions in PTSD symptoms from pre- to post-treatment, though consistent with a priori hypotheses there were no group differences on PTSD variables. However, compared to the EXP group, participants in the TMT group showed increased frequency in social activities and greater time spent in social activities. These changes occurred from mid-treatment (after completion of exposure therapy) to post-treatment (after completion of the social emotional rehabilitation component); supporting the hypothesis that TMT alone would result in improved social functioning. Although the TMT group also had a significant decrease in episodes of physical rage, that change occurred prior to introduction of the social emotional component of TMT. This study demonstrates efficacy of exposure therapy for treating the core symptoms of PTSD among combat veterans with a severe and chronic form of this disorder. Moreover, multi-component CBT shows promise for improving social functioning beyond that provided by exposure therapy alone, particularly by increasing social engagement/interpersonal functioning in a cohort of veterans with severe and chronic PTSD.

Castillo, D. T., Chee, C. L., Nason, E., Keller, J., C'de Baca, J., Qualls, C., … Keane, T. M. (2016). **Group-delivered cognitive/exposure therapy for PTSD in women veterans: A randomized controlled trial.** *Psychological Trauma: Theory, Research, Practice, and Policy, 8*, 404-412. doi:10.1037/tra0000111 *Objective:* Group delivery of posttraumatic stress disorder (PTSD) treatment has several advantages, however group research is not comparable to individual trials. This study extends the group literature by improving methodology in examining the efficacy of a 3-module (cognitive, exposure, skills) group treatment for PTSD, establishes a format for the delivery of group exposure therapy, and compares 3 treatment modules within the group. *Method:* Eighty-six Operation Enduring Freedom (OEF)/Operation Iraqi Freedom (OIF) women veterans were randomized to a 16-week, 3-member group treatment (Tx) or a waitlist (WL) condition. The primary (Clinician Administered PTSD Scale [CAPS]) and secondary (Medical Outcomes Study Short Form-36 [SF-36], Quality of Life Inventory [QOLI], and PTSD Checklist [PCL]) outcome measures were administered at baseline, post Tx/WL, and at 3- and 6-months post Tx (PCL additionally at pre/post for each treatment module). *Results:* PTSD symptoms significantly improved in Tx arm participants (p < .001, ES = 1.72; unit of analysis group: n = 14), as did mental and physical life functioning (SF-36; p < .001), and quality of life (QOLI; p < .001). The WL significantly improved on the SF-36 (mental; p = .04) and QOLI (p = .02). Clinical improvement (CAPS) in the Tx arm reflected a treatment response (≥10-point decrease) in 77% and loss of PTSD diagnosis (<45) in 52% of participants, comparable to individual prolonged exposure (PE) treatment. Finally, PCL scores significantly lowered in exposure and cognitive modules. *Conclusions:* This study supports the use of group format for PTSD with 3 modules using improved methodology, with a novel, 3-member group which allows repeated in-session weekly imaginal exposures. The results suggest future examination of group delivered PE.

Chard, K. M. (2005). **An evaluation of cognitive processing therapy for the treatment of posttraumatic stress disorder related to childhood sexual abuse.** *Journal of Consulting and Clinical Psychology, 73*, 965-971. doi:10.1037/0022-006X.73.5.965 This study compared the effectiveness of cognitive processing therapy for sexual abuse survivors (CPT-SA) with that of the minimal attention (MA) given to a wait-listed control group. Seventy-one women were randomly assigned to 1 of the 2 groups. Participants were assessed at pretreatment and 3 times during posttreatment: immediately after treatment and at 3-month and 1-year follow-up, using the Clinician-Administered posttraumatic stress disorder (PTSD) Scale (D. Blake et al., 1995), the Beck Depression Inventory (A. T. Beck, R. A. Steer, & G. K. Brown, 1996), the Structured Clinical Interview for the DSM-IV (R. L. Spitzer, J. B. W. Williams, & M. Gibbon, 1995; M. B. First et al., 1995), the Dissociative Experiences Scale-II (E. M. Bernstein & F. W. Putnam, 1986), and the Modified PTSD Symptom Scale (S. A. Falsetti, H. S. Resnick, P. A. Resick, & D. G. Kilpatrick, 1993). Analyses suggested that CPT-SA is more effective for reducing trauma-related symptoms than is MA, and the results were maintained for at least 1 year.

Classen, C. C., Palesh, O. G., Cavanaugh, C. E., Koopman, C., Kaupp, J. W., Kraemer, H. C., . . . Spiegel, D. (2011). **A comparison of trauma-focused and present-focused group therapy for survivors of childhood sexual abuse: A randomized controlled trial.** *Psychological Trauma: Theory, Research, Practice, and Policy, 3*, 84-93. doi:10.1037/a0020096 This randomized controlled trial compared trauma-focused group psychotherapy (TFGT) with present-focused group psychotherapy (PFGT) and a waitlist condition for 166 survivors of childhood sexual abuse who were at risk for HIV infection. Primary outcomes included risk for HIV infection (based on sexual revictimization, drug and alcohol use, and risky sex) and posttraumatic stress disorder (PTSD) symptoms. It was hypothesized that TFGT would be superior to the PFGT and waitlist conditions and that receiving either treatment (combining both TFGT and PFGT) would be superior to no treatment (waitlist condition). Intention-to-treat analyses for HIV risk found that all conditions reduced risk; however, there was no effect for condition on HIV risk. Intention-to-treat analyses for PTSD symptoms found a reduction for all conditions. There was no advantage for either TFGT or PFGT in reducing PTSD symptoms; however, there was an effect for treatment compared with the waitlist condition. On secondary outcomes, there was a greater reduction in anger for TFGT compared with PFGT, and when comparing treatment with the waitlist condition, there was a greater reduction in hyperarousal, reexperiencing, anger, and impaired self-reference for the treatment condition. Adequate dose analyses generally confirmed the intention-to-treat findings and additionally found that treatment led to reductions in depression, dissociation, and sexual concerns.

Cloitre, M., & Koenen, K. C. (2001). **The impact of borderline personality disorder on process group outcome among women with posttraumatic stress disorder related to childhood abuse.** *International Journal of Group Psychotherapy, 51*, 379-398. doi:10.1521/ijgp.51.3.379.49886 The outcome of a 12-week interpersonal process group therapy for women with posttraumatic stress disorder (PTSD) related to childhood sexual abuse with and without borderline personality disorder (BPD) was assessed by comparing three naturally occurring treatment conditions: groups that did not have any members with borderline personality disorder (BPD-) (n = 18), groups in which at least one member carried the diagnosis (BPD+)(n = 16), and a 12-week waitlist (WL) (n = 15). PTSD, anger, depression, and other symptoms were significantly reduced in the BPD- groups. However, the BPD+ and WL conditions did not show any pre- to posttreatment improvements. Furthermore, the BPD+ condition showed a significant worsening on measures of anger. Analyses within the BPD+ condition indicated that women with and without the diagnosis experienced equal posttreatment increases in anger problems. These latter results suggest the presence of an anger "contagion" effect. That is, women without BPD did well in the BPD- groups but showed increased anger similar to the BPD+ women when treated in groups with them. Implications for client-treatment matching considerations in PTSD group therapy are discussed.

Dunn, N. J., Rehm, L. P., Schillaci, J., Souchek, J., Mehta, P., Ashton, C. M., ... & Hamilton, J. D. (2007). **A randomized trial of self-management and psychoeducational group therapies for comorbid chronic posttraumatic stress disorder and depressive disorder.** *Journal of Traumatic Stress, 20*, 221-237. doi:10.1002/jts.20214 The authors randomized 101 male veterans with chronic combat-related posttraumatic stress disorder (PTSD) and depressive disorder to an evidence-based depression treatment (self-management therapy; n = 51) or active-control therapy (n = 50). Main outcome measures for efficacy, using intention-to-treat analyses, were subjective and objective PTSD and depression scales at pretest, posttest, and 3-, 6-, and 12-month follow-up. Other measures included treatment compliance, satisfaction, treatment-targeted constructs, functioning, service utilization, and costs. Self-management therapy's modestly greater improvement on depression symptoms at treatment completion disappeared on follow-up. No other differences on symptoms or functioning appeared, although psychiatric outpatient utilization and overall outpatient costs were lower with self-management therapy. Despite success in other depressed populations, self-management therapy produced no clinically significant effect in depression with chronic PTSD.

Foy, D. W., Glynn S. M., Schnurr, P. P., Jankowski, M. K., Wattenberg, M. S., Weiss, D. S., . . . Gusman, F. D. (2000). Group therapy. In E. Foa, T. Keane, & M. Friedman (Eds.), *Effective treatments for PTSD: Practice guidelines from the International Society for Traumatic Stress Studies* (pp. 155-175). New York: Guilford Press. Group therapy for posttraumatic stress disorder (PTSD) offers cohesion, encouragement, and support from other members in either "covering" or "uncovering" formats, referring to whether or not traumatic experiences are addressed directly. Representative of the covering format is supportive group therapy, and of uncovering format are psychodynamic groups and cognitive-behavioral therapy. Group treatment for PTSD is recommended as potentially effective based upon consistent positive evidence from 14 recent studies. The course of treatment involving group therapy is described, as well as clinical recommendations.

Hien, D. A., Wells, E. A., Jiang, H., Suarez-Morales, L., Campbell, A. N. C., Cohen, L. R., . . . Nunes, E. V. (2009). **Multisite randomized trial of behavioral interventions for women with co-occurring PTSD and substance use disorders.** *Journal of Consulting and Clinical Psychology, 77*, 607-619. doi:10.1037/a0016227 The authors compared the effectiveness of the Seeking Safety group, cognitive–behavioral treatment for substance use disorder and posttraumatic stress disorder (PTSD), to an active comparison health education group (Women's Health Education [WHE]) within the National Institute on Drug Abuse's Clinical Trials Network. The authors randomized 353 women to receive 12 sessions of Seeking Safety (M = 6.2 sessions) or WHE (M = 6.0 sessions) with follow-up assessment 1 week and 3, 6, and 12 months posttreatment. Primary outcomes were the Clinician Administered PTSD Scale (CAPS), the PTSD Symptom Scale–Self Report (PSS-SR), and a substance use inventory (self-reported abstinence and percentage of days of use over 7 days). Intention-to-treat analysis showed large, clinically significant reductions in CAPS and PSS-SR symptoms (d = 1.94 and 1.12, respectively) but no reliable difference between conditions. Substance use outcomes were not significantly different over time between the two treatments and at follow-up showed no significant

change from baseline. Study results do not favor Seeking Safety over WHE as an adjunct to substance use disorder treatment for women with PTSD and reflect considerable opportunity to improve clinical outcomes in community-based treatments for these co-occurring conditions.

Hundt, N. E., Robinson, A., Arney, J., Stanley, M. A., & Cully, J. A. (2015). **Veterans' perspectives on benefits and drawbacks of peer support for posttraumatic stress disorder.** *Military Medicine, 180*, 851-856. doi:10.7205/MILMED-D-14-00536 Peer support has been increasingly utilized within the Department of Veterans Affairs and offers an opportunity to augment existing care for posttraumatic stress disorder (PTSD). The current study sought to examine veterans' perspectives on the potential benefits and drawbacks of peer support for PTSD. A sample of 23 veterans with substantial treatment experience completed one-time qualitative interviews that were transcribed and coded for thematic content using grounded theory methodology. Results indicated that veterans identified numerous potential benefits to a peer support program, including social support, purpose and meaning, normalization of symptoms and hope, and therapeutic benefits. Veterans also identified ways that peer support could complement psychotherapy for PTSD by increasing initiation and adherence to treatment and supporting continued use of skills after termination. Results also indicated that veterans may prefer peer support groups that are separated according to trauma type, gender, and era of service. Other findings highlighted the importance of the leadership and interpersonal skills of a peer support group leader. Overall, veterans found peer support to be a highly acceptable complement to existing PTSD treatments with few drawbacks.

Morland, L. A., Mackintosh, M. A., Greene, C. J., Rosen, C. S., Chard, K. M., Resick, P., & Frueh, B. C. (2014). **Cognitive processing therapy for posttraumatic stress disorder delivered to rural veterans via telemental health: A randomized noninferiority clinical trial.** *Journal of Clinical Psychiatry, 75*, 470-476. doi:10.4088/JCP.13m08842 *Objective:* To compare clinical and process outcomes of cognitive processing therapy-cognitive only version (CPTC) delivered via videoteleconferencing (VTC) to in-person in a rural, ethnically diverse sample of veterans with posttraumatic stress disorder (PTSD). *Method:* A randomized clinical trial with a noninferiority design was used to determine if providing CPT-C via VTC is effective and "as good as" in-person delivery. The study took place between March 2009 and June 2013. PTSD was diagnosed per *DSM-IV* Participants received 12 sessions of CPT-C via VTC (n = 61) or in-person (n = 64). Assessments were administered at baseline, midtreatment, immediately posttreatment, and 3 and 6 months posttreatment. The primary clinical outcome was posttreatment PTSD severity, as measured by the Clinician-Administered PTSD Scale. *Results:* Clinical and process outcomes found VTC to be noninferior to in-person treatment. Significant reductions in PTSD symptoms were identified at posttreatment (Cohen $d = 0.78$, $P < .05$) and maintained at 3- and 6-month follow-up ($d = 0.73$, $P < .05$ and $d = 0.76$, $P < .05$, respectively). High levels of therapeutic alliance, treatment compliance, and satisfaction and moderate levels of treatment expectancies were reported, with no differences between groups (for all comparisons, $F < 1.9$, $P > .17$). *Conclusions:* Providing CPT-C to rural residents with PTSD via VTC produced outcomes that were "as good as" in-person treatment. All participants demonstrated significant reductions in PTSD symptoms posttreatment and at follow-up. Results indicate that VTC can offer increased access to specialty mental health care for residents of rural or remote areas.

Najavits, L. M., & Hien, D. (2013). **Helping vulnerable populations: A comprehensive review of the treatment outcome literature on substance use disorder and PTSD.** *Journal of Clinical Psychology, 69*, 433-479. doi:10.1002/jclp.21980 We review treatment studies for comorbid substance use disorder (SUD) and posttraumatic stress disorder (PTSD). Results show positive outcomes on multiple domains. Most models had more effect on PTSD than SUD, suggesting SUD is harder to treat. Seeking Safety (SS) is the most studied model. It shows positive outcomes, and is the only treatment outperforming a control on both PTSD and SUD. Partial-dose SS had more mixed results than the full dose. This first-generation of PTSD/SUD research addresses complex samples excluded from "gold standard" PTSD-alone literature. Treatments for PTSD/SUD are generally longer than PTSD-alone treatments and present-focused, emphasizing stabilization and coping. The few models with past-focused (exposure-based) components also incorporated present-focused approaches for these vulnerable clients. We discuss public health perspectives to advance the field.

Ray, R. D., & Webster, R. (2010). **Group interpersonal psychotherapy for veterans with posttraumatic stress disorder: A pilot study.** *International Journal of Group Psychotherapy, 60*, 131-140. doi:10.1521/ijgp.2010.60.1.131 Group-based interpersonal psychotherapy (IPT-G) was provided to nine male Vietnam veterans with posttraumatic stress disorder (PTSD) to reduce interpersonal difficulties. Standardized measures of posttraumatic stress, depression, interpersonal problems, and functioning were administered pre- and posttreatment and at 2- and 4-month follow-ups. Individual (reliable change indices) and group analyses (repeated measures ANOVAs) indicated improvements in interpersonal and global functioning (not maintained at follow-up), as well as for PTSD and depressive symptoms (maintained at follow-up). Qualitative feedback indicated reduced levels of anger and stress as well as improved relationships. IPT-G for Vietnam veterans shows promise in improving interpersonal functioning and reducing psychological distress. However, since not all improvements were maintained over time, future studies may need to explore relapse prevention strategies.

Ready, D. J., Thomas, K. R., Worley, V., Backscheider, A. G., Harvey, L. A. C., Baltzell, D., & Rothbaum, B. O. (2008). **A field test of group based exposure therapy with 102 veterans with war-related posttraumatic stress disorder.** *Journal of Traumatic Stress, 21*, 150-157. doi:10.1002/jts.20326 Group-based exposure therapy (GBET) was field-tested with 102 veterans with war-related posttraumatic stress disorder. Nine to 11 patients attended 3 hours of group therapy per day twice weekly for 16–18 weeks. Stress management and a minimum of 60 hours of exposure was included (3 hours of within-group war-trauma presentations per patient, 30 hours of listening to recordings of own war-trauma presentations and 27 hours of hearing other war-trauma presentations). Analysis of assessments conducted by treating clinicians pre-, post- and 6-month posttreatment suggests that GBET produced clinically significant and lasting reductions in PTSD symptoms for most patients on both clinician symptoms ratings (6-month posttreatment effect size $\delta = 1.22$) and self-report measures with only three dropouts.

Resick, P. A., & Schnicke, M. K. (1992). **Cognitive processing therapy for sexual assault victims.** *Journal of Consulting and Clinical Psychology, 60*, 748-756. doi:10.1037/0022-006X.60.5.748 Cognitive processing therapy (CPT) was developed to treat the symptoms of posttraumatic stress disorder (PTSD) in rape victims. CPT is based on an information processing theory of PTSD and includes education, exposure, and cognitive components. Nineteen sexual assault survivors received CPT, which consists of 12 weekly sessions in a group format. They were assessed at pretreatment, posttreatment, and 3- and 6-month follow-up. CPT subjects were compared with a 20-subject comparison sample, drawn from the same pool who waited for group therapy for at least 12 weeks. CPT subjects improved significantly from pre- to posttreatment on both PTSD and depression measures and maintained their improvement for 6 months. The comparison sample did not change from the pre- to the posttreatment assessment sessions.

Resick, P. A., Wachen, J. S., Mintz, J., Young-McCaughan, S., Roache, J. D., Borah, A. M., … Peterson, A. L. (2015). **A randomized clinical trial of group cognitive processing therapy compared with group present-centered therapy for PTSD among active duty military personnel.** *Journal of Consulting and Clinical Psychology, 83*, 1058-1068. doi:10.1037/ccp0000016 *Objective:* To determine whether group therapy improves symptoms of posttraumatic stress disorder (PTSD), this randomized clinical trial compared efficacy of group cognitive processing therapy (cognitive only version; CPT-C) with group present-centered therapy (PCT) for active duty military personnel. *Method:* Patients attended 90-min groups twice weekly for 6 weeks at Fort Hood, Texas. Independent assessments were administered at baseline, weekly before sessions, and 2 weeks, 6 months, and 12 months posttreatment. A total of 108 service members (100 men, 8 women) were randomized. Inclusion criteria included PTSD following military deployment and medication stability. Exclusion criteria included suicidal/homicidal intent or other severe mental disorders requiring immediate treatment. Follow-up assessments were administered regardless of treatment completion. Primary outcome measures were the PTSD Checklist (Stressor Specific Version; PCL-S) and Beck Depression Inventory-II. The Posttraumatic Stress Symptom Interview (PSS-1) was a secondary measure. Results: Both treatments resulted in large reductions in PTSD severity, but improvement was greater in CPT-C. CPT-C also reduced depression, with gains remaining during follow-up. In PCT, depression only improved between baseline and before Session 1. There were few adverse events associated with either treatment. Conclusions: Both CPT-C and PCT were tolerated well and reduced PTSD symptoms in group format, but only CPT-C improved depression. This study has public policy implications because of the number of active military needing PTSD treatment, and demonstrates that group format of treatment of PTSD results in significant improvement and is well tolerated. Group therapy may an important format in settings in which therapists are limited.

Schnurr, P. P., Friedman, M. J., Foy, D. W., Shea, M. T., Hsieh, F. Y., Lavori, P. W., . . . Bernardy, N. C. (2003). **Randomized trial of trauma-focused group therapy for posttraumatic stress disorder: Results from a Department of Veterans Affairs cooperative study.** *Archives of General Psychiatry, 60*, 481-489. doi:10.1001/archpsyc.60.5.481 *Background:* Department of Veterans Affairs Cooperative Study 420 is a randomized clinical trial of 2 methods of group psychotherapy for treating posttraumatic stress disorder (PTSD) in male Vietnam veterans. *Methods:* Vietnam veterans (360 men) were randomly assigned to receive trauma-focused group psychotherapy or a present-centered comparison treatment that avoided trauma focus. Treatment was provided weekly to groups of 6 members for 30 weeks, followed by 5 monthly booster sessions. Severity of PTSD was the primary outcome. Additional measures were other psychiatric symptoms, functional status, quality of life, physical health, and service utilization. Follow-up assessments were conducted at the end of treatment (7 months) and at the end of the booster sessions (12 months); 325 individuals participated in 1 or both assessments. Additional follow-up for PTSD severity was performed in a subset of participants at 18 and 24 months. *Results:* Although posttreatment assessments of PTSD severity and other measures were significantly improved from baseline, intention-to-treat analyses found no overall differences between therapy groups on any outcome. Analyses of data from participants who received an adequate dose of treatment suggested that trauma-focused group therapy reduced avoidance and numbing and, possibly, PTSD symptoms. Dropout from treatment was higher in trauma-focused group treatment. Average improvement was modest in both treatments, although approximately 40% of participants showed clinically significant change. *Conclusions:* This study did not find a treatment effect for trauma-focused group therapy. The difference between the effectiveness and adequate dose findings suggests the possible value of methods to enhance the delivery of cognitive-behavioral treatments in clinical practice settings.

Sikkema, K. J., Hansen, N. B., Kochman, A., Tarakeshwar, N., Neufeld, S., Meade, C. S., & Fox, A. M. (2007). **Outcomes from a group intervention for coping with HIV/AIDS and childhood sexual abuse: reductions in traumatic stress.** *AIDS and Behavior, 11*, 49-60. doi:10.1007/s10461-006-9149-8 Childhood sexual abuse is common among HIV-infected persons, though few empirically supported treatments addressing sexual abuse are available for men and women with HIV/AIDS. This study reports the outcome from a randomized controlled trial of a group intervention for coping with HIV and sexual abuse. A diverse sample of 202 HIV-positive men and women who were sexually abused as children was randomly assigned to one of three conditions: a 15-session HIV and trauma coping group intervention, a 15-session support group comparison condition, or a waitlist control (later randomly assigned to an intervention condition). Traumatic stress symptoms were assessed at baseline and post-intervention, with analysis conducted for the three-condition comparison followed by analysis of the two-condition comparison between the coping and support group interventions. Participants in the coping group intervention exhibited reductions in intrusive traumatic stress symptoms compared to the waitlist condition and in avoidant traumatic stress symptoms compared to the support group condition. No differences were found between the support group intervention and waitlist conditions. Tests of clinical significance documented the meaningfulness of change in symptoms.

Sloan, D. M., Feinstein, B. A., Gallagher, M. W., Beck, J. G., & Keane, T. M. (2013). **Efficacy of group treatment for posttraumatic stress disorder symptoms: A meta-analysis.** *Psychological Trauma: Theory, Research, Practice, and Policy, 5*, 176-183. doi:10.1037/a0026291 This study conducted a meta-analysis of published randomized clinical group trials for adult survivors of trauma to examine the efficacy of the group format. Effect sizes for posttraumatic stress disorder (PTSD) severity outcome were examined. Sixteen studies were included, with a total of 1686 participants. Results of a random effects model meta-analysis indicated that group treatments are associated with significant pre- to posttreatment reduction in PTSD symptom severity (within treatment d = .71, 95% CI [.51, .91]), and result in superior treatment effects relative to a wait list comparison condition (d = .56, 95% CI [.31, .82]). However, no significant findings were obtained for group interventions relative to active treatment comparison conditions (d = .09, 95% CI [–.03, .22]). Moderator analyses also indicated that gender and type of trauma moderated treatment effects for PTSD outcome, with smaller effect sizes associated with males relative to females and combined gender samples, and smaller effect sizes for combat and child sexual assault trauma samples relative to mixed-trauma sample studies. Taken together, group treatment for trauma symptoms is better than no treatment but not better relative to comparison conditions that control for nonspecific benefits of therapy. Additional work is needed to identify effective group treatments for PTSD, especially for patients with repeated or chronic traumatization.

Sloan, D. M., Unger, W., & Beck, J. G. (2016). **Cognitive-behavioral group treatment for veterans diagnosed with PTSD: Design of a hybrid efficacy-effectiveness clinical trial.** *Contemporary Clinical Trials, 47*, 123-130. doi:10.1016/j.cct.2015.12.016 Despite significant advances in individual treatment approaches for PTSD, knowledge of group approaches has lagged behind. Much of the reason knowledge for group treatment for PTSD has been limited is due to the complexity of conducting randomized controlled trials in the group treatment context. This limited empirical knowledge is unfortunate given the frequency with which group treatment for PTSD is used in clinical settings, including the Department of Veteran Affairs. The goal of this study is to examine the efficacy of a group cognitive-behavioral treatment (GCBT) for PTSD relative to group supportive counseling approach (i.e. group present centered treatment; GPCT). The sample will consist of 196 veterans diagnosed with PTSD who will be randomly assigned to either GCBT (n = 98) or GPCT (n = 98). Both treatments will be administered by two therapists over the course of 14 sessions. Assessments will take place at baseline, mid-treatment, and 1-, 3-, 6-, and 12-months follow-up. The primary outcome measure will be PTSD symptom severity assessed with a semi-structured diagnostic instrument. Given the rise of veterans presenting for PTSD treatment services, identifying efficacious group treatment approaches will be invaluable.

Zlotnick, C., Johnson, J., & Najavits, L. M. (2009). **Randomized controlled pilot study of cognitive-behavioral therapy in a sample of incarcerated women with substance use disorder and PTSD.** *Behavior Therapy, 40*, 325-336. doi:10.1016/j.beth.2008.09.004 This randomized controlled pilot study compared a cognitive-behavioral therapy (Seeking Safety; SS) plus treatment-as-usual (TAU) to TAU-alone in 49 incarcerated women with substance use disorder (SUD) and posttraumatic stress disorder (PTSD); full or subthreshold. Seeking Safety consisted of a voluntary group treatment during incarceration and individual treatment after prison release. TAU was required in the prison and comprised 180 to 240 hours of individual and group treatment over 6 to 8 weeks. Assessments occurred at intake, 12 weeks after intake, and 3 and 6 months after release from prison. There were no significant differences between conditions on all key domains (PTSD, SUD, psychopathology, and legal problems); but both conditions showed significant improvements from intake to later time points on all of these outcomes across time. Secondary analyses at follow-up found trends for SS participants improving on clinician-rated PTSD symptoms and TAU participants worsening on self-reported PTSD symptoms. Also, SS demonstrated continued improvement on psychopathology at 3 and 6 months, whereas TAU did not. However, alcohol use improved more for TAU during follow-up. Satisfaction with SS was high, and a greater number of SS sessions was associated with greater improvement on PTSD and drug use. Six months after release from prison, 53% of the women in both conditions reported a remission in PTSD. Study limitations include lack of assessment of SS outcomes at end of group treatment; lack of blind assessment; omission of the SS case management component; and possible contamination between the two conditions. The complex needs of this population are discussed.

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Implementation of Evidence-Based Treatment for PTSD

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There is relatively little adoption of evidence-based treatments (EBTs) into routine practice. Dissemination of EBTs or practice guidelines through traditional educational activities (e.g., formal continuing education programs) has limited impact on day-to-day clinical practice. Implementation science is an emerging field that has developed as the gap between research and practice has been identified across a variety of health care settings. The field is concerned with the study of methods to promote the integration of research findings into health care practice and policy.

A high priority need exists for implementation of EBTs for PTSD in a broad range of mental health training and service delivery organizations (Ruzek & Rosen, 2009). Large-scale dissemination of EBTs for PTSD and other trauma-related problems is well underway in the United States (US) and abroad (e.g., CATS Consortium, 2007; Ebert et al., 2012; Karlin et al., 2010). For example, beginning in 2006-2007, the US Department of Veterans Affairs (VA) developed national training initiatives to disseminate two EBTs for PTSD, Prolonged Exposure (PE) and Cognitive Processing Therapy (CPT). These sizable endeavors have been the subject of research on factors that impact implementation success. Although much of the research has been observational in nature rather than experimental, there have been studies comparing EBT implementation to usual care. Research indicates that when EBTs are implemented into routine care settings, patients with PTSD and related disorders experience substantial symptom reduction. For example, program evaluation data from mental health providers who have participated in the VA PE and CPT training initiatives indicate significant improvements in their patients' PTSD and depressive symptomatology (Chard, Ricksecker, Healy, Karlin, & Resick, 2012; Eftekhari et al., 2013).

Similarly, Ehlers and colleagues (2013) demonstrated substantial PTSD symptom reduction among a large consecutive sample of patients in a United Kingdom National Health Service outpatient clinic. Recent work in developing countries using a task-shifting strategy in which health workers without advanced degrees deliver the EBTs indicates that these treatments can be effective in under-resourced settings. CPT is more effective than usual care even when adapted significantly for non-literate women in high-conflict areas (Bass et al., 2013). Similarly, Murray and colleagues (2015) demonstrated that lay counselors in developing countries can be trained to effectively deliver Trauma-Focused Cognitive Behavioral Therapy (TF-CBT) to traumatized orphans. Despite evidence showing that clinicians can be trained to effectively deliver trauma-focused EBTs, several studies indicate that their use is relatively low in outpatient mental health settings (e.g., Finley et al., 2015; Shiner et al., 2013; Sigel, Benton, Lynch, & Kramer, 2013). Implementation researchers have been working to determine what factors predict initial and sustained use of EBTs. Over the past two decades, implementation frameworks have been developed to guide implementation efforts and their formal study (Tabak, Khoong, Chambers, & Brownson, 2012). These models specify factors to consider at the level of the provider and patient dyad, the intervention itself, and the organization and system into which new treatments are implemented. The existing research evidence strongly suggests that factors at each level are predictive of implementation success, and that there may be interactions between levels that influence such success.

Continued on page 2

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Continued from cover

Relatively few studies on implementation of EBTs for PTSD use a theoretical model (e.g., Cook et al., 2015; Couineau & Forbes, 2011; Watts et al., 2014). While the lack of operationalization and psychometrically strong measures of relevant constructs from implementation models has likely hindered progress in the traumatic stress field, more recently, validated measures have been developed or used (Cook, Thompson, & Schnurr, in press; Cook et al., 2012). Cook and colleagues (2015) used a well-known framework, *Diffusion of Innovations*, to study PE and CPT in 38 VA residential PTSD programs across the United States. They found that supportive context (dedicated time and resources and incentives and mandates) as well as positive views of the treatments were related to successful implementation. They also developed a Perceived Characteristics of Innovation Scale, in which favorable attitudes towards each of these EBTs appear unidimensional, and were associated with greater self-reported adoption. Watts et al. (2014) used the *Promoting Action on Research Implementation in Health Services* framework to study the implementation of PE and CPT in New England VA specialty PTSD clinics. Several factors were associated with increased use of EBTs, including prior use of the treatments, customization of training, and extended interaction with the training team. Couineau and Forbes (2011) utilized a behavior change model to promote CBT trauma-focused interventions in Australia. They found while providers' knowledge, skills, and confidence improved through training and supervision, successful implementation depended on providers' views on perceived risks associated with providing these types of therapies as well as on beliefs about the best timing of the interventions. Despite these concerns, however, there was a significant increase of imaginal exposure in the treatment plans of patients with PTSD.

Some research exists on the role of providers or clinic administrators in the implementation of EBTs for PTSD. For example, VA providers' treatment orientation, professional discipline, level of clinical experience treating PTSD, and prior PE training experience were unrelated to their PE patients' outcome in therapy (Eftekhari et al., 2015). Although many VA residential providers did not perceive any patient factors that dissuaded their use of PE or CPT, three broad categories emerged regarding reasons that patients were perceived to be less suitable or "ready" for the treatments: the presence of psychiatric comorbidities, cognitive limitations, and low levels of patient motivation (Cook, Dinnen, Simiola, Thompson, & Schnurr, 2014). There is also some evidence that providers' theoretical orientation and setting are associated with attitudes toward EBTs, with those who endorse CBT orientations and those who work in PTSD specialty care settings less likely to endorse a belief that PE would increase patient distress (Ruzek et al., 2014). These findings regarding perceived appropriateness, readiness for and timing or sequencing in the delivery of EBTs for PTSD have been echoed elsewhere (Couineau & Forbes, 2011; Hamblen et al., 2015).

Further exploration is needed on the perceptions of EBTs for PTSD from multiple stakeholders, including patients. A recent study that examined preferences for medication versus different CBTs for PTSD, found that Veteran patients preferred combined medication and therapy, with over half preferring CPT over several other CBTs and other therapies (Schumm, Walter, Bartone & Chard, 2015). One innovative way for increasing engagement in EBTs for PTSD is to work directly with patient and provider dyads through shared decision-making (Mott, Stanley, Street, Grady & Teng, 2014). Given the substantial variability in the way EBT treatment decisions are likely made, current evidence indicates that a brief shared decision-making intervention to assist providers in explaining the treatment rationale standardized to their patients along with a framework for treatment decisions could positively impact preference for and engagement in an EBT for PTSD.

A variety of strategies to assist in the implementation of EBTs for PTSD, such as mandates, provision of organization-level support through involvement of site supervisors or evidence-based coordinators, and an assessment of organizational culture, have been used (Karlin et al., 2010) but rarely formally studied. Training has been one of the most extensively researched implementation strategies. A number of studies focused on PTSD and related problems have attempted to identify the most effective strategies for training clinicians. Kolko and colleagues (2013) conducted a randomized controlled trial (RCT) of training strategies and demonstrated that the use of workshop training and consultation in Alternatives for Families-Cognitive Behavioral Therapy (AF-CBT) for families resulted in greater knowledge and use of AF-CBT, as well as lower rates of clinician turnover, than training as usual (TAU). Ebert and colleagues (2014) demonstrated the feasibility of a Learning Collaborative model, which uses a blend of training and support strategies, to implement integrated smoking cessation with PTSD care. Train-the-trainer models have also been tested as potentially accessible strategies for scaling up EBT implementation in under-resourced settings. For instance, Jacob and colleagues' (2014) RCT found evidence that clinicians trained by newly-trained peers can produce clinical outcomes that are comparable to treatment delivered by expert-trained clinicians. Two ongoing RCTs are testing the impact of different consultation and supervision strategies for TF-CBT and CPT on treatment fidelity and clinical outcomes (e.g., session review, model fidelity, outcome monitoring, skill-building; Dorsey et al., 2013; Stirman et al., 2013) and thus should provide information on how to optimally support providers delivering EBTs for PTSD.

The role of web-based technologies in increasing the dissemination and implementation of EBTs for PTSD has only recently received empirical attention. National trainers in TF-CBT noted the potential value of innovative, technology-based solutions to enhance provider fidelity and competence as well as patient engagement (Hanson et al., 2014). Other studies have investigated the use of technology to enhance training and consultation outcomes and to examine more scalable models of EBT training (Ruzek et al., 2014).

In conclusion, tremendous progress has been made in the dissemination of EBTs for PTSD in children and adults. However, their integration into everyday practice remains a challenge. A large majority of the treatment implementation literature in the traumatic stress field is descriptive rather than experimental. We need formal studies of the implementation process using a theory-driven or empirically guided theoretical model with solid operationalization and measurement of implementation constructs. Closing the gap between science and practice is a complex process that involves multiple levels of a health care system from training and supervising providers to competently deliver the treatments to addressing organizational and systems barriers to their delivery. Whereas research has confirmed some factors related to implementation success, further methodologically sound research is needed to understand optimal dissemination and implementation strategies to assist providers to use EBTs with a balance between fidelity and flexibility. Advancing the treatment of PTSD in public and private health care systems and with independent providers is critical to improving the lives of traumatized individuals. Implementation science is crucial in this endeavor.

FEATURED ARTICLES

Bass, J.K., Annan, J., McIvor Murray, S., Kaysen, D., Griffiths, S., Cetinoglu, T., . . . Bolton, P.A. (2013). **Controlled trial of psychotherapy for Congolese survivors of sexual violence.** *New England Journal of Medicine, 368*, 2182-2191. doi:10.1056/NEJMoa1211853 Survivors of sexual violence have high rates of depression, anxiety, and PTSD. Although treatment for symptoms related to sexual violence has been shown to be effective in high-income countries, evidence is lacking in low-income, conflict-affected countries. In this trial in the Democratic Republic of Congo, we randomly assigned 16 villages to provide CPT (1 individual session and 11 group sessions) or individual support to female sexual-violence survivors with high levels of PTSD symptoms and combined depression and anxiety symptoms. One village was excluded owing to concern about the competency of the psychosocial assistant, resulting in 7 villages that provided therapy (157 women) and 8 villages that provided individual support (248 women). Assessments of combined depression and anxiety symptoms (average score on the Hopkins Symptom Checklist [range, 0 to 3, with higher scores indicating worse symptoms]), PTSD symptoms (average score on the PTSD Checklist [range, 0 to 3, with higher scores indicating worse symptoms]), and functional impairment (average score across 20 tasks [range, 0 to 4, with higher scores indicating greater impairment]) were performed at baseline, at the end of treatment, and 6 months after treatment ended. A total of 65% of participants in the therapy group and 52% of participants in the individual-support group completed all three assessments. Mean scores for combined depression and anxiety improved in the individual-support group (2.2 at baseline, 1.7 at the end of treatment, and 1.5 at 6 months after treatment), but improvements were significantly greater in the therapy group (2.0 at baseline, 0.8 at the end of treatment, and 0.7 at 6 months after treatment) ($P<0.001$ for all comparisons). Similar patterns were observed

FEATURED ARTICLES *continued*

for PTSD and functional impairment. At 6 months after treatment, 9% of participants in the therapy group and 42% of participants in the individual-support group met criteria for probable depression or anxiety ($P<0.001$), with similar results for PTSD. In this study of sexual-violence survivors in a low-income, conflict-affected country, group psychotherapy reduced PTSD symptoms and combined depression and anxiety symptoms and improved functioning.

Chard, K.M., Ricksecker, E.G., Healy, E.T., Karlin, B.E., & Resick, P.A. (2012). **Dissemination and experience with cognitive processing therapy.** *Journal of Rehabilitation Research and Development, 49*, 667-678. doi:10.1682/JRRD.2011.10.0198 Clinical practice guidelines suggest that cognitive behavioral therapies are recommended for the treatment of PTSD. One of these treatments, CPT, is an EBT that has been shown to be effective at treating combat, assault, and interpersonal violence trauma in randomized controlled trials. The VA Office of Mental Health Services has implemented an initiative to disseminate CPT as part of a broad effort to make evidence-based psychotherapies widely available throughout the VA healthcare system. This article provides an overview of CPT and reviews the efficacy and program evaluation data supporting its use in a variety of settings. In addition, we report on survey data from individuals who have participated in the VA initiative and on outcome data from patients treated by rollout-trained therapists. Our data suggest that many clinicians trained in the rollout show good adoption of the CPT model and demonstrate solid improvements in their patients' PTSD and depressive symptomatology. Finally, we offer recommendations for using CPT in clinical settings.

Cook, J.M., Dinnen, S., Thompson, R., Ruzek, J., Coyne, J.C., & Schnurr, P.P. (2015). **A quantitative test of an implementation framework in 38 VA residential PTSD programs.** *Administration and Policy in Mental Health and Mental Health Services Research, 42*, 462-473. doi:10.1007/s10488-014-0590-0 This study examines the implementation of two evidence-based psychotherapies, PE and CPT, in the VA residential PTSD treatment programs. Two hundred and one providers from 38 programs completed an online survey concerning implementation of PE delivered on an individual basis and CPT delivered in individual and group formats. For PE, a supportive organizational context (dedicated time and resources, and incentives and mandates) and overall positive view of the treatment was related to its implementation. For both group and individual CPT, only the supportive organizational context was significantly associated with outcome. Implications for implementation efforts are discussed.

Couineau, A.-L., & Forbes, D. (2011). **Using predictive models of behavior change to promote evidence-based treatment for PTSD.** *Psychological Trauma: Theory, Research, Practice, and Policy, 3*, 266-275. doi:10.1037/a0024980 While there is a strong evidence base regarding effective treatment of PTSD, and an increased number of treatment guidelines available internationally, research indicates that there is significant variation in clinical practice. This study aimed to identify effective ways to promote adoption of trauma-focused interventions in community services

offering mental health care to people who have experienced trauma. The study sought to do so by identifying factors influencing the uptake of evidence-based practice at both an individual and organizational level, and trialing competency training and support strategies based on these factors across 6 community trauma services. The effectiveness of the training and support strategies was investigated using self-report surveys and prospective recording of clinicians' treatment planning for PTSD clients. The study found that while lack of skills and confidence were identified as significant barriers to the uptake of trauma-focused interventions, expectations about treatment outcomes and organizational factors also influenced clinical behavior. This finding highlighted the importance of considering factors other than knowledge and skills when developing training and other interventions to support the implementation of evidence-based practice. Furthermore, it was found that a training and implementation process tailored to organizational and individual barriers, and based on currently recognized theories of behavior change, led to a significant increase in the use of imaginal exposure in the treatment plans of clients assessed as having PTSD. This change was maintained 6 months following training.

Ebert, L., Malte, C., Hamlett-Berry, K., Beckham, J., McFall, M., & Saxon, A. (2014). **Use of a learning collaborative to support implementation of integrated care for smoking cessation for veterans with posttraumatic stress disorder.** *American Journal of Public Health, 104*, 1935-1942. doi:10.2105/AJPH.2013.301776
We evaluated the feasibility of incorporating integrated care (IC) for smoking cessation into routine treatment for PTSD at the VA Medical Centers and the utility of the Learning Collaborative (LC) model in facilitating implementation. *Methods:* We conducted two LCs aimed at implementing IC for smoking cessation using multidisciplinary teams comprising 70 staff members from 12 VA PTSD clinics. Using questionnaires, we evaluated providers' perceptions of the LC methodology and the effectiveness and feasibility of routine IC delivery. We assessed number of providers delivering and patients receiving IC using medical record data. More than 85% of participating VA staff considered the LC to be an effective training and implementation platform. The majority thought IC effectively addressed an important need and could be delivered in routine PTSD care. All LC participants who planned to deliver IC did so (n = 52). Within 12 months of initial training, an additional 46 locally trained providers delivered IC and 395 Veterans received IC. The LC model effectively facilitated rapid and broad implementation of IC. Facilitators and barriers to sustained use of IC are unknown and should be identified to understand how best to promote ongoing access to EBT for smoking cessation in mental health populations.

Eftekhari, A., Crowley, J.J., Ruzek, J.I., Garvert, D.W., Karlin, B.E., & Rosen, C.S. (2015). **Training in the implementation of prolonged exposure therapy: Provider correlates of treatment outcome.** *Journal of Traumatic Stress, 28*, 65-68. doi:10.1002/jts.21980
The authors examined the degree to which provider characteristics, such as profession, treatment orientation, prior experience in treating PTSD, prior experience with PE therapy, and attitudes about PE, were related to the clinical outcomes of Veterans receiving care from clinicians participating in the national VA PE Training Program. Positive patient outcomes were achieved by providers of every profession, theoretical orientation, level of clinical experience treating PTSD, and prior PE training experience. With 1,105 providers and 32 predictors (13 provider variables), power was at least 90% power to detect an effect of $\beta = .15$. Profession was the only provider characteristic significantly related to outcomes, but the mean effect (a two point difference on the PTSD Checklist) was too small to be clinically meaningful. The results support the intensive training model used in the VA PE training program and demonstrate that clinicians of varying backgrounds can be trained using interactive training workshops followed by case consultation to deliver PE effectively.

Eftekhari, A., Ruzek, J.I., Crowley, J.J., Rosen, C.S., Greenbaum, M.A., & Karlin, B.E. (2013). **Effectiveness of national implementation of prolonged exposure therapy in Veterans Affairs care.** *JAMA Psychiatry, 70*, 949-955. doi:10.1001/jamapsychiatry.2013.36
Importance: PTSD is a pervasive and often debilitating condition that affects many individuals in the general population and military service members. Effective treatments for PTSD are greatly needed for both Veterans returning from Iraq and Afghanistan and Veterans of other eras. PE therapy has been shown to be highly efficacious in clinical trials involving women with noncombat trauma, but there are limited data on its effectiveness in real-world clinical practice settings and with Veterans. *Objective:* To evaluate the effectiveness of PE as implemented with Veterans with PTSD in a large health care system. *Design, Setting, and Participants:* This evaluation included 1931 Veterans treated by 804 clinicians participating in the VA PE Training Program. After completing a 4-day experiential PE training workshop, clinicians implemented PE (while receiving consultation) with a minimum of 2 Veteran patients who had a primary diagnosis of PTSD. *Main Outcomes and Measures:* Changes in PTSD and depression symptoms were assessed with the PTSD Checklist and the Beck Depression Inventory II, measured at baseline and at the final treatment session. Multiple and single imputation were used to estimate the posttest scores of patients who left treatment before completing 8 sessions. Demographic predictors of treatment dropout were also examined. *Results:* Intent-to-treat analyses indicate that PE is effective in reducing symptoms of both PTSD (pre-post $d = 0.87$) and depression (pre-post $d = 0.66$), with effect sizes comparable to those reported in previous efficacy trials. The proportion of patients screening positive for PTSD on the PTSD Checklist decreased from 87.6% to 46.2%. *Conclusions:* Clinically significant reductions in PTSD symptoms were achieved among male and female Veterans of all war eras and Veterans with combat-related and noncombat-related PTSD. Results also indicate that PE is effective in reducing depression symptoms, even though depression is not a direct target of the treatment.

Ehlers, A., Grey, N., Wild, J., Stott, R., Liness, S., Deale, A., . . . Clark, D.M. (2013). **Implementation of cognitive therapy for PTSD in routine clinical care: Effectiveness and moderators of outcome in a consecutive sample.** *Behaviour Research and Therapy, 51*, 742-752. doi:10.1016/j.brat.2013.08.006 Trauma-focused psychological treatments are recommended as first-line treatments for PTSD,

but clinicians may be concerned that the good outcomes observed in RCTs may not generalize to the wide range of traumas and presentations seen in clinical practice. This study investigated whether Cognitive Therapy for PTSD (CT-PTSD) can be effectively implemented into a UK National Health Service Outpatient Clinic serving a defined ethnically mixed urban catchment area. A consecutive sample of 330 patients with PTSD (age 17–83) following a wide range of traumas were treated by 34 therapists, who received training and supervision in CT-PTSD. Pre- and post-treatment data (PTSD symptoms, anxiety, and depression) were collected for all patients, including dropouts. Hierarchical linear modeling investigated candidate moderators of outcome and therapist effects. CT-PTSD was well tolerated and led to very large improvement in PTSD symptoms, depression and anxiety. The majority of patients showed reliable improvement/clinically significant change: intent-to-treat: 78.8%/57.3%; completer: 84.5%/65.1%. Dropouts and unreliable attenders had worse outcome. Statistically reliable symptom exacerbation with treatment was observed in only 1.2% of patients. Treatment gains were maintained during follow-up (M = 280 days, n = 220). Few of the selection criteria used in some RCTs, demographic, diagnostic and trauma characteristics moderated treatment outcome, and only social problems and needing treatment for multiple traumas showed unique moderation effects. There were no random effects of therapist on symptom improvement, but therapists who were inexperienced in CT-PTSD had more dropouts than those with greater experience. The results support the effectiveness of CT-PTSD and suggest that trauma-focused cognitive behavior therapy can be successfully implemented in routine clinical services treating patients with a wide range of traumas.

Jacob, N., Neuner, F., Maedl, A., Schaal, S., & Elbert, T. (2014). **Dissemination of psychotherapy for trauma spectrum disorders in postconflict settings: A randomized controlled trial in Rwanda.** *Psychotherapy and Psychosomatics, 83*, 354-363. doi:10.1159/000365114 *Background:* Dissemination of psychotherapeutic modules to local counselors seems a key requirement for coping with mental health disasters in conflict regions. We tested a train-the-trainer (TTT) dissemination model for the treatment of PTSD. *Methods:* We randomly assigned widowed or orphaned survivors of the 1994 Rwandan genocide with a PTSD diagnosis to narrative exposure therapy (NET) treatment (NET-1, n = 38) or to a 6-month waiting list (WL) condition to be followed by treatment (WL/ NET-2, n = 38). Expert therapists trained a first dissemination generation of local Rwandan psychologists in NET complemented by 2 sessions of interpersonal psychotherapy modules. Under the supervision of the experts, these Rwandan psychologists (a) provided NET to the NET-1 participants and (b) subsequently trained and supervised a second generation of local psychologists. This second dissemination generation provided treatment to the WL/NET-2 group. The primary outcome measure was the Clinician-Administered PTSD Scale total score before therapy and at 3- and 12-month follow-ups. *Results:* At the 3-month follow-up, the NET-1 participants suffered significantly and substantially less from PTSD symptoms than the participants in the WL group. The treatment gains of NET-1 were maintained and increased at follow-up, with a within-group effect size of Cohen's d = 1.47 at the 12-month follow-up. After treatment by the second dissemination generation of therapists, the WL/NET-2 participants improved to an extent similar to that of the NET-1 group at follow-ups, with an effect size of Cohen's d = 1.37 at the 12-month follow-up. *Conclusions:* A TTT model of PTSD treatment dissemination can be effective in resource-poor post-conflict societies.

Kolko, D.J., Baumann, B.L., Herschell, A.D., Hart, J.A., Holden, E.A., & Wisniewski, S.R. (2012). **Implementation of AF-CBT by community practitioners serving child welfare and mental health: A randomized trial.** *Child Maltreatment, 17*, 32-46. doi:10.1177/1077559511427346 The Partnerships for Families project is a randomized clinical trial designed to evaluate the implementation of Alternatives for Families: A CBT (AF-CBT), an EBT for family conflict, coercion, and aggression, including child physical abuse. To evaluate the effectiveness of a training program in this model, 182 community practitioners from 10 agencies were randomized to receive AF-CBT training (n = 90) using a learning community model (workshops, consultation visits) or TAU (n = 92) which provided trainings per agency routine. Practitioners completed self-report measures at four time points (0, 6, 12, and 18 months following baseline). Of those assigned to AF-CBT, 89% participated in at least one training activity and 68% met a "training completion" definition. A total of 80 (44%) practitioners were still active clinicians in the study by 18-month assessment in that they had not met our staff turnover or study withdrawal criteria. Using an intent-to-train design, hierarchical linear modeling analyses revealed significantly greater initial improvements for those in the AF-CBT training condition (vs. TAU condition) in CBT-related knowledge and use of AF-CBT teaching processes, abuse-specific skills, and general psychological skills. In addition, practitioners in both groups reported significantly more negative perceptions of organizational climate through the intervention phase. These significant, albeit modest, findings are discussed in the context of treatment training, research, and work force issues as they relate to the diverse backgrounds, settings, and populations served by community practitioners.

Murray, L.K., Skavenski, S., Kane, J.C., Mayeya, J., Dorsey, S., Cohen, J.A., . . . Bolton, P.A. (2015). **Effectiveness of trauma-focused cognitive behavioral therapy among trauma-affected children in Lusaka, Zambia: A randomized clinical trial.** *JAMA Pediatrics.* doi:10.1001/jamapediatrics.2015.0580 Orphans and vulnerable children (OVC) are at high risk for experiencing trauma and related psychosocial problems. Despite this, no randomized clinical trials have studied EBTs for OVC in low-resource settings. To evaluate the effectiveness of lay counselor-provided TF-CBT to address trauma and stress-related symptoms among OVC in Lusaka, Zambia. This randomized clinical trial compared TF-CBT and treatment as usual (TAU) (varying by site) for children recruited from August 1, 2012, through July 31, 2013, and treated until December 31, 2013, for trauma-related symptoms from five community sites within Lusaka, Zambia. Children were aged 5 through 18 years and had experienced at least one traumatic event and reported significant trauma-related symptoms. Analysis was with intent to treat. The intervention group received 10 to 16 sessions of TF-CBT (n = 131). The TAU group (n = 126) received usual community services offered to OVC. The primary outcome

was mean item change in trauma and stress-related symptoms using a locally validated version of the UCLA Posttraumatic Stress Disorder Reaction Index (range, 0-4) and functional impairment using a locally developed measure (range, 0-4). Outcomes were measured at baseline and within 1 month after treatment completion or after a waiting period of approximately 4.5 months after baseline for TAU. At follow-up, the mean item change in trauma symptom score was −1.54 (95% CI, −1.81 to −1.27), a reduction of 81.9%, for the TF-CBT group and −0.37 (95% CI, −0.57 to −0.17), a reduction of 21.1%, for the TAU group. The mean item change for functioning was −0.76 (95% CI, −0.98 to −0.54), a reduction of 89.4%, and −0.54 (95% CI, −0.80 to −0.29), a reduction of 68.3%, for the TF-CBT and TAU groups, respectively. The difference in change between groups was statistically significant for both outcomes ($P < .001$). The effect size (Cohen *d*) was 2.39 for trauma symptoms and 0.34 for functioning. Lay counselors participated in supervision and assessed whether the intervention was provided with fidelity in all 5 community settings. The TF-CBT adapted for Zambia substantially decreased trauma and stress-related symptoms and produced a smaller improvement in functional impairment among OVC having experienced high levels of trauma.

Ruzek, J.I., & Rosen, R.C. (2009). **Disseminating evidence-based treatments for PTSD in organizational settings: A high priority focus area.** *Behaviour Research and Therapy, 47*, 980-989. doi:10.1016/j.brat.2009.07.008 Dissemination of EBTs for PTSD has become an important focus of activity in the aftermath of recent terrorist attacks (e.g., London underground and US 9/11 attacks), natural disasters (e.g., Indian Ocean tsunami and Hurricane Katrina), and wars (e.g., in Iraq and Afghanistan). This has become a high-priority need for all mental health training and service delivery organizations. Researchers and educators have begun to examine clinician and client perceptions and preferences regarding PTSD treatment processes, and health care systems are organizing more comprehensive efforts at training and system change. As this evolution of services moves forward, effective dissemination should be a major focus of health policy research for the next decade or more. This review critically evaluates the PTSD-related research and emerging theory related to four major sets of variables that affect dissemination: (1) Practitioner factors, (2) Training methods, (3) The practice innovation(s) being disseminated; and (4) Organization or system factors. We evaluate findings from recent studies in light of emerging models of dissemination, and in the final section of the paper, we consider five broad topics with particular implications for dissemination of PTSD-specific treatments. They are: (1) The content of dissemination (i.e., which treatment protocols or intervention methods should be prioritized); (2) Strict adherence versus flexibility in the use of treatment manuals and the role of fidelity assessment; (3) The need for collaboration with user audiences; (4) The potential role of web-based technologies in increasing the effectiveness and efficiency of dissemination; and (5) Development of dissemination infrastructures within organizations.

Schumm, J.A., Walter, K.H., Bartone, A.S., & Chard, K.M. (2015). **Veteran satisfaction and treatment preferences in response to a posttraumatic stress disorder specialty clinic orientation group.** *Behaviour Research and Therapy, 69*, 75-82. doi:10.1016/j.brat.2015.04.006 To maximize accessibility to EBTs for PTSD, the VA has widely disseminated CPT and PE therapy to VA clinicians. However, there is a lack of research on Veteran preferences when presented with a range of psychotherapy and medication options. This study uses a mixed-method approach to explore Veteran satisfaction with a VA PTSD specialty clinic pre-treatment orientation group, which provides education about available PTSD treatment options. This study also tested differences in treatment preference in response to the group. Participants were 183 US Veterans. Most were White, male, and referred to the clinic by a VA provider. Results indicated high satisfaction with the group in providing an overview of services and helping to inform treatment choice. Most preferred psychotherapy plus medications (63.4%) or psychotherapy only (30.1%). Participants endorsed a significantly stronger preference for CPT versus other psychotherapies. PE was significantly preferred over nightmare resolution therapy and present-centered therapy, and both PE and cognitive-behavioral conjoint therapy were preferred over virtual reality exposure therapy. Results suggest that by informing consumers about EBTs for PTSD, pre-treatment educational approaches may increase consumer demand for these treatment options.

Shiner, B., D'Avolio, L.W., Nguyen, T.M., Zayed, M.H., Young-Xu, Y., Desai, R.A., . . . Watts, B.V. (2013). **Measuring use of evidence based psychotherapy for posttraumatic stress disorder.** *Administration and Policy in Mental Health and Mental Health Services Research, 40*, 311-318. doi:10.1007/s10488-012-0421-0 To improve methods of estimating use of evidence-based psychotherapy for PTSD in the Veteran's health administration, we evaluated administrative data and note text for patients newly enrolling in six Veterans Health Administration (VHA) outpatient PTSD clinics in New England during the 2010 fiscal year (n = 1,924). Using natural language processing, we developed machine learning algorithms that mimic human raters in classifying note text. We met our targets for algorithm performance as measured by precision, recall, and F-measure. We found that 6.3 % of our study population received at least one session of evidence-based psychotherapy during the initial 6 months of treatment. Evidence-based psychotherapies appear to be infrequently utilized in VHA outpatient PTSD clinics in New England. Our method could support efforts to improve use of these treatments.

Watts, B.V., Shiner, B., Zubkoff, L., Carpenter-Song, E., Ronconi, J.M., & Coldwell, C.M. (2014). **Implementation of evidence-based psychotherapies for posttraumatic stress disorder in VA specialty clinics. Psychiatric Services, 65**, 648-653. doi:10.1176/appi.ps.201300176 *Objectives:* The VA has engaged in substantial efforts to promote the use of evidence-based psychotherapies for PTSD. The authors evaluated the effectiveness of these efforts. *Methods:* This study used a cross-sectional, mixed-methods evaluation of treatment provided by the VA at specialty PTSD clinics in New England during the first six months of fiscal year 2010. Natural language processing algorithms were applied to clinical notes to determine utilization of evidence-based psychotherapy (prolonged exposure therapy and cognitive-processing therapy) among patients who were newly diagnosed as having PTSD.

FEATURED ARTICLES *continued*

Data regarding efforts to implement evidence-based psychotherapy and other clinic characteristics were obtained through qualitative interviews with clinical and administrative staff (*N* = 30), and the Promoting Action on Research Implementation in Health Services framework was used to identify clinic factors associated with use of evidence-based psychotherapy. *Results:* Six percent of patients (*N* = 1,924) received any sessions of an evidence-based psychotherapy for PTSD (median=five sessions). Several clinic factors were associated with an increased rate of implementation, including prior experience with use of the treatments, customization of training, and prolonged contact with the implementation and training team. Facilitation with broad training goals and clinics with highly organized systems of care were negatively associated with implementation. *Conclusions:* Few patients with PTSD received evidence-based psychotherapy for PTSD during their first six months of treatment at a VA specialty PTSD clinic. The implementation framework poorly predicted factors associated with uptake of evidence-based psychotherapy. These results suggest that additional research is needed to understand implementation of evidence-based therapy in mental health settings.

ADDITIONAL CITATIONS

CATS Consortium. (2007). **Implementing CBT for traumatized children and adolescents after September 11: Lessons learned from the Child and Adolescent Trauma Treatments and Services (CATS) Project.** *Journal of Clinical Child and Adolescent Psychology, 36*, 581-592. doi:10.1080/15374410701662725 The Child and Adolescent Trauma Treatments and Services Consortium (CATS) was the largest youth trauma project associated with the September 11 World Trade Center disaster, created as a collaborative project involving New York State policymakers; academic scientists; clinical treatment developers; and routine practicing clinicians, supervisors, and administrators. The CATS project was established to deliver evidence-based cognitive-behavioral trauma treatments for children and adolescents affected by the September 11 terrorist attack in New York City and to examine implementation processes and outcomes associated with delivery of these treatments. This article outlines the major challenges, describes strategies CATS employed to address them, and makes recommendations based on critical lessons learned.

Cook, J.M., Dinnen, S., Simiola, V., Thompson, R., & Schnurr, P.P. (2014). **VA residential provider perceptions of dissuading factors to the use of two evidence-based PTSD treatments.** *Professional Psychology: Research and Practice, 45*, 136-142. doi:10.1037/a0036183 Providers (*N* = 198) from 38 Department of Veterans Affairs residential PTSD treatment programs across the US completed qualitative interviews regarding implementation of two EBTs: prolonged exposure and cognitive processing therapy. Many indicated that they did not perceive any patient factors that dissuaded their use of either evidence-based treatment, but three broad categories emerged regarding perceived suitability candidates for treatment: the presence of psychiatric comorbidities, cognitive limitations, and low levels of patient motivation.

ADDITIONAL CITATIONS *continued*

Cook, J.M., O'Donnell, C., Dinnen, S.D. Coyne, J.C., Ruzek, J.I., & Schnurr, P.P. (2012). **Measurement of a model of implementation for health care: Toward a testable theory.** *Implementation Science, 7*, 59. doi:10.1186/1748-5908-7-59 The present paper represents a first step in operationalizing Greenhalgh et al.'s model of implementation of innovations in health care organizations (2004) by providing background, rationale, working definitions and measurement of key constructs. A systematic review of the literature and iterative process of team consensus identified three types of data that can be used to operationalize the constructs in the model: survey items, interview questions and administrative data. Testing of psychometric properties and subsequent refinement should enhance the utility of the measures.

Cook, J.M., Thompson, R., & Schnurr, P.P. (in press). **Perceived Characteristics of Intervention Scale: Development and psychometric properties.** *Assessment.* doi:10.1177/1073191114561254 The Perceived Characteristics of Intervention Scale (PCIS), a 20-item assessment measure was developed to assess health care providers' views of interventions. In a study with two hundred and fifteen Department of Veterans Affairs' residential treatment providers from 38 programs across the United States, the PCIS was demonstrated to be a reliable measure of perceived characteristics of interventions, with some preliminary support for its validity.

Dorsey, S., Pullmann, M.D., Deblinger, E., Berliner, L., Kerns, S.E., Thompson, K., . . . Garland, A.F. (2013). **Improving practice in community-based settings: A randomized trial of supervision – study protocol.** *Implementation Science, 8*, 89. doi:10.1186/1748-5908-8-89 This current federally-funded investigation leverages the Washington State Trauma-Focused Cognitive Behavioral Therapy Initiative to describe usual supervision practices and to test the impact of systematic implementation of gold standard supervision strategies on treatment fidelity and clinical outcomes. Study results will provide insight into how supervisors can optimally support clinicians delivering EBTs, and will be one of the first experimental studies of gold standard supervision strategies in community mental health, yielding needed information about how to leverage supervision to improve clinician fidelity and client outcomes.

Ebert, L., Amaya-Jackson, L., Markiewicz, J.M., Kisiel, C., & Fairbank, J.A. (2012). **Use of the Breakthrough Series Collaborative to support broad and sustained use of evidence-based trauma treatment for children in community practice settings.** *Administration and Policy in Mental Health and Mental Health Services Research, 39*, 187-199. doi:10.1007/s10488-011-0347-y This observational study evaluates the feasibility and utility of adapting the Institute for Healthcare's Breakthrough Series Collaborative (BSC) to support the broad implementation and sustained use of TF-CBT in community practice settings. Study findings indicated that agency staff in diverse roles viewed the BSC methodology as a valuable practicable, and potentially effective approach for facilitating skillful delivery of TF-CBT with fidelity.

ADDITIONAL CITATIONS *continued*

Finley, E.P., Garcia, H.A., Ketchum, N.S., McGeary, D.D., McGeary, C.A., Stirman, S.W., & Peterson, A.L. (2015). **Utilization of evidence-based psychotherapies in Veterans Affairs posttraumatic stress disorder outpatient clinics.** *Psychological Services, 12*, 73-82. doi:10.1037/ser0000014 A national survey of providers (N = 128) within VA PTSD clinical teams (PCTs) was conducted to describe utilization of PE and CPT and to identify individual and organizational factors associated with treatment uptake and adherence. Perceived effectiveness of PE and CPT were significantly associated with utilization of and adherence to those treatments. Reported number of hours conducting supportive care was positively associated with feeling the clinic was not sufficiently staffed (p = .05), and adherence to the PE treatment manual was positively associated with receiving emotional support from coworkers (p < .01).

Hamblen, J.L., Bernardy, N.C., Sherrieb, K, Norris, F.H., Cook, J.M., Louis, C.A., & Schnurr, P.P. (2015). **VA PTSD clinic director perspectives: How perceptions of readiness influence delivery of evidence-based PTSD treatment.** *Professional Psychology: Research and Practice, 46*, 90-96. doi:10.1037/a0038535 Qualitative interviews were conducted with a nationally representative sample of 38 directors of specialized PTSD outpatient programs in VA medical centers about implementation of two EBTs. While every director confirmed that EBTs, specifically prolonged exposure and cognitive processing therapy, were provided in their program, it was nearly universal for these treatments to be preceded by preparatory groups. The concept of readiness for trauma-focused EBTs guided program development and flow throughout the programs.

Hanson, R.F., Gros, K.S., Davidson, T.M., Barr, S., Cohen, J., Deblinger, E., . . . Ruggiero, K J. (2014). **National trainers' perspectives on challenges to implementation of an empirically supported mental health treatment.** *Administration and Policy in Mental Health and Mental Health Services Research, 41*, 522-534. doi:10.1007/s10488-013-0492-6 Thematic interviews were conducted with 19 approved national (TF-CBT) trainers to assess their perspectives about challenges to implementation of TF-CBT and to explore their perceptions about the potential value of innovative, technology-based solutions to enhance provider fidelity and improve quality of care. These data offer some important insights and implications for training in EBTs, provider fidelity and competence, and patient engagement, particularly for those interventions targeting trauma-related symptoms among youth.

Karlin, B.E., Ruzek, J.I., Chard, K.M., Eftekhari, A., Monson, C.M., Hembree, E.A., . . . Foa, E.B. (2010). **Dissemination of evidence-based psychological treatments for posttraumatic stress disorder in the Veterans Health Administration.** *Journal of Traumatic Stress, 23*, 663-673. doi:10.1002/jts.20588 The VA has developed national initiatives to train mental health staff in the delivery of CPT and PE therapy and has implemented a variety of strategies to promote local implementation. In this article, the authors examine VA's national CPT and PE training initiatives and report initial patient, therapist, and system-level program evaluation results.

Meyers, L.L., Strom, T.Q., Leskela, J., Thuras, P., Kehle-Forbes, S.M., & Curry, K.T. (2013). **Service utilization following participation in cognitive processing therapy or prolonged exposure therapy for post-traumatic stress disorder.** *Military Medicine, 178*, 95-99. doi:10.7205/MILMED-D-12-00302 Data on VA health service utilization and health care costs were obtained from national VA databases for 70 Veterans who completed prolonged exposure or cognitive processing therapy at a Midwestern VA medical center. Results demonstrated a significant decrease in the use of individual and group psychotherapy, as well as a 39.4% decrease in direct costs associated with mental health care. Primary care and emergency department services remained unchanged.

Mott, J.M., Stanley, M.A., Street, R.L., Grady, R.H., & Teng, E.J. (2014). **Increasing engagement in evidence-based PTSD treatment through shared decision-making: A pilot study.** *Military Medicine, 179*, 143-149. doi:10.7205/MILMED-D-13-00363 This study sought to develop (phase 1) and pilot test the feasibility and potential effectiveness (phase 2) of a brief shared decision-making intervention to promote engagement in evidence-based PTSD treatment. Among the 20 study completers, a greater proportion of participants in the intervention condition preferred an EBT and received an adequate (≥9 sessions) dose of psychotherapy.

Powell, B J., Waltz, T.J., Chinman, M.J., Damschroder, L J., Smith, J.L., Matthieu, M.M., . . . Kirchner, J.E. (2015). **A refined compilation of implementation strategies: Results from the Expert Recommendations for Implementing Change (ERIC) project.** Implementation Science, 10, 21. doi:10.1186/s13012-015-0209-1 Using a modified Delphi process, a panel of experts in implementation and clinical practice generated consensus on 73 implementation strategies and definitions. This list can be helpful in constructing multifaceted, multilevel implementation strategies for implementation efforts or comparative effectiveness research.

Ruzek, J.I., Rosen, R.C., Garvert, D.W., Smith, L.D., Sears, K.C., Marceau, L., . . . Stoddard, A.M. (2014). **Online self-administered training of PTSD treatment providers in cognitive–behavioral intervention skills: Results of a randomized controlled trial.** *Journal of Traumatic Stress, 27*, 703-711. doi:10.1002/jts.21977 This study compared web-based training in 3 intervention skills (motivation enhancement [ME], goal setting [GS], behavioral task assignment [BTA]) with web-based training plus telephone consultation, and a no-training control. The overall tests of differences among the groups were statistically significant for ME and BTA skills (p < .001 and p = .005, respectively), but not for GS (p = .245). Overall, these findings support the use of web-based dissemination for large-scale training programs for trauma providers in health care delivery systems.

Sigel, B.A., Benton, A.H., Lynch, C.E., & Kramer, T.L. (2013). **Characteristics of 17 statewide initiatives to disseminate trauma-focused cognitive-behavioral therapy (TF-CBT).** *Psychological Trauma: Theory, Research, Practice, and Policy, 5*, 323-333. doi:10.1037/a0029095 The purpose of this study was to explore large-scale initiatives and dissemination models in the United States to promote TF-CBT, an evidence-based practice

ADDITIONAL CITATIONS *continued*

for childhood PTSD. Approximate total costs, approximate number of therapists trained, and duration of training and consultation ranged considerably across 17 statewide projects. Differences between two dissemination models in duration of training and approximate number of trained therapists were noted; however, approximate funding per year, and approximate total costs did not differ between the two models.

Stirman, S.W., Shields, N., Deloriea, J., Landy, M.S.H., Belus, J.M., Maslej, M.M., & Monson, C.M. (2013). **A randomized controlled dismantling trial of post-workshop consultation strategies to increase effectiveness and fidelity to an evidence-based psychotherapy for posttraumatic stress disorder.** *Implementation Science, 8*, 82. doi:10.1186/1748-5908-8-82 This study investigates whether clinicians receiving different forms of post-workshop support (six-month duration) will deliver CPT with greater fidelity (i.e., psychotherapy adherence and competence) and have improved patient outcomes compared with clinicians receiving no formal post-workshop support. The study results will inform how best to implement and transfer evidence-based psychotherapy (e.g., CPT) to clinical settings to attain comparable outcomes to those observed in research settings.

Tabak, R.G., Khoong, E.C., Chambers, D.A., & Brownson, R.C. (2012). **Bridging research and practice: Models for dissemination and implementation research.** *American Journal of Preventive Medicine, 43*, 337-350. doi:10.1016/j.amepre.2012.05.024 This paper provides a synthesis of 61 implementation theories and frameworks used in research. These findings provide guidance on how to select a model to inform implementation science study design and execution.

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New Research in Treating Child and Adolescent Trauma

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Research into the effective treatment of child and adolescent PTSD continues to blossom. The expanding quality and scope of child PTSD randomized controlled trials (RCT) published or in press between January 2012 and June 2015 are the primary focuses of this commentary.

Increasingly, researchers are attempting to *prevent* the development of pediatric PTSD. The only existing such evidence-based intervention prevents the development of chronic PTSD (Berkowitz et al., 2011). In 2014, Kramer & Landolt compared an early, two session cognitive behavioral therapy (CBT) to treatment as usual (TAU) for two 16-year-old children at elevated risk for developing PTSD following road accidents or burns. Preschool children did not show significant benefit from the intervention, but school-aged children who received the intervention had significantly fewer internalizing symptoms and marginally lower PTSD intrusion symptoms at a 3-month follow-up compared to children in the TAU condition. This is the first study that provided *an entire intervention* within the first month after trauma exposure. The extreme brevity of the intervention and promising results suggest the potential for very early brief CBT interventions to prevent the development of PTSD in children and adolescents. More studies like this are needed; especially as new methods (e.g., biomarkers) become available to identify high-risk children. Kassam-Adams and colleagues (2013) provide an excellent overview of preventive intervention models including risk factors, likely effective components and the need for early identification and referral.

Since children are typically brought to treatment by caregivers who are seeking treatment for negative child behaviors rather than children's trauma experiences per se, engaging families in trauma treatment can be challenging. Two recent studies provide insight into successful strategies for retaining families in trauma treatment. In the first, Dorsey and colleagues (2014) randomized 47 children and adolescents in foster care with one of their foster parents to receive either standard Trauma-Focused Cognitive Behavioral Therapy (TF-CBT); or TF-CBT with enhanced evidence-based engagement strategies. Youth and foster parents who received the enhanced engagement strategies were significantly more likely to be retained in therapy through four sessions and were less likely to drop out of treatment prematurely. In a smaller study, Saxe and colleagues (2012) randomized 20 youth with prominent PTSD symptoms to Trauma Systems Therapy (TST) or care as usual (CAU). At three-month assessment, 90% of the youth in the TST condition were still in treatment while only 10% of the CAU youth remained in treatment, documenting the effectiveness of TST for retaining youth in treatment. Together these studies provide therapists with important information about how to successfully engage families in evidence-based trauma treatment.

Several international studies are evaluating evidence-based treatments across cultures, settings and trauma experiences. Jensen and colleagues (2014) randomized 156 Norwegian youth ages 10-18 years who had experienced diverse traumas, to TF-CBT or TAU in eight community treatment centers across Norway. Results indicated that youth receiving TF-CBT experienced significantly greater improvement in PTSD, depression and general mental health symptoms and significantly greater improvement in functional impairment compared to youth receiving TAU. Interestingly, the authors found that therapeutic alliance predicted positive child outcomes only in the TF-CBT condition (Ormhaug et al., 2014).

Murray and colleagues (2015) randomized 257 orphans and vulnerable Zambian children (OVC)

Continued on page 2

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Continued from cover

ages 5-17 years to TF-CBT provided by trained lay counselors, or to TAU. The TF-CBT group experienced significantly greater improvement in PTSD and functional impairment than the TAU group. This study used gold standard mixed methodologies for developing locally validated assessment instruments.

In companion RCTs, O'Callaghan, McMullen, and colleagues culturally modified TF-CBT for group delivery to youth with complex trauma in the Democratic Republic of Congo. Sexually exploited girls ages 12-17 were randomized to group TF-CBT provided in thrice weekly sessions over 5 weeks by trained lay counselors, or a wait list control group (WL; O'Callaghan et al., 2013). The TF-CBT group experienced significantly greater improvement in PTSD, depression, anxiety, conduct problems, psychosocial distress, and pro-social behaviors. Former boy soldiers and other war-affected boys ages 13-17 years were randomized to receive group TF-CBT provided by lay counselors or a WL control (McMullen et al., 2013). Youth receiving TF-CBT experienced significantly greater improvement in PTSD, depression, anxiety, conduct problems, psychosocial distress and pro-social behaviors compared to the WL group. In both studies treatment effects for the TF-CBT groups were maintained over a 3-month follow-up period. The cultural modifications to the TF-CBT model in the Congolese and Zambian studies were modest (e.g., using local folktales as metaphors during psychoeducation; incorporating the importance of witchcraft during cognitive processing; addressing cultural reluctance to discuss sexuality as prelude to education about healthy sexuality and developing trauma narration).

Two quasi-randomized controlled trials conducted in schools evaluated interventions for children impacted by the conflict in the Middle East. Barron and colleagues (2013) randomized children in Nablus, Palestine ages 11-14 by classroom to receive Teaching Recovery Techniques (TRT), a CBT school-based group intervention, or a WL control condition. Children did not differ significantly on demographic or mental health variables at pre-treatment; Analysis of Covariance (ANCOVA) indicated significant group X time differences in favor of the TRT group with regard to PTSD, grief and depression, supporting the efficacy of the TRT model for children exposed to ongoing violence. In the second study, Berger and colleagues (2012) used a quasi-randomized controlled design to assign 154 7th and 8th graders in Sderot, Israel to receive Extended Enhancing Resiliency Amongst Students Experiencing Stress (ERASE-Stress), a manualized, universal teacher-delivered skills-based program that does not target traumatic memories, or a WL control group. At baseline, 43.5% of students had a likely diagnosis of PTSD. One month after the intervention, students in ERASE-Stress had statistically significantly greater reduction in PTSD, anxiety, somatic complaints, and functional impairment scores compared to the WL group.

Finally, a Dutch team conducted a RCT to directly compare outcomes of Eye Movement Desensitization and Reprocessing (EMDR) and TF-CBT. This study also has relevance to complex trauma, which is discussed in more detail below. EMDR is widely used in many European countries and there is a strong belief that it is more efficient than other treatments for resolving PTSD symptoms. Diehle and colleagues (2015) randomized 40 traumatized Dutch children ages 8-19 years to TF-CBT or EMDR. Both treatments were highly effective for improving PTSD symptoms. However, contrary to the researchers' hypothesis, there was no significant difference in efficiency between the treatments. As predicted, children receiving TF-CBT experienced significantly greater improvement in comorbid problems common in complex trauma than children receiving EMDR, including depressive and hyperactive symptoms.

Back in the United States (US), lively discussion continues regarding the Diagnostic and Statistical Manual of Mental Disorders (DSM) PTSD diagnostic criteria for children and adolescents, and its impact on treatment outcome research. Specifically, since no single diagnosis or assessment instrument fully describes youth with complicated trauma presentations, researchers are using creative strategies to design treatment outcome studies for this population. Ford and colleagues (2012) evaluated Trauma Affect Regulation: Guide for Education and Therapy (TARGET), an emotion regulation therapy for complex trauma. This team randomized 59 delinquent girls ages 13-17 years who met full or partial PTSD diagnostic criteria to receive TARGET or enhanced TAU (ETAU), a relational supportive therapy. Almost half of these girls were in residential treatment during treatment, making this a very challenging study to conduct, since residential treatment facilities for adjudicated youth exist to address severe behavioral problems and typically are not focused on providing trauma services. Multiple instruments were used to assess diverse outcomes. Group X Time analyses showed significantly greater improvement in youth receiving TARGET for changes in PTSD, emotion regulation, anxiety and posttraumatic cognitions, but there was also improvement in the ETAU cohort with respect to hope and anger management. This study documented the promise of using evidence-based trauma treatments for traumatized youth within the juvenile justice system, and highlighted the importance of carefully evaluating how trauma impacts these youth's complex clinical presentations. Studies like this and a previous TF-CBT deconstructive study (Deblinger et al., 2011) suggest the possibility of matching treatments to individual children's presenting problems.

It is difficult to untangle the question of how to treat complicated PTSD from the issue of how to address co-occurring psychiatric conditions such as substance abuse, violence and risk behaviors. Two important studies address these questions. The first study evaluated the efficacy of Risk Reduction through Family Therapy (RRTF), a modification of TF-CBT for youth with substance abuse. Danielson and colleagues randomized 30 adolescents with comorbid sexual assault history and substance abuse history to RRTF or TAU (Danielson et al., 2012). Multiple instruments assessed substance abuse, family and mental health outcomes in addition to PTSD. Mixed effects regressions showed that the RRTF group experienced significantly greater improvement in PTSD, depression, substance use, and internalizing symptoms than the WL group, but because of baseline differences in symptom severity we need to be cautious before drawing conclusions about effectiveness from this pilot study.

The second study evaluated a collaborative care model targeting violence risk behaviors, substance abuse, PTSD and depression in youth who were hospitalized after acute physical injuries (Zatzick et al., 2014). The intervention included motivational interviewing targeting risk behaviors and substance use as well as medication and CBT targeting PTSD and depression. At a level 1 trauma center, 120, 12 to 18-year-olds were randomized

to the collaborative care intervention or a no-treatment control. Follow-ups at 2, 5, and 12 months used standard instruments for violence risk behaviors, substance use, PTSD and depression. At baseline, a third of the youth endorsed carrying a weapon. The intervention group experienced significantly greater reductions in weapon carrying compared to controls during the year after injury. Other outcomes were not significantly different. The lack of significant differences on other outcomes may have been due to the fact that reported baseline symptoms were low relative to weapon carrying.

Since most children and adolescents attend school, providing trauma screening and treatment in these settings offers and important opportunity for meeting the needs of children who otherwise would not receive services (Kataoka et al., 2012). A study by Foa et al. (2013) highlights the value of embedding existing evidence based treatments in usual community provider organizations and shows the effectiveness of one such treatment, Prolonged Exposure, for adolescents.

Empirical evidence from the few well controlled, scientifically rigorous studies conducted to date has failed to support the efficacy of any pharmacologic agent in improving PTSD symptoms in children an excellent review is provided in Wilkinson & Carrion (2012). Despite this, psychotropic medications are often used to treat traumatized children; particularly those involved in the child welfare and juvenile justice systems. The following study is important because it offers potentially promising data. Scheeringa & Weems (2014) provided children ages 7-18 with PTSD with a 12 session CBT manualized treatment. Those remaining in treatment at session 5 (N = 57) were randomized to CBT + D-Cycloserine (DSC) or CBT+ Placebo. DSC may enhance exposure-based therapies for anxiety as a partial NDMA agonist. Results showed no significant differences between the two groups, however, there was a trend toward DSC speeding recovery during the exposure sessions of CBT and evidence that the CBT+DSC group sustained greater improvement in inattention than the CBT + Placebo group at 3-month follow-up. This finding is of potential significance for children with comorbid PTSD and Attention Deficit Hyperactivity Disorder, or for those with PTSD-related inattention. More research into the use of DSC for augmenting CBT treatment in children and adolescents is warranted.

Finally, therapists can only provide face-to-face treatment for a small fraction of the traumatized children around the world. Web-based treatment offers the possibility of greatly magnifying the reach of therapist-delivered evidence-based treatment. Marsac and colleagues (2013) describe an ongoing RCT to test a game for preventive intervention following acute injury. No doubt more tablet, smart phone, and computer-assisted options are coming for children to access trauma treatment. For example, the TF-CBT Triangle of Life, for implementing TF-CBT cognitive processing, is now available from Google+ and Apple stores. From promising new preventive interventions for acute trauma to the growing number of evidence-based treatments for complex trauma presentations across the developmental spectrum, to technological applications to assist in treatment implementation, the future of child trauma treatment looks bright.

FEATURED ARTICLES

Barron, I. G., Abdallah, G., & Smith, P.A. (2013). **Randomized control trial of a CBT trauma recovery program in Palestinian schools.** *Journal of Loss and Trauma, 18*, 306-321. doi:10.1080/15325024.2012.688712 The current study aimed to assess the TRT trauma recovery program within the context of ongoing violence. Utilizing a randomized controlled trial, 11-14-year-old students in Nablus, Palestine, were allocated by class to intervention or wait-list control conditions. Standardized measures assessed trauma exposure, PTSD, grief, and depression. Program fidelity and participant experiences were measured by adherence questionnaires and focus groups. Analyses involved paired t-tests, ANCOVAs, and thematic analysis. Intervention students reported significant decreases in PTSD, grief, and depression. Findings indicate that the TRT program has the potential to ameliorate children's trauma symptoms during situations of ongoing violence.

Berger, R., Gelkopf, M., & Heineberg, Y. (2012). **A teacher-delivered intervention for adolescents exposed to ongoing and intense traumatic war-related stress: A quasi-randomized controlled study.** *Journal of Adolescent Health, 51*, 453-461. doi:10.1016/j.jadohealth.2012.02.011 *Purpose:* For the past 8 years, the residents of Sderot — a town in southern Israel — have been exposed to ongoing and intense war-related threat due to daily rocket attacks and mortar shelling from the adjacent Gaza region. This study first evaluates the prevalence of posttraumatic symptomatology in a sample of seventh- and eighth-grade students, and then assesses the efficacy of a universal teacher-delivered skill-oriented and present-focused intervention in preventing and reducing adolescents' posttraumatic stress-related symptoms. *Method:* In a quasi-randomized controlled trial, 154 seventh- and eighth-grade students with significant levels of war-related exposure were assigned to participate in either a manualized active 16-session intervention (ERASE-Stress) or a waiting-list control group. They were assessed using self-report measures before and after the intervention on posttraumatic stress-related symptoms, somatic complaints, functional impairment, and anxiety. *Results:* At baseline, 43.5% were found to have a likely diagnosis of PTSD. A month after the intervention ended, students in the active intervention showed statistically significant reduction on all outcome measures compared with those in the waiting-list control group. *Conclusions:* Extended ERASE-Stress — a universal teacher-delivered skill-oriented program not targeting traumatic memories and involving trained and supervised homeroom teachers — may help students suffering from significant war-related posttraumatic symptoms reduce their level of symptomatology and can serve as an important and effective component of a community mental health policy for communities affected by chronic trauma, such as war and terrorism.

Danielson, C.K., McCart, M.R., Walsh, K., de Arellano, M.A., White, D., & Resnick, H.S. (2012). **Reducing substance use risk and mental health problems among sexually assaulted adolescents: A pilot randomized controlled trial.** *Journal of Family Psychology, 26*, 628-635. doi:10.1037/a0028862 The current study reports results from a pilot randomized controlled trial evaluating the feasibility and

efficacy of Risk Reduction through Family Therapy (RRFT) for reducing substance use risk and trauma-related mental health problems among sexually assaulted adolescents. Thirty adolescents (aged 13–17 years; *M* = 14.80; SD = 1.51) who had experienced at least one sexual assault and their caregivers were randomized to RRFT or TAU conditions. Participants completed measures of substance use, substance use risk factors (e.g., family functioning), mental health problems (i.e., PTSD, depression, and general internalizing/externalizing symptoms) and risky sexual behavior at four time points (baseline, post treatment, and 3- and 6-month follow-up). Mixed-effects regression models yielded significantly greater reductions in substance use, specific substance use risk factors, and (parent-reported) PTSD, depression, and general internalizing symptoms among youth in the RRFT condition relative to youth in the TAU condition. However, significant baseline differences in functioning between the two conditions warrant caution in interpreting between-groups findings. Instead, emphasis is placed on replication of feasibility findings and within-group improvements over time among the RRFT youth.

Diehle, J., Opmeer, B. C., Boer, F., Mannarino, A. P., & Lindauer, R. J. L. (2015). T**rauma-focused cognitive behavioral therapy or eye movement desensitization and reprocessing: What works in children with posttraumatic stress symptoms? A randomized controlled trial.** *European Child & Adolescent Psychiatry, 24*, 227-236. doi:10.1007/s00787-014-0572-5 To prevent adverse long-term effects, children who suffer from posttraumatic stress symptoms (PTSS) need treatment. Trauma-focused cognitive behavioral therapy (TF-CBT) is an established treatment for children with PTSS. However, alternatives are important for non-responders or if TF-CBT trained therapists are unavailable. Eye movement desensitization and reprocessing (EMDR) is a promising treatment for which sound comparative evidence is lacking. The current randomized controlled trial investigates the effectiveness and efficiency of both treatments. Forty-eight children (8–18 years) were randomly assigned to eight sessions of TF-CBT or EMDR. The primary outcome was PTSS as measured with the Clinician-Administered PTSD Scale for Children and Adolescents (CAPS-CA). Secondary outcomes included parental report of child PTSD diagnosis status and questionnaires on comorbid problems. The Children's Revised Impact of Event Scale was administered during the course of treatment. TF-CBT and EMDR showed large reductions from pre- to post-treatment on the CAPS-CA (–20.2; 95 % CI –12.2 to –28.1 and –20.9; 95 % CI –32.7 to –9.1). The difference in reduction was small and not statistically significant (mean difference of 0.69, 95 % CI –13.4 to 14.8). Treatment duration was not significantly shorter for EMDR (p = 0.09). Mixed model analysis of monitored PTSS during treatment showed a significant effect for time ($p < 0.001$) but not for treatment (p = 0.44) or the interaction of time by treatment (p = 0.74). Parents of children treated with TF-CBT reported a significant reduction of comorbid depressive and hyperactive symptoms. TF-CBT and EMDR are effective and efficient in reducing PTSS in children.

Dorsey, S., Pullmann, M. D., Berliner, L., Koschmann, E., McKay, M. M., & Deblinger, E. (2014). **Engaging foster parents in treatment: A randomized trial of supplementing trauma-focused cognitive behavioral therapy with evidence-based engagement strategies.** *Child Abuse and Neglect, 38*, 1508-1520. doi:10.1016/j.chiabu.2014.03.020 The goal of this study was to examine the impact of supplementing TF-CBT (Cohen et al., 2006) with evidence-based engagement strategies on foster parent and foster youth engagement in treatment, given challenges engaging foster parents in treatment. A randomized controlled trial of TF-CBT standard delivery compared to TF-CBT plus evidence-based engagement strategies was conducted with 47 children and adolescents in foster care and one of their foster parents. Attendance, engagement, and clinical outcomes were assessed 1 month into treatment, end of treatment, and 3 months post-treatment. Youth and foster parents who received TF-CBT plus evidence-based engagement strategies were more likely to be retained in treatment through four sessions and were less likely to drop out of treatment prematurely. The engagement strategies did not appear to have an effect on the number of canceled or no-show sessions or on treatment satisfaction. Clinical outcomes did not differ by study condition, but exploratory analyses suggest that youth had significant improvements with treatment. Strategies that specifically target engagement may hold promise for increasing access to evidence-based treatments and for increasing likelihood of treatment completion.

Ford, J.D., Steinberg, K.L., Hawke, J.M., Levine, J., & Zhang, W. (2012). **Randomized trial comparison of emotion regulation and relational psychotherapies for PTSD with girls involved in delinquency.** *Journal of Clinical Child and Adolescent Psychology, 41*, 27-37. doi:10.1080/15374416.2012.632343 PTSD is prevalent in youth involved in delinquency, but it is often not effectively treated. A randomized clinical trial was conducted comparing the outcomes of an emotion regulation therapy (TARGET) with a relational supportive therapy (ETAU) with 59 delinquent girls (age 13-17 years) who met criteria for full or partial PTSD. Mixed model regression analyses demonstrated generally large effects for pre-post change in PTSD symptoms for both therapies but not in emotion regulation. Both therapies had small to medium effect size changes in anxiety, anger, depression, and posttraumatic cognitions. Treatment x Time interactions showed small to medium effects favoring TARGET for change in PTSD (intrusive reexperiencing and avoidance) and anxiety symptoms, posttraumatic cognitions, and emotion regulation, and favoring ETAU for change in hope and anger. Results provide preliminary support for TARGET as a potentially efficacious therapy for PTSD with delinquent girls. Relational therapies such as ETAU also may be beneficial for delinquent girls with PTSD, particularly to enhance optimism and self-efficacy and reduce anger.

Jensen, T.K., Holt, T., Ormhaug, S. M., Egeland, K., Granly, L., Hoaas, L.C., & Wentzel-Larsen, T. (2014). **A randomized effectiveness study comparing trauma-focused cognitive behavioral therapy with therapy as usual for youth.** *Journal of Clinical Child and Adolescent Psychology, 43*, 356-369. doi:10.1080/15374416.2013.822307 The efficacy of TF-CBT has been shown in several randomized controlled trials. However, few trials have been conducted in community clinics, few have used TAU as a comparison group, and none have been conducted outside of the US. The objective of this study was to evaluate the effectiveness of TF-CBT in regular community settings compared with TAU. One hundred fifty-six traumatized youth (M age = 15.1 years, range = 10-18; 79.5% girls) were randomly assigned to TF-CBT or TAU.

Intent-to-treat analysis using mixed effects models showed that youth receiving TF-CBT reported significantly lower levels of posttraumatic stress symptoms (est. = 5.78, *d* = 0.51), 95% CI [2.32, 9.23]; depression (est. = 7.00, *d* = 0.54), 95% CI [2.04, 11.96]; and general mental health symptoms (est. = 2.54, *d* = 0.45), 95% CI [0.50, 4.58], compared with youth in the TAU group. Youth assigned to TF-CBT showed significantly greater improvements in functional impairment (est. = -1.05, *d* = -0.55), 95% CI [-1.67, -0.42]. Although the same trend was found for anxiety reduction, this difference was not statistically significant (est. = 4.34, *d* = 0.30), 95% CI [-1.50, 10.19]. Significantly fewer youths in the TF-CBT condition were diagnosed with PTSD compared to youths in the TAU condition, chi-square(1, *N* = 116) = 4.61, *p* = .031, Phi = .20). Findings indicate that TF-CBT is effective in treating traumatized youth in community mental health clinics and that the program may also be successfully implemented in countries outside the US.

Kramer, D.N., & Landolt, M.A. (2014). **Early psychological intervention in accidentally injured children ages 2-16: A randomized controlled trial.** *European Journal of Psychotraumatology, 5*. doi:10.3402/ejpt.v5.24402 *Background:* Road traffic accidents (RTA) and burns are frequent events in children. Although many children recover spontaneously, a considerable number develop long-term psychological sequelae. Evidence on early psychological interventions to prevent such long-term problems is still scarce for school-age children and completely lacking for pre-school children. *Objectives:* To evaluate the efficacy of an early two-session cognitive-behavioral intervention in 108 children ages 2–16 after RTAs and burns. *Methods:* Children assessed at risk for the development of PTSD were randomly assigned to either a control group offered treatment as usual or an intervention group. Primary outcomes were PTSD, behavioral problems, and depression symptoms. Baseline and blinded 3- and 6-month follow-up assessments were conducted. *Results:* In pre-school children, no intervention effects were found. School-age children in the intervention group exhibited significantly fewer internalizing problems at 3-month follow-up relative to controls and a borderline significant time-by-group effect for PTSD intrusion symptoms was found (*p* = 0.06). *Conclusions:* This is the first study examining the efficacy of an indicated, early psychological intervention among both school-age and pre-school-age children. Because the intervention was ineffective for young children, no evidence-based practice can currently be suggested. Given that parents of pre-school children perceived the intervention as helpful, brief counseling of parents in terms of psychoeducation and training in coping skills still should be provided by clinicians, despite the current lack of evidence. To prevent trauma-related disorders in school-age children, the intervention might be used in a step-wise manner, where only children at risk for long-term psychological maladjustment are provided with psychological support.

Marsac, M.L., Kohser, K.L., Winston, F.K., Kenardy, J.A., March, S., & Kassam-Adams, N. (2013). **Using a web-based game to prevent posttraumatic stress in children following medical events: Design of a randomized controlled trial.** *European Journal of Psychotraumatology, 4*, doi:10.3402/ejpt.v4i0.21311 *Background:* Medical events including acute illness and injury are among the most common potentially traumatic experiences for children. Despite the scope of the problem, only limited resources are available for prevention of posttraumatic stress symptoms (PTSS) after pediatric medical events. Web-based programs provide a low-cost, accessible means to reach a wide range of families and show promise in related areas of child mental health. *Objectives:* To describe the design of a randomized controlled trial that will evaluate feasibility and estimate preliminary efficacy of Coping Coach, a web-based preventive intervention to prevent or reduce PTSS after acute pediatric medical events. *Method:* Seventy children and their parents will be randomly assigned to either an intervention or a waitlist control condition. Inclusion criteria require that children are aged 8-12 years, have experienced a medical event, have access to Internet and telephone, and have sufficient competency in the English language to complete measures and understand the intervention. Participants will complete baseline measures and will then be randomized to the intervention or waitlist control condition. Children in the intervention condition will complete module 1 (Feelings Identification) in the hospital and will be instructed on how to complete modules 2 (Appraisals) and 3 (Avoidance) online. Follow-up assessments will be conducted via telephone at 6, 12, and 18 weeks after the baseline assessment. Following the 12-week assessment, children in the waitlist control condition will receive instructions for completing the intervention. *Results:* Primary study outcomes include data on intervention feasibility and outcomes (child appraisals, coping, PTSS and health-related quality of life). *Discussion:* Results will provide data on the feasibility of the implementation of the Coping Coach intervention and study procedures as well as estimations of efficacy to determine sample size for a larger study. Potential strengths and limitations of this design are discussed.

McMullen, J., O'Callaghan, P., Shannon, C., Black, A., & Eakin, J. (2013). **Group trauma-focused cognitive-behavioural therapy with former child soldiers and other war-affected boys in the DR Congo: A randomised controlled trial.** *Journal of Child Psychology and Psychiatry, 54*, 1231-1241. doi:10.1111/jcpp.12094 *Background:* The Democratic Republic of Congo (DRC) has been home to the world's deadliest conflict since World War II and is reported to have the largest number of child soldiers in the world. Despite evidence of the debilitating impact of war, no group-based mental health or psychosocial intervention has been evaluated in a randomised controlled trial for psychologically distressed former child soldiers. *Method:* A randomised controlled trial involving 50 boys, aged 13-17, including former child soldiers (*n* = 39) and other war-affected boys (*n* = 11). They were randomly assigned to an intervention group, or wait-list control group. The intervention group received a 15-session, group-based, culturally adapted TF-CBT intervention. Assessment interviews were completed at baseline, postintervention, and 3-month follow-up (intervention group). *Results:* ANCOVA demonstrated that, in comparison to the wait-list control group, the TF-CBT intervention group had highly significant reductions in posttraumatic stress symptoms, overall psychosocial distress, depression or anxiety-like symptoms, conduct problems, and a significant increase in prosocial behaviour ($p < .001$ for all). Effect sizes were higher when former child soldier scores were separated for sub-analysis. Three-month follow-up of the intervention group found that treatment gains were maintained.

Conclusions: A culturally modified, group-based TF-CBT intervention was effective in reducing posttraumatic stress and psychosocial distress in former child soldiers and other war-affected boys.

Murray, L.K., Skavenski, S., Kane, J.C. Mayeya, J., Dorsey, S., Cohen, J.A., & Bolton, P.A. (2015). **Effectiveness of trauma-focused cognitive behavioral therapy among trauma-affected children in Lusaka, Zambia: A randomized controlled trial.** *JAMA Pediatrics.* doi:10.1001/jamapediatrics.2015.0580 *Importance:* Orphans and vulnerable children (OVC) are at high risk for experiencing trauma and related psychosocial problems. Despite this, no randomized clinical trials have studied evidence-based treatments for OVC in low-resource settings. *Objective:* To evaluate the effectiveness of lay counselor-provided TF-CBT to address trauma and stress-related symptoms among OVC in Lusaka, Zambia. *Design, Setting, and Participants:* This randomized clinical trial compared TF-CBT and treatment as usual (TAU) (varying by site) for children recruited from August 1, 2012, through July 31, 2013, and treated until December 31, 2013, for trauma-related symptoms from 5 community sites within Lusaka, Zambia. Children were aged 5 through 18 years and had experienced at least one traumatic event and reported significant trauma-related symptoms. Analysis was with intent to treat. *Interventions:* The intervention group received 10 to 16 sessions of TF-CBT (*n* = 131). The TAU group (*n* = 126) received usual community services offered to OVC. *Main Outcomes and Measures:* The primary outcome was mean item change in trauma and stress-related symptoms using a locally validated version of the UCLA Posttraumatic Stress Disorder Reaction Index (range, 0-4) and functional impairment using a locally developed measure (range, 0-4). Outcomes were measured at baseline and within 1 month after treatment completion or after a waiting period of approximately 4.5 months after baseline for TAU. *Results:* At follow-up, the mean item change in trauma symptom score was -1.54 (95% CI, -1.81 to -1.27), a reduction of 81.9%, for the TF-CBT group and -0.37 (95% CI, -0.57 to -0.17), a reduction of 21.1%, for the TAU group. The mean item change for functioning was -0.76 (95% CI, -0.98 to -0.54), a reduction of 89.4%, and -0.54 (95% CI, -0.80 to -0.29), a reduction of 68.3%, for the TF-CBT and TAU groups, respectively. The difference in change between groups was statistically significant for both outcomes (P < .001). The effect size (Cohen d) was 2.39 for trauma symptoms and 0.34 for functioning. Lay counselors participated in supervision and assessed whether the intervention was provided with fidelity in all 5 community settings. *Conclusions and Relevance:* The TF-CBT adapted for Zambia substantially decreased trauma and stress-related symptoms and produced a smaller improvement in functional impairment among OVC having experienced high levels of trauma. *Trial Registration:* clinicaltrials.gov Identifier: NCT01624298.

O'Callaghan, P., McMullen, J., Shannon, C., Rafferty, H., & Black, A. (2013). **A randomized controlled trial of trauma-focused cognitive behavioral therapy for sexually exploited, war-affected Congolese girls.** *Journal of the American Academy of Child and Adolescent Psychiatry, 52*, 359-369. doi:10.1016/j.jaac.2013.01.013 *Objective:* To assess the efficacy of TF-CBT delivered by nonclinical facilitators in reducing posttraumatic stress, depression, and anxiety and conduct problems and increasing prosocial behavior in a group of war-affected, sexually exploited girls in a single-blind, parallel-design, randomized + controlled trial. *Method:* Fifty-two 12- to 17-year-old, war-affected girls exposed to rape and inappropriate sexual touch in the Democratic Republic of Congo were screened for trauma, depression and anxiety, conduct problems, and prosocial behavior. They were then randomized to a 15 session, group-based, culturally modified TF-CBT (*n* = 24) group or a wait-list control group (*n* = 28). Primary analysis, by intention-to-treat, involving all randomly assigned participants occurred at pre- and postintervention and at 3-month follow-up (intervention group only). *Results:* Compared to the wait list control, the TF-CBT group experienced significantly greater reductions in trauma symptoms (F(1,49) = 52.708, p<0·001, χ(p)2 = 0.518). In addition, the TF-CBT group showed a highly significant improvement in symptoms of depression and anxiety, conduct problems, and prosocial behavior. At 3-months follow-up the effect size (Cohen's d) for the TF-CBT group was 2.04 (trauma symptoms), 2.45 (depression and anxiety), 0.95 (conduct problems), and-1.57 (prosocial behavior). *Conclusions:* A group-based, culturally modified, TF-CBT intervention delivered by nonclinically trained Congolese facilitators resulted in a large, statistically significant reduction in posttraumatic stress symptoms and psychosocial difficulties among war-affected girls exposed to rape or sexual violence. Clinical trial registration information-An RCT of TF-CBT with sexually-exploited, war-affected girls in the DRC; http://clinicaltrials.gov/; NCT01483261.

Saxe, G.N., Ellis, B.H., Fogler, J., & Navalta, C.P. (2012). **Innovations in practice: Preliminary evidence for effective family engagement in treatment for child traumatic stress–trauma systems therapy approach to preventing dropout.** *Child and Adolescent Mental Health, 17*, 58-61. doi:10.1111/j.1475-3588.2011.00626.x *Background:* This study aimed to obtain preliminary evidence for the extent to which a novel intervention embedded within a systems-oriented treatment model (trauma systems therapy [TST]) engages and retains traumatized children and their families in treatment. *Method:* Twenty youth who had prominent symptoms of posttraumatic stress were randomly assigned to receive TST or CAU. *Results:* At the 3-month assessment, 90% of TST participants were still in treatment, whereas only 10% of CAU participants remained. Within-group analyses of TST participants demonstrated significant reductions in posttraumatic stress and aggression as well as a slight improvement in home safety. *Conclusions:* These preliminary findings point to the need to utilize effective engagement approaches to retain traumatized children and their families in treatment.

Scheeringa, M.S. & Weems, C.F. (2014). **Randomized placebo-controlled D-cycloserine with cognitive behavior therapy for pediatric posttraumatic stress.** *Journal of Child and Adolescent Psychopharmacology, 24*, 69-77. doi:10.1089/cap.2013.0106 *Objective:* Research on D-cycloserine (DCS), a partial *N*-methyl-d-aspartic acid (NMDA) agonist, has suggested that it may enhance exposure-based therapies for anxiety disorders. Results with DCS in adult PTSD have been conflicting; however, no data have been reported on children with PTSD. Although many individuals with PTSD respond to exposure-based CBT, there are subgroups of individuals who are nonresponders, and many responders still have substantial residual symptoms.

This randomized, triple-blind, placebo-controlled study tested DCS as an adjunct to CBT to improve and speed treatment response for PTSD in youth. *Methods:* Seven to 18 year-old youth with exposure to trauma and PTSD were offered a 12-session, manualized CBT treatment. Those who remained in treatment at the fifth session were randomly allocated (n = 57) to either CBT and DCS or CBT and placebo. *Results:* Youth in the CBT and DCS group had significant reductions in symptoms, but these reductions were not greater than those in the CBT and placebo group. There was a trend toward DCS speeding PTSD symptom recovery during the exposure-based sessions, and evidence that the CBT and DCS group better maintained stability of gains on inattention ratings from posttreatment to the 3-month follow-up. *Conclusions:* This initial study of CBT and DCS to treat pediatric PTSD provided suggestive and preliminary evidence for more rapid symptom recovery and beneficial effects on attention, but did not show an overall greater effect for reducing PTSD symptoms. It appears that augmentation with DCS represents unique challenges in PTSD. Because PTSD involves complex, life-threatening trauma memories, as opposed to the imagined dreadful outcomes of other anxiety disorders, the use of DCS may require greater attention to how its use is coupled with exposure-based techniques. DCS may have inadvertently enhanced reconsolidation of trauma memories rather than more positive and adaptive memories. In addition, the results suggest that future research could focus on the longer-term benefits of DCS on attention and ways to capitalize on attention-enhancing therapies. *ClinicalTrials.gov registry:* Effect of D-cycloserine on Treatment of PTSD in Youth, NCT01157416, http://clinicaltrials.gov/ct2/results?term=NCT01157416&Search=Search, and D-cycloserine Adjunctive Treatment for PTSD in Adolescents, NCT01157429, http://clinicaltrials.gov/ct2/results?term=NCT01157429&Search=Search.

Zatzick, D., Russo. J., Lord, S.P., Varley, C., Wang, J., Berliner, L., & Rivara, F. P. (2014). **Collaborative care intervention targeting violence risk behaviors, substance use, and posttraumatic stress and depressive symptoms in injured adolescents: a randomized clinical trial.** *JAMA Pediatrics, 168*, 532-539. doi:10.1001/jamapediatrics.2013.4784 *Importance:* Violence and injury risk behaviors, alcohol and drug use problems, and PTSD and depressive symptoms occur frequently among adolescents presenting to acute care medical settings after traumatic physical injury. *Objective:* To test the effectiveness of a stepped collaborative care intervention targeting this constellation of risk behaviors and symptoms in randomly sampled hospitalized adolescents with and without traumatic brain injury. *Design, Setting, and Participants:* A pragmatic randomized clinical trial was conducted at a single US level I trauma center. Participants included 120 adolescents aged 12 to 18 years randomized to intervention (n = 59) and control (n = 61) conditions. *Interventions:* Stepped collaborative care intervention included motivational interviewing elements targeting risk behaviors and substance use as well as medication and cognitive behavioral therapy elements targeting PTSD and depressive symptoms. *Main Outcomes and Measures:* Adolescents were assessed at baseline before randomization and 2, 5, and 12 months after injury hospitalization. Standardized instruments were used to assess violence risk behaviors, alcohol and drug use, and PTSD and depressive symptoms.

FEATURED ARTICLES *continued*

Results: The investigation attained more than 95% adolescent follow-up at each assessment point. At baseline, approximately one-third of the participants endorsed the violence risk behavior of carrying a weapon. Regression analyses demonstrated that intervention patients experienced significant reductions in weapon carrying compared with controls during the year after injury (group × time effect, $F_{3,344} = 3.0$; $P = .03$). At 12 months after the injury, 4 (7.3%) intervention patients vs 13 (21.3%) control patients reported currently carrying a weapon (relative risk, 0.31; 95% CI, 0.11-0.90). The intervention was equally effective in reducing the risk of weapon carrying among injured adolescents with and without traumatic brain injury. Other treatment targets, including alcohol and drug use problems and high levels of PTSD and depressive symptoms, occurred less frequently in the cohort relative to weapon carrying and were not significantly affected by the intervention. *Conclusions and Relevance:* Collaborative care intervention reduced the risk of adolescent weapon carrying during the year after the injury hospitalization. Future investigation should replicate this preliminary observation. If the finding is replicated, orchestrated investigative and policy efforts could systematically implement and evaluate screening and intervention procedures targeting youth violence prevention at US trauma centers. *Trial Registration:* Clinicaltrials.gov identifier: NCT00619255.

ADDITIONAL CITATIONS

Berkowitz, S.J., Stover, C.S., & Marans, S.R. (2011). **The child and family traumatic stress intervention: Secondary prevention for youth at risk of developing PTSD.** *Journal of Child Psychology and Psychiatry, 52*, 676-685. doi:10.1111/j.1469-7610.2010.02321.x This article describes the randomized controlled trial of a 4-session child and caregiver preventive intervention for 106, 7 to 17-year-olds begun within 30 days of exposure to a potentially traumatic event. The Child and Family Traumatic Stress Intervention was significantly superior to a supportive comparison condition in preventing the development of full or partial chronic PTSD at 3-month follow-up.

Deblinger, E., Mannarino, A.P., Cohen, J.A., Runyon, M.K. & Steer, R.A. (2011). **Trauma-focused cognitive behavioral therapy for children: Impact of trauma narrative and treatment length.** *Depression and Anxiety, 28*, 67-75. doi:10.1002/da.20744 This randomized controlled TF-CBT study used a 2X2 design to evaluate the impact of including vs. not including the TF-CBT trauma narrative (TN) phase, and of providing TF-CBT in 8 vs. 16 sessions for 210, 4- to 11-year-old children after sexual abuse. Findings indicated that 1) all conditions effectively improved PTSD; 2) 8 sessions with the TN phase was most effective and efficient for improving child fear and anxiety symptoms and parental abuse-specific distress; and 3) 16 sessions without TN led to greater improvement in parenting skills and children's externalizing behavior symptoms.

Foa, E.B., McLean, C.P., Capaldi, S., & Rosenfield, D. (2013). **Prolonged exposure vs supportive counseling for sexual abuse-related PTSD in adolescent girls: A randomized clinical trial.** *JAMA, 310*, 2650-2657. doi:10.1001/jama.2013.282829 This study compared

ADDITIONAL CITATIONS *continued*

Prolonged Exposure (PE) to supportive counseling (SC) in 61 adolescent females with sexual abuse-related PTSD. No information about participants' sexual abuse or other trauma experiences was included; and it appeared that caregivers were not involved in treatment. Adolescents receiving PE experienced significantly greater improvement in PTSD and depressive symptoms than those receiving SC.

Kassam-Adams, N.L., Marsac, L.M., Hildenbrand, A. & Winston, F.K. (2013). **Posttraumatic stress following pediatric injury: update on diagnosis, risk factors, and intervention.** *JAMA Pediatrics, 167*, 1158-1165. doi:10.1001/jamapediatrics.2013.2741 This review provides an excellent update on risk factors for developing PTSD following pediatric injury and intervention strategies including web-based models.

Kataoka, S.H., Langley, A.K., Wong, M., Baweja, S., & Stein, B.D. (2012). **Responding to students with posttraumatic stress disorder in schools.** *Child and Adolescent Psychiatric Clinics of North America, 21*, 119-133. doi:10.1016/j.chc.2011.08.009 This paper reviews risks for students to develop PTSD and the role that schools and mental health consultants can play in addressing unmet needs.

Ormhaug, S.M., Jensen, T.K., Wentzel-Larsen, T., & Shirk, S.R. (2014). **The therapeutic alliance in treatment of traumatized youth: relation to outcome in a randomized clinical trial.** *Journal of Consulting and Clinical Psychology, 82*, 52-64. doi:10.1037/a0033884 This study evaluated the impact of the therapeutic alliance in the context of a randomized controlled treatment trial of TF-CBT versus TAU in 8 usual care clinics in Norway. Therapeutic alliance was comparable across the treatment conditions, but positive treatment alliance only significantly predicted better treatment outcome in the TF-CBT condition.

Wilkinson, J.M. & Carrion, V.G. (2012). **Pharmacotherapy in Pediatric PTSD: A developmentally focused review of the evidence.** *Current Psychopharmacology, 1*, 252-270. doi:10.2174/2211556011201030252 This article provides an excellent review of the evidence for efficacy of treating PTSD symptoms. The review is divided by both medication class and developmental level.

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Technology and PTSD Care: An Update

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Introduction

Telemental health technologies such as clinical video teleconferencing (CVT), web-based interventions, and mobile devices offer innovative mechanisms for delivering mental health services to trauma survivors. Only a small proportion of individuals in need of psychological care actually receive treatment and individual psychotherapy alone is not likely to be able to fully meet that need (Kazdin & Blase, 2011). These technologies can facilitate delivery of care and provide critical support before therapy, in-between therapy sessions and following therapy for maintenance and relapse prevention. These modalities may make care more manageable for individuals who may not otherwise be able to access treatment. Research has demonstrated feasibility and shown high levels of satisfaction with these technologies, but we have yet to determine the efficacy of many tools intended to help survivors of trauma. Research on CVT is advanced and implementation of CVT service delivery is well underway. However, research related to online interventions and mobile applications (apps) is just beginning to evolve.

Clinical Videoconferencing Technology (CVT)

A CVT technology is often used to enhance or expand the reach of clinician-delivered psychotherapy. CVT allows for real-time, interactive, face-to-face communication between clinicians and patients located in different locations through the delivery of psychotherapy via a television, computer monitor or tablet screen. PTSD therapy delivered by CVT has been extensively studied for both individual and group treatment formats and has become progressively more available in a variety of service systems.

Typically, CVT is office-based, with the therapist located at a larger medical facility and the patient located at the more remote satellite clinic. However, more recently there has been movement into home-based CVT.

Studies have indicated that CVT can achieve comparable clinical outcomes to in-person delivery across various therapies with diverse patient populations (Backhaus et al., 2012). Randomized clinical trials (RCTs) have demonstrated that PTSD outcomes with CVT delivery of trauma-focused therapies are generally comparable to outcomes associated with traditional service delivery methods. These specific RCTs often employ a noninferiority methodological approach. Noninferiority trials are intended to show that the effect of a new treatment, or in this case the CVT modality, is not worse or "noninferior" to the active already established control condition, or in this case the traditional in-person face-to-face modality. A recent RCT conducted with Veterans with PTSD confirmed the noninferiority of using CVT to deliver an evidence-based treatment (EBT) for PTSD, Cognitive Processing Therapy (CPT; Resick et al., 2007), relative to CPT delivered in-person (Morland et al., 2014). A pilot study of Prolonged Exposure (PE; Foa, Hembree, & Rothbaum, 2007) delivered via CVT to 12 Veterans with PTSD evidenced significant decreases in clinical outcomes and provided support for the feasibility and safety of trauma-focused treatments delivered via CVT (Tuerk, Yoder, Ruggiero, Gros, & Acierno, 2010). A recent RCT found that a collaborative care model, which included treatment with CPT, medication and case management, and psychiatric consultations delivered via telehealth, produced larger

Continued on page 2

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Continued from cover

reductions in PTSD symptoms compared to outcomes found in the treatment-as-usual condition and thus, enhanced treatment engagement and increased access to and delivery of EBTs relative to usual care (UC; Fortney et al., 2015).

Veterans with PTSD have shown high degrees of patient and clinician satisfaction (Deitsch, Frueh, & Santos, 2000) and rates of attendance (Greene et al., 2010) comparable to in-person care in other CVT studies. Furthermore, research investigating therapist effects in CVT indicates that therapist adherence (Morland et al., 2011), therapist competence, and therapist fidelity when delivering manualized treatment protocols is similar in CVT and in-person modalities (Frueh et al., 2007).

Based on positive results for office-based CVT, there is growing interest regarding whether CVT can be used to safely and effectively deliver PTSD therapy to patients in their own homes, thereby reducing travel burden for patients. A number of ongoing trials of in-home delivery of PTSD treatments with Veterans are currently underway. Yuen and colleagues (in press) reported the preliminary results of a RCT of home-based PE delivered via CVT for combat-related PTSD, which provided evidence that clinical outcomes and patient satisfaction for home-based PTSD treatment was similar between the CVT and in-person conditions. Another ongoing trial is assessing in-home delivery of an exposure therapy for co-occurring PTSD and depression in Operation New Dawn/Operation Enduring Freedom Veterans. Preliminary results demonstrated significant reductions in symptoms of PTSD, depression, and anxiety in both the home-based CVT and in-person conditions (Strachan, Gros, Ruggiero, Lejuez, & Acierno, 2012). Future large scale RCTs on PTSD treatments delivered via various telehealth modalities (e.g., home-based CVT, online, apps) are warranted.

Online Interventions

Online tools offer a convenient way of providing information, screening and self-assessment, intervention, and social support to people who might otherwise not access formal treatment (Amstadter, Broman-Fulks, Zinzow, Ruggiero, & Cercone, 2009). Reputable websites that provide mental health information for trauma survivors include the websites of the National Center for PTSD, International Society of Traumatic Stress Studies, American Psychological Association, Anxiety and Depression Association of America, and Afterdeployment.org. There has been little empirical research on the effects of online educational material. In an uncontrolled study with 445 military families, Roy and colleagues (2012) found that family member scores on a PTSD knowledge test improved by 34% after a single session of using an educational website. Sadler and colleagues (2013) tested an online screening and information program designed for female Reserve and National Guard troops returning from deployment (N = 131). Thirty-one percent said using the site made them feel more comfortable seeking mental health care and 42% said they planned to seek mental health treatment. Another online screening and recommendation program has been developed for disaster survivors (Ruggiero et al., 2012).

Interapy is an online, therapist-supported, narrative writing intervention for PTSD. Over a 5-week period, participants engage in writing exercises that include elements of exposure, cognitive reappraisal, and farewell rituals. Therapists provide email feedback after each writing assignment. Three trials have tested *Interapy* among trauma-exposed individuals with PTSD symptoms. Although the first trial with *Interapy* showed large effects on PTSD and other symptoms among completers, the nearly 50% drop-out rate and lack of an intent-to-treat (ITT) analysis raised questions about its overall effectiveness (Lange et al., 2003). In subsequent trials with trauma-exposed individuals (Knaevelsrud & Maercker, 2007) and parents who lost a child during pregnancy (Kersting et al., 2013), retention was over 84% and ITT analyses showed *Interapy* produced large improvements in PTSD symptoms, depression and anxiety (d = .82-1.41) relative to controls. Furthermore, stronger therapeutic alliance with the online clinician predicted greater improvement in two studies, suggesting that email contact is an important component of *Interapy* (Knaevelsrud & Maercker, 2007; Wagner, Brand, Schulz, & Knaevelsrud, 2012). Among survivors of the 9/11 Pentagon attack, another online CBT intervention with email support produced steeper reductions in PTSD symptoms than did online supportive counseling (Litz, Engel, Bryant, & Papa, 2007).

My Disaster Recovery (http://disaster.bluesunsupport.com) is an online tool designed to improve trauma survivor coping skills, which involves no written disclosure and is self-administered without any clinician contact. It consists of six modules: social support, self-talk, relaxation, trauma triggers, unhelpful coping, and professional help. A trial among 56 survivors of Hurricane Ike showed that using *My Disaster Recovery* for an average of 1.8 hours reduced worry more than use of a non-interactive electronic book (e-book) or usual care; changes on other symptoms were non-significant (Steinmetz, Benight, Bishop, & James, 2012). A Chinese variant of the website *My Trauma Recovery* (Wang, Wang, & Maercker, 2013) was tested in both an urban sample exposed to a variety of traumas (n = 93, retention rate < 38%) and rural survivors of the 2008 Szechuan earthquake (n = 93, retention rate > 87%). ITT analyses in both samples showed that PTSD symptoms improved more among those using the tool than among controls.

VetChange is a self-administered online intervention that uses elements of motivational interviewing, CBT strategies and self-control training to address problematic drinking in people with PTSD. A study conducted with 600 Veterans found that participants completed an average of four of eight modules. Both alcohol problems and PTSD symptoms declined more in the treatment than in the control condition (Brief et al., 2013). In another study evaluating the PTSD module of the self-administered intervention *Afterdeployment.org*, four of eleven Veterans showed reductions in PTSD symptoms (Bush et al., 2014). Taken together, these studies suggest that both therapist-supported and fully self-administered online interventions can produce psychological benefits for trauma survivors, but the effects for therapist-mediated interventions appear to be larger.

mHealth Technologies

Phone and other mobile health technologies (i.e., tablet computers, e-books) hold significant promise for improving the assessment and treatment of PTSD. Similar to online interventions, they can provide information, facilitate screening/assessment, provide intervention, mobilize social support, potentially increase the

reach of psychosocial interventions at minimal incremental cost, strengthen self-management, and enhance process and outcomes assessment. A study focusing on assessment methodology demonstrated that PTSD Checklist (PCL) symptom assessments obtained via mobile device were equivalent to those recorded using traditional paper and pencil measures (Price et al., in press). By virtue of their relatively continuous access between treatment sessions, they can mobilize treatment processes in the natural environment by increasing situational coping, offering as-needed access to supportive resources, facilitating self-monitoring, enabling scheduling and reminding patients of therapeutic tasks. Initial publications have focused on descriptions of newly developed mobile apps and assessments of provider and patient perceptions of the technologies. To date, no research has investigated the impact of these tools on patient outcomes, either as adjuncts to treatment or as stand-alone interventions.

The most used PTSD-related app is PTSD Coach, now downloaded over 180,000 times in 89 countries. This app is designed to educate users about PTSD, enable self-assessment of PTSD symptoms, and increase self-management of symptoms by providing coping tools and promoting use of social support and community resources. Kuhn, Greene, Hoffman, and colleagues (2014) surveyed 45 Veterans receiving PTSD treatment about their perceptions of the PTSD Coach app. After using the app over a brief three-day period, almost 90% of Veterans indicated that they were moderately or extremely satisfied with the app and ratings of app helpfulness were very positive. Ratings of helpfulness and satisfaction were unrelated to the Veteran's age. A larger survey of 188 Veterans receiving outpatient VA PTSD treatment found that 85% were interested in using apps as part of treatment. Access to the technology was good (76% reported owning a smartphone or tablet) and, while age was correlated with ownership of a device, it was unrelated to use of apps in treatment (Erbes et al., 2014).

An important potential role for mobile apps involves support for delivery of EBTs (Reger et al. 2013) described the PE Coach app, designed to enable patients to understand psychoeducational content, schedule upcoming sessions, complete and self-monitor in vivo and imaginal exposure homework assignments, master breathing retraining, and measure PTSD symptom change. A survey on perceptions of PE Coach completed by 163 VA mental health clinicians found that perceptions of the relative advantage, compatibility with care, and complexity of using the app were mildly favorable (Kuhn, Eftekhari, Hoffman, et al., 2014). The study was conducted prior to the launch of the app, thus ratings were obtained in response to written descriptions of app capabilities rather than experiences with use. Younger clinicians (<40 years old) rated PE Coach significantly more favorably than older clinicians and reported greater levels of intention to use the app.

Summary

A solid research base does exist that supports the use of CVT to deliver EBTs. Some research has demonstrated efficacy of online interventions; however, research on outcomes of mobile apps is in its infancy. For both online and mobile app interventions, more research is needed to establish their efficacy, identify active elements and core processes of change, determine effective ways of increasing uptake and engagement, and explore ways of combining these modalities to maximize the impact of unique features associated with each technology. There is little data demonstrating the efficacy of these tools; however, many of these psychoeducational tools that support delivery of established treatments pose little risk of harm and can be used to augment psychotherapy or case management and provide initial psychoeducation to patients not yet receiving formal treatment. Given the potential utility of online materials, clinicians should explore including them as supplements to face-to-face care. It also seems reasonable to use apps designed to support established psychotherapies (e.g., PE Coach) as they offer advantages over paper-and-pencil workbooks and pose no risk. Clinicians using any telemedicine tools should familiarize themselves with the content and processes of the tools and actively monitor their use and impact on patient care.

The technologies outlined here offer a path toward improving the efficiency and effectiveness of trauma-related interventions. Potentially, they can improve outcomes while at the same time enabling mental health professionals to serve greater numbers of patients. They can also form a core element of public health interventions that can reach large numbers of trauma survivors and help them to better self-manage their post-trauma difficulties. Given the anticipated spread of these technologies around the world in the next decade or so, they hold promise of making a significant contribution to reducing the global burden of mental health problems experienced by trauma survivors.

FEATURED ARTICLES

Backhaus, A., Agha, Z., Maglione, M. L., Repp, A., Ross, B., Zuest, D., et al. (2012). **Videoconferencing psychotherapy: A systematic review.** *Psychological Services, 9*, 111-131. doi:10.1037/a0027924
Individuals with mental health problems may face barriers to accessing effective psychotherapies. Videoconferencing technology, which allows audio and video information to be shared concurrently across geographical distances, offers an alternative that may improve access. We conducted a systematic literature review of the use of videoconferencing psychotherapy (VCP), designed to address 10 specific questions, including therapeutic types/formats that have been implemented, the populations with which VCP is being used, the number and types of publications related to VCP, and available satisfaction, feasibility, and outcome data related to VCP. After electronic searches and reviews of reference lists, 821 potential articles were identified, and 65 were selected for inclusion. The results indicate that VCP is feasible, has been used in a variety of therapeutic formats and with diverse populations, is generally associated with good user satisfaction, and is found to have similar clinical outcomes to traditional face-to-face psychotherapy. Although the number of articles being published on VCP has increased in recent years, there remains a need for additional large-scale clinical trials to further assess the efficacy and effectiveness of VCP.

Erbes, C. R., Stinson, R., Kuhn, E., Polusny, M., Urban, J., Hoffman, J., et al. (2014). **Access, utilization, and interest in mHealth applications among Veterans receiving outpatient care for PTSD.** *Military Medicine, 179*, 1218-1222. doi:10.7205/MILMED-D-14-00014 Mobile health (mHealth) refers to the use of mobile technology (e.g., smartphones) and software (i.e., apps) to facilitate or enhance health care. Several mHealth programs act as either stand-alone aids for Veterans with PTSD or adjuncts to conventional psychotherapy approaches. Veterans enrolled in a Veterans Affairs (VA) outpatient treatment program for PTSD (N = 188) completed anonymous questionnaires that assessed Veterans' access to mHealth-capable devices and their utilization of and interest in mHealth programs for PTSD. The majority of respondents (n = 142, 76%) reported having access to a cell phone or tablet capable of running apps, but only a small group (n = 18) reported use of existing mHealth programs for PTSD. Age significantly predicted ownership of mHealth devices, but not utilization or interest in mHealth apps among device owners. Around 56% to 76% of respondents with access indicated that they were interested in trying mHealth programs for such issues as anger management, sleep hygiene, and management of anxiety symptoms. Findings from this sample suggest that Veterans have adequate access to, and interest in, using mHealth apps to warrant continued development and evaluation of mobile apps for the treatment of PTSD and other mental health conditions.

Foa, E. B., Hembree, E. A., & Rothbaum, B. O. (2007). *Prolonged Exposure therapy for PTSD: Emotional processing of traumatic experience: Therapist guide.* New York: Oxford University Press. This guide gives clinicians the information they need to treat clients who exhibit the symptoms of PTSD. It is based on the principles of Prolonged Exposure Therapy, the most scientifically-tested and proven treatment that has been used to effectively treat victims of all types of trauma. Whether your client is a veteran of combat, a victim of a physical or sexual assault, or a casualty of a motor vehicle accident, the techniques and strategies outlined in this book will help.

Fortney, J. C., Pyne, J. M., Kimbrell, T. A., Hudson, T. J., Robinson, D. E., Schneider, R., et al. (2015). **Telemedicine-based collaborative care for posttraumatic stress disorder: A randomized clinical trial.** *JAMA Psychiatry, 72*, 58-67. doi:10.1001/jamapsychiatry.2014.1575 *Importance:* PTSD is prevalent, persistent, and disabling. Although psychotherapy and pharmacotherapy have proven efficacious in randomized clinical trials, geographic barriers impede rural Veterans from engaging in these evidence-based treatments. *Objective:* To test a telemedicine-based collaborative care model designed to improve engagement in evidence-based treatment of PTSD. *Design, Setting, and Participants:* The Telemedicine Outreach for PTSD (TOP) study used a pragmatic randomized effectiveness trial design with intention-to-treat analyses. Outpatients were recruited from 11 Department of Veterans Affairs (VA) community-based outpatient clinics serving predominantly rural Veterans. Inclusion required meeting diagnostic criteria for current PTSD according to the Clinician-Administered PTSD Scale. Exclusion criteria included receiving PTSD treatment at a VA medical center or a current diagnosis of schizophrenia, bipolar disorder, or substance dependence. Two hundred sixty-five Veterans were enrolled from November 23, 2009, through September 28, 2011, randomized to UC or the TOP intervention, and followed up for 12 months. *Interventions:* SD care teams located at VA medical centers supported on-site community-based outpatient clinic providers. Off-site PTSD care teams included telephone nurse care managers, telephone pharmacists, telepsychologists, and telepsychiatrists. Nurses conducted care management activities. Pharmacists reviewed medication histories. Psychologists delivered cognitive processing therapy via interactive video. Psychiatrists supervised the team and conducted interactive video psychiatric consultations. *Main Outcomes and Measures:* The primary outcome was PTSD severity as measured by the Posttraumatic Diagnostic Scale. Process-of-care outcomes included medication prescribing and regimen adherence and initiation of and adherence to cognitive processing therapy. *Results:* During the 12-month follow-up period, 73 of the 133 patients randomized to TOP (54.9%) received cognitive processing therapy compared with 16 of 132 randomized to UC (12.1%) (odds ratio, 18.08 [95% CI, 7.96-41.06]; P < .001). Patients in the TOP arm had significantly larger decreases in Posttraumatic Diagnostic Scale scores (from 35.0 to 29.1) compared with those in the UC arm (from 33.5 to 32.1) at six months (β = -3.81; P = .002). Patients in the TOP arm also had significantly larger decreases in Posttraumatic Diagnostic Scale scores (from 35.0 to 30.1) compared with those in the UC arm (from 33.5 to 31.7) at 12 months (β = -2.49; P = .04). There were no significant group differences in the number of PTSD medications prescribed and adherence to medication regimens were not significant. Attendance at eight or more sessions of cognitive processing therapy significantly predicted improvement in Posttraumatic Diagnostic Scale scores (β = -3.86 [95% CI, -7.19 to -0.54]; P = .02) and fully mediated the intervention effect at 12 months. *Conclusions and Relevance:* Telemedicine-based collaborative care can successfully engage rural Veterans in evidence-based psychotherapy to improve PTSD outcomes.

Kazdin, A. E., & Blase, S. L. (2011). **Rebooting psychotherapy research and practice to reduce the burden of mental illness.** *Perspectives on Psychological Science, 6*, 21-37. doi:10.1177/1745691610393527 Psychological interventions to treat mental health issues have developed remarkably in the past few decades. Yet this progress often neglects a central goal—namely, to reduce the burden of mental illness and related conditions. The need for psychological services is enormous, and only a small proportion of individuals in need actually receive treatment. Individual psychotherapy, the dominant model of treatment delivery, is not likely to be able to meet this need. Despite advances, mental health professionals are not likely to reduce the prevalence, incidence, and burden of mental illness without a major shift in intervention research and clinical practice. A portfolio of models of delivery will be needed. We illustrate various models of delivery to convey opportunities provided by technology, special settings and nontraditional service providers, self-help interventions, and the media. Decreasing the burden of mental illness also will depend on integrating prevention and treatment, developing assessment and a national database for monitoring mental illness and its

burdens, considering contextual issues that influence delivery of treatment, and addressing potential tensions within the mental health professions. Finally, opportunities for multidisciplinary collaborations are discussed as key considerations for reducing the burden of mental illness.

Kersting, A., Dölemeyer, R., Steinig, J., Walter, F., Krokoer, K., Baust, K., et al. (2013). **Brief internet-based intervention reduces posttraumatic stress and prolonged grief in parents after the loss a child during pregnancy: A randomized controlled trial.** *Psychotherapy and Psychosomatics, 82*, 372-381. doi:10.1159/000348713 *Background:* The loss of a child during pregnancy causes significant psychological distress for many women and their partners, and may lead to long-lasting psychiatric disorders. Internet-based interventions using exposure techniques and cognitive restructuring have proved effective for PTSD and prolonged grief. This study compared the effects of an Internet-based intervention for parents after prenatal loss with a waiting list condition (WLC). *Methods:* The Impact of Event Scale—Revised assessed symptoms of PTSD; the Inventory of Complicated Grief and the Brief Symptom Inventory assessed depression, anxiety, and general mental health. The 228 participants (92% female) were randomly allocated to a treatment group (TG; n = 115) or a WLC group (n = 113). The TG received a five-week cognitive behavioral intervention including (1) self-confrontation, (2) cognitive restructuring, and (3) social sharing. *Results:* The TG showed significantly reduced symptoms of posttraumatic stress, prolonged grief, depression, and anxiety relative to the WLC control group. Intention-to-treat analysis revealed treatment effects of between d = 0.84 and d = 1.02 for posttraumatic stress and prolonged grief from pre- to posttreatment time points. Further significant improvement in all symptoms of PTSD and prolonged grief was found from the posttreatment evaluation to the 12-month follow-up. The attrition rate of 14% was relatively low. *Conclusions:* The Internet-based intervention proved to be a feasible and cost-effective treatment, reducing symptoms of posttraumatic stress, grief, depression, anxiety, and general mental health after pregnancy loss. Low-threshold e-health interventions should be further evaluated and implemented routinely to improve psychological support after pregnancy loss.

Knaevelsrud, C., & Maercker, A. (2007). **Internet-based treatment for PTSD reduces distress and facilitates the development of a strong therapeutic alliance: a randomized controlled clinical trial.** BMC Psychiatry 2007, 7:13 doi:10.1186/1471-244X-7-13 *Background:* The present study was designed to evaluate the efficacy of an internet-based therapy (Interapy) for PTSD in a German speaking population. Also, the quality of the online therapeutic relationship, its development and its relevance as potential moderator of the treatment effects was investigated. *Method:* Ninety-six patients with posttraumatic stress reactions were allocated at random to ten sessions of Internet-based cognitive behavioural therapy (CBT) conducted over a five-week period or a waiting list control group. Severity of PTSD was the primary outcome. Secondary outcome variables were depression, anxiety, dissociation and physical health. Follow-up assessments were conducted at the end of treatment and three months after treatment. *Results:* From baseline to post-treatment assessment, PTSD severity and other psychopathological symptoms were significantly improved for the treatment group (intent-to-treat group × time interaction effect size d = 1.40). Additionally, patients of the treatment condition showed significantly greater reduction of co-morbid depression and anxiety as compared to the WLC. These effects were sustained during the three-month follow-up period. High ratings of the therapeutic alliance and low drop-out rates indicated that a positive and stable therapeutic relationship could be established online. Significant improvement of the online working alliance in the course of treatment and a substantial correlation between the quality of the online relationship at the end of treatment and treatment outcome emerged. *Conclusion:* Interapy proved to be a viable treatment alternative for PTSD with large effect sizes and sustained treatment effects. A stable and positive online therapeutic relationship can be established through the Internet which improved during the treatment process.

Kuhn, E., Eftekhari, A., Hoffman, J. E., Crowley, J. J., Ramsey, K. M., Reger, G. M., et al. (2014). **Clinician perceptions of using a smartphone app with prolonged exposure therapy.** *Administration and Policy in Mental Health and Mental Health Services, 41*, 800-807. doi:10.1007/s10488-013-0532-2 Clinician perceptions of clinical innovations affect their adoption and spread. This study investigated mental health clinicians' (n = 163) perceptions of a patient-facing smartphone app for prolonged exposure (PE) therapy for PTSD, before its public release. After reading a description of the app, participants rated perceptions of it based on diffusion of innovations theory constructs. Perceptions were generally favorable regarding the app's relative advantage over existing PE practices, compatibility with their values and needs, and complexity. Age (< 40 years), smartphone ownership, and having used apps in care related to more favorable perceptions. Smartphone ownership, relative advantage, and complexity significantly predicted intention to use the app if it were available. These findings suggest that clinicians are receptive to using a PE app and that dissemination efforts should target sub-groups of PE clinicians to maximize adoption.

Kuhn, E., Greene, C., Hoffman, J., Nguyen, T., Wald, L., Schmidt, J., Ramsey, K. M., & Ruzek, J. (2014). **Preliminary evaluation of PTSD Coach, a smartphone app for post-traumatic stress symptoms.** *Military Medicine, 179*, 12-18. doi:10.7205/MILMED-D-13-00271 PTSD Coach is a mobile application (app) designed to help individuals who have PTSD symptoms better understand and self-manage their symptoms. It has wide-scale use (over 130,000 downloads in 78 countries) and very favorable reviews but has yet to be evaluated. Therefore, this study examines user satisfaction, perceived helpfulness, and usage patterns of PTSD Coach in a sample of 45 Veterans receiving PTSD treatment. After using PTSD Coach for several days, participants completed a survey of satisfaction and perceived helpfulness and focus groups exploring app use and benefit from use. Data indicate that participants were very satisfied with PTSD Coach and perceived it as being moderately to very helpful with their PTSD symptoms. Analysis of focus group data resulted in several categories of app use: to manage acute distress and PTSD

symptoms, at scheduled times, and to help with sleep. These findings offer preliminary support for the acceptability and perceived helpfulness of PTSD Coach and suggest that it has potential to be an effective self-management tool for PTSD. Although promising, future research is required to validate this, given study limitations.

Lange, A., Rietdijk, D., Hudcovicova, M., van de Ven, J.-P., Schrieken, B., & Emmelkamp, P. M. G. (2003). **Interapy: A controlled randomized trial of the standardized treatment of posttraumatic stress through the internet.** *Journal of Consulting and Clinical Psychology, 71*, 901-909. doi:10.1037/0022-006X.71.5.901 Online therapy offers many advantages over face-to-face therapy. Interapy includes psychoeducation, screening, effect measures, and a protocol-driven treatment via the Internet for people suffering from posttraumatic stress. The present article reports the results of a controlled trial on the Internet-driven treatment of posttraumatic stress and grief in a group of people who manifested mild to relatively severe trauma symptoms. Participants in the treatment condition (n = 69) improved significantly more than participants in the waiting-list control condition (n = 32) on trauma-related symptoms and general psychopathology. The effect sizes were large. On most subscales, more than 50% of the treated participants showed reliable change and clinically significant improvement, with the highest percentages being found for depression and avoidance.

Litz, B. T., Engel, C. C., Bryant, R. A., & Papa, A. (2007). **A randomized, controlled proof-of-concept trial of an internet-based, therapist-assisted self-management treatment for posttraumatic stress disorder.** *American Journal of Psychiatry, 164*, 1676-1683. doi:10.1176/appi.ajp.2007.06122057 *Objective:* The authors report an 8-week randomized, controlled proof-of-concept trial of a new therapist-assisted, Internet-based, self-management cognitive behavior therapy versus Internet-based supportive counseling for PTSD. *Method:* Service members with PTSD from the attack on the Pentagon on September 11th or Operation Enduring Freedom (OEF) / Operation Iraqi Freedom (OIF) / Operation New Dawn (OND) were randomly assigned to self-management cognitive behavior therapy (N = 24) or supportive counseling (N = 21). *Results:* The dropout rate was similar to regular cognitive behavior therapy (30%) and unrelated to treatment arm. In the intent-to-treat group, self-management cognitive behavior therapy led to sharper declines in daily log-on ratings of PTSD symptoms and global depression. In the completer group, self-management cognitive behavior therapy led to greater reductions in PTSD, depression, and anxiety scores at six months. One-third of those who completed self-management cognitive behavior therapy achieved high-end state functioning at six months. *Conclusions:* Self-management cognitive behavior therapy may be a way of delivering effective treatment to large numbers with unmet needs and barriers to care.

Morland, L. A., Mackintosh, M., Greene, C. J., Rosen, C. S., Chard, K. M., Resick, P., et al. (2014). **Cognitive Processing Therapy for posttraumatic stress disorder delivered to rural Veterans via telemental health: A randomized noninferiority clinical trial.** *Journal of Clinical Psychiatry, 75*, 470-476. doi:10.4088/JCP.13m08842 *Objective:* To compare clinical and process outcomes of cognitive processing therapy-cognitive only version (CPT-C) delivered via videoteleconferencing (VTC) to in-person in a rural, ethnically diverse sample of Veterans with PTSD. *Method:* A randomized clinical trial with a noninferiority design was used to determine if providing CPT-C via VTC is effective and "as good as" in-person delivery. The study took place between March 2009 and June 2013. PTSD was diagnosed per *DSM-IV*. Participants received 12 sessions of CPT-C via VTC (n = 61) or in-person (n = 64). Assessments were administered at baseline, midtreatment, immediately posttreatment, and three and six months posttreatment.The primary clinical outcome was posttreatment PTSD severity, as measured by the Clinician-Administered PTSD Scale. *Results:* Clinical and process outcomes found VTC to be noninferior to in-person treatment. Significant reductions in PTSD symptoms were identified at posttreatment (Cohen d = 0.78, P < .05) and maintained at three- and six-month follow-up (d = 0.73, P< .05 and d = 0.76, P < .05, respectively). High levels of therapeutic alliance, treatment compliance, and satisfaction and moderate levels of treatment expectancies were reported, with no differences between groups (for all comparisons, F< 1.9, P > .17). *Conclusions:* Providing CPT-C to rural residents with PTSD via VTC produced outcomes that were "as good as" in-person treatment. All participants demonstrated significant reductions in PTSD symptoms posttreatment and at follow-up. Results indicate that VTC can offer increased access to specialty mental health care for residents of rural or remote areas.

Resick P. A., Monson, C. M., & Chard, K. M. (2007). *Cognitive Processing Therapy treatment manual: Veteran/military version.* Boston, MA: U.S. Department of Veterans Administration. Cognitive Processing Therapy (CPT) is a 12-session therapy that has been found effective for both PTSD and other corollary symptoms following traumatic events (Monson et al, 2006; Resick et al, 2002; Resick & Schnicke, 1992, 1993). Although the research on CPT focused on rape victims originally, we have used the therapy successfully with a range of other traumatic events, including military-related traumas. This revision of the manual is in response to requests for a treatment manual that focuses exclusively on military trauma. The manual has been updated to reflect changes in the therapy over time, particularly with an increase in the amount of practice that is assigned and with some of the handouts. It also includes suggestions from almost two decades of clinical experience with the therapy.

Roy, M. J., Taylor, P., Runge, W., Grigsby, E., Woolley, M., & Torgeson, T. (2012). **Web-based post-traumatic stress disorder education for military family members.** *Military Medicine, 177(3)*, 284-290. doi:10.7205/MILMED-D-11-00350 *Objective:* Since PTSD is common after military deployment and affects both military service members and their families, we sought to both improve PTSD-related knowledge of military family members and to foster actions to help service members with their symptoms. *Methods:* Focus groups were conducted with military family members and their feedback was incorporated into an educational website to improve family members' knowledge of PTSD. We pilot-tested the site and a 25-item questionnaire, then used it to assess the knowledge of 497 family members before and after their use of

the website. *Results:* Use of this educational website improved military family members' PTSD-related knowledge on a 25-item test, with an increase from a mean 13.9 correct responses beforehand to 18.7 after website use ($p < 0.001$; effect size 1.2). In addition, 217 family members returned to the site ≥10 days after their initial visit; 57% had taken actions such as discussing the service member's symptoms with them or persuading them to get medical attention, and 82 to 95% of them believed their actions to be beneficial. *Conclusion:* A web-based intervention can both improve PTSD-related knowledge and foster behavioral changes in military family members.

Sadler, A. G., Mengeling, M. A., Torner, J. C., Smith, J. L., Franciscus, C. L., Erschens, H. J., et al. (2013). **Feasibility and desirability of web-based mental health screening and individualized education for female OEF/OIF Reserve and National Guard war Veterans.** *Journal of Traumatic Stress, 26*, 401-404. doi:10.1002/jts.21811 OEF/OND Reserve and National Guard (RNG) service members have an increased risk for postdeployment mental health (MH) and readjustment problems, yet most do not access needed care. It is unknown if RNG servicewomen experiencing postdeployment readjustment symptoms are aware these may signify treatable MH concerns or if this knowledge activates care-seeking. The aims of this proof-of-concept study were to determine the feasibility of web-based MH screening for postdeployment MH symptoms to inform individualized psychoeducation, and to assess user perceptions about the online instrument and process, MH care access, and VA and other MH care. A midwestern sample ($N = 131$) of recently deployed (past 24 months) OEF/OIF RNG Army and Air Force servicewomen participated. High rates of combat experiences (95%) and military sexual trauma (50%) were reported. Positive screens for key symptoms of MH problems were prevalent. One third (31%) of satisfaction survey completers indicated online information reduced discomfort with seeking MH care; 42% reported they would subsequently seek MH assessment. Participants interviewed by telephone indicated that stigma and limited knowledge about women-specific services were key reasons servicewomen do not use MH care. This study demonstrated web-based screenings with individualized psychoeducation are implementable and favorable to RNG servicewomen.

Steinmetz, S. E., Benight, C. C., Bishop, S. L., & James, L. E. (2012). **My disaster recovery: A pilot randomized controlled trial of an internet intervention.** *Anxiety, Stress & Coping, 25*, 593-600. doi:10.1080/10615806.2011.604869 This pilot study tested the efficacy of the *My Disaster Recovery* (MDR) website to decrease negative affect and increase coping self-efficacy. Fifty-six survivors of Hurricane Ike were recruited from a larger study being conducted at the University of Texas Medical Branch at the first anniversary of the storm. Restricted randomization was used to assign participants to the MDR website, an information-only website, or an UC condition. Group × time interactions indicated that MDR reduced participant worry more than the other conditions. A similar trend was also identified for depression. Both websites were accessed a small to moderate amount and participants reported mixed satisfaction for both websites. Although the effect sizes for worry and depression were in the moderate to large range, small sample size and timing of the intervention qualify the findings. These preliminary findings encourage further evaluation of MDR with a larger, demographically diverse sample and indicate that the MDR website might be helpful in reducing worry and depression.

Strachan, M., Gros, D. F., Ruggiero, K. J., Lejuez, C. W., & Acierno, R. (2012). **An integrated approach to delivering exposure-based treatment for symptoms of PTSD and depression in OIF/OEF Veterans: Preliminary findings.** *Behavior Therapy, 43*, 560-569. doi:10.1016/j.beth.2011.03.003 Combat-exposed military personnel from the wars in Iraq and Afghanistan report high rates of PTSD and associated psychiatric problems. A formidable body of research supports exposure therapy as a front-line intervention for PTSD; however, relative to studies of civilians, fewer investigations have evaluated the effectiveness of exposure therapy using military samples. Specifically, barriers to care (e.g., stigma associated with receiving mental health services) may compromise utilization of evidence-based psychotherapy. As such, researchers have argued that Veterans with PTSD may require an integrated and innovative approach to the delivery of exposure techniques. This paper presents the rationale for and preliminary data from an ongoing clinical trial that compares the home-based telehealth (HBT) application of a brief, behavioral treatment (Behavioral Activation and Therapeutic Exposure; BA-TE) for Veterans with PTSD to the standard, in-person application of the same treatment. Forty OIF/OEF Veterans with PTSD and MDD were consented, enrolled, and randomized to condition (BA-TE in-person, or BA-TE HBT) and symptoms of anxiety and depression were assessed at pre- and posttreatment. Participants in both conditions experienced reductions in depression, anxiety, and PTSD symptoms between pre- and posttreatment, suggesting that HBT application of an integrated PTSD treatment may be feasible and effective.

Tuerk, P. W., Yoder, M., Ruggiero, K. J., Gros, D. F., & Acierno, R. (2010). **A pilot study of prolonged exposure therapy for posttraumatic stress disorder delivered via telehealth technology.** *Journal of Traumatic Stress, 23*, 116-123. doi:10.1002/jts.20494 The authors present a pilot study of 12 Veterans diagnosed with combat-related PTSD and treated with PE therapy via telehealth technology. A reference sample of 35 combat Veterans treated with in-person PE in the same clinic is also included for a comparison. Feasibility and clinical outcomes of interest include technical performance and practicality of the telehealth equipment, patient safety, treatment completion rates, number of sessions required for termination, and clinical outcomes. Results indicated large statistically significant decreases in self-reported pathology for Veterans treated with PE via telehealth technology. Preliminary results support the feasibility and safety of the modality. Suggestions for the implementation of PE via telehealth technology are discussed.

Wang, Z., Wang, J., & Maercker, A. (2013). **Chinese My Trauma Recovery, a web-based intervention for traumatized persons in two parallel samples: Randomized controlled trial.** *Journal of Medical Internet Research, 15(9)*, e213. doi:10.2196/jmir.2690 *Background:* Guided self-help interventions for PTSD are a

promising tool for the dissemination of contemporary psychological treatment. *Objective:* This study investigated the efficacy of the Chinese version of the My Trauma Recovery (CMTR) website. *Methods:* In an urban context, 90 survivors of different trauma types were recruited via Internet advertisements and allocated to a randomized controlled trial (RCT) with a waiting list control condition. In addition, in a rural context, 93 survivors mainly of the 2008 Sichuan earthquake were recruited in-person for a parallel RCT in which the website intervention was conducted in a counseling center and guided by volunteers. Assessment was completed online on a professional Chinese survey website. The primary outcome measure was the Post-traumatic Diagnostic Scale (PDS); secondary outcome measures were Symptom Checklist 90-Depression (SCL-D), Trauma Coping Self-Efficacy Scale (CSE), Post-traumatic Cognitive Changes (PCC), and Social Functioning Impairment (SFI) questionnaires adopted from the My Trauma Recovery website. *Results:* For the urban sample, findings indicated a significant group×time interaction in post-traumatic symptom severity ($F_{1,88}$ = 7.65, P = .007). CMTR reduced post-traumatic symptoms significantly with high effect size after one month of treatment ($F_{1,45}$ = 15.13, Cohen's d = 0.81, P < .001) and the reduction was sustained over a three-month follow-up ($F_{1,45}$=17.29, Cohen's d = 0.87, P < .001). In the rural sample, the group×time interaction was also significant in post-traumatic symptom severity ($F_{1,91}$ = 5.35, P = .02). Post-traumatic symptoms decreased significantly after treatment ($F_{1,48}$ = 43.97, Cohen's d = 1.34, P < .001) and during the follow-up period ($F_{1,48}$ = 24.22, Cohen's d = 0.99, P < .001). Additional outcome measures (post-traumatic cognitive changes, depression) indicated a range of positive effects, in particular in the urban sample (group×time interactions: $F_{1,88}$ = 5.32-8.37, all Ps < .03), contributing to the positive evidence for self-help interventions. Differences in the effects in the two RCTs are exploratorily explained by sociodemographic, motivational, and setting feature differences between the two samples. *Conclusions:* These findings give support for the short-term efficacy of CMTR in the two Chinese populations and contribute to the literature that self-help web-based programs can be used to provide mental health help for traumatized persons.

Yuen, E. K., Gros, D. F., Price, M., Zeigler, S., Tuerk, P. W., Foa, E. B., et al. (in press). **Randomized controlled trial of home-based telehealth versus in-person Prolonged Exposure for combat-related PTSD in Veterans: Preliminary results.** *Journal of Clinical Psychology*. doi:10.1002/jclp.22168 *Objectives:* Telehealth technology may reduce the effect of treatment barriers and improve participation in treatment for Veterans with PTSD. The present study is an ongoing randomized controlled trial comparing the effectiveness of PE delivered via in person or home-based video telehealth modalities. *Method:* A total of 52 Veterans with combat-related PTSD were randomized to receive 8-12 weeks of PE through either home-based telehealth or standard in-person office-based care. *Results:* Participants evidenced significant reductions in symptoms of PTSD, depression, and anxiety from pre- to posttreatment across both conditions. Analyses conducted within a noninferiority framework suggested nonsignificant treatment outcome differences in clinician-reported PTSD and self-reported anxiety between the conditions. Results were inconclusive for self-reported PTSD and depression symptoms.

FEATURED ARTICLES *continued*

Patient satisfaction ratings did not significantly differ between the two groups. *Conclusions:* Results suggest that PE can be delivered via home-based telehealth with outcomes and satisfaction ratings comparable to in-person practices for certain symptoms, however additional research is needed. This modality has the potential to address stigma- and geographic-related barriers to treatment, such as travel time and cost.

ADDITIONAL CITATIONS

Amstadter, A. B., Broman-Fulks, J., Zinzow, H., Ruggiero, K. J., & Cercone, J. (2009). **Internet-based interventions for traumatic stress-related mental health problems: A review and suggestion for future research.** *Clinical Psychology Review, 29*, 410-420 doi:10.1016/j.cpr.2009.04.001 This article is a review of the research literature on computerized and internet-based interventions (IBIs) for traumatic stress-related conditions. Effect sizes comparable to in-person psychological treatment were found for computerized or IBIs for depression and anxiety, while lower effect sizes were evidence for interventions aimed at alcohol and smoking cessation. The authors identify directions for future research, including mechanisms of change in IBI and novel web-based approaches to treatment.

Brief, D. J., Rubin, A., Keane, T. M., Enggasser, J. L., Roy, M., Helmuth, E., et al. (2013). **Web intervention for OEF/OIF Veterans with problem drinking and PTSD symptoms: A randomized clinical trial.** *Journal of Consulting and Clinical Psychology, 81*, 890-900. doi:10.1037/a0033697 Veterans who served in Operation Enduring Freedom (OEF) and Operation New Dawn (OND) with alcohol misuse and symptoms of PTSD, recruited through targeted Facebook ads, were randomized to evaluate the efficacy of a newly developed, eight-module, self-management web intervention (VetChange) based on motivational and cognitive-behavioral principles to reduce alcohol consumption, alcohol-related problems, and PTSD symptoms. Six hundred and four participants were randomized to an Initial Intervention Group (IIG); four and 196 to a Delayed Intervention Group (DIG) that waited eight weeks for access to VetChange. Intent-to-treat analyses showed that IIG and DIG as well as within-group changes. *Results:* IIG participants demonstrated greater reductions in drinking (p < .001) and PTSD symptoms (p = .009) between baseline and end-of-intervention than did DIG participants. DIG participants showed similar improvements following participation in VetChange. Improvement in alcohol symptoms was sustained at three-month follow-up.

Bush, N. E., Prins, A., Laraway, S., O'Brien, K., Ruzek, J., et al. (2014). **A pilot evaluation of the AfterDeployment.org online posttraumatic stress workshop for military service members and Veterans.** *Psychological Trauma: Theory, Research, Practice, and Policy, 6*, 109-119. doi:10.1037/a0032179 This pilot study examined the impact of an eight-week online self-management posttraumatic stress (PTS) workshop on symptoms of PTS, depression, and functional impairment on Veterans (N = 11) with PTS. Reductions in symptoms and improvements in general functioning were found for some of the Veterans. These preliminary findings suggest the online PTS workshop may be effective in reducing PTS symptoms for some Veterans.

ADDITIONAL CITATIONS *continued*

Deitsch, S. E., Frueh, B. C., & Santos, A. B. (2000). **Telepsychiatry for post-traumatic stress disorder**. *Journal of Telemedicine and Telecare, 6(3)*, 184-186. doi:10.1258/1357633001935194 This study investigated the one time use of a group therapy delivered to male combat Veterans (*N* = 4) via CVT. Results indicated that group members were satisfied with the CVT equipment and reported CVT as a valuable alternative treatment delivery modality. The authors concluded that CVT can contribute to therapy group cohesion.

Frueh, B. C., Monnier, J., Grubaugh, A. L., Elhai, J. D., Yim, E., & Knapp, R. (2007). **Therapist adherence and competence with manualized cognitive-behavioral therapy for PTSD delivered via videoconferencing technology.** *Behavior Modification, 31*, 856-866. doi:10.1177/0145445507302125 This project was the first study to test CVT for PTSD. The therapist adherence and competence ratings were compared between CBT for PTSD delivered via an in-person or CVT modality to 38 male Veterans. Clinical and process outcomes between the two conditions were similar; however, Veterans in the in-person condition reported more comfort in talking to their therapist at post-treatment compared to Veterans receiving CBT via CVT. The findings of this study suggest that therapist competence and adherence to CBT is similar between in-person and CVT delivery modalities.

Germain, V., Marchand, A., Bouchard, S., Drouin, M.-S., & Guay, S. (2009). **Effectiveness of cognitive behavioural therapy administered by videoconference for posttraumatic stress disorder.** *Cognitive Behaviour Therapy, 38*, 42-53. doi:10.1080/16506070802473494 The effectiveness of CBT for PTSD delivered via CVT (*n* = 16) compared to in-person delivery (*n* = 32) was examined in this study. Significant decreases in PTSD symptoms and improvements in overall functioning were found in participants in both conditions. The effectiveness of the treatment did not differ between the two delivery modalities.

Greene, C. J., Morland, L. A., Macdonald, A., Frueh, B. C., Grubbs, K. M., & Rosen, C. S. (2010). **How does tele-mental health affect group therapy process? Secondary analysis of a noninferiority trial.** *Journal of Consulting and Clinical Psychology, 78*, 746-750. doi:10.1037/a0020158 The effect of CVT on group therapy processes was examined in this secondary analysis of a randomized noninferiority trial (Morland et al., 2010) of an anger management treatment conducted with Veterans (*N* = 111) via a CVT compared to an in-person delivery modality. No significant differences were found on most process variables between the CVT and in-person groups. Results support the use of CVT to deliver group psychotherapy.

Gros, D. F., Yoder, M., Tuerk, P. W., Lozano, B. E., & Acierno, R. (2011). **Exposure therapy for PTSD delivered to Veterans via telehealth: Predictors of treatment completion and outcome and comparison to treatment delivered in person.** *Behavior Therapy, 42*, 276-283. doi:10.1016/j.beth.2010.07.005 This study investigated the effectiveness of 12-session exposure therapy delivered either via telehealth (n = 62) or in person (n = 27) in Veterans with PTSD. Exposure therapy delivered via telehealth was effective in reducing the symptoms of PTSD, anxiety, depression, stress, and general impairment with large effect sizes. Interestingly, exposure therapy via telehealth was less effective than exposure therapy delivered in person; however, lack of random assignment to condition limits conclusions of differential effectiveness. Overall, these findings support the utility of telehealth services to provide effective, evidence-based psychotherapies.

Morland, L. A., Hynes, A. K., Mackintosh, M.-A., Resick, P. A., & Chard, K. M. (2011). **Group cognitive processing therapy delivered to Veterans via telehealth: A pilot cohort.** *Journal of Traumatic Stress, 24*, 465-469. doi:10.1002/jts.20661 A pilot investigation of the clinical and process outcomes of a non-inferiority designed RCT examining group CPT delivered to combat Veterans with PTSD (*N* = 13) via an in-person or CVT modality was reported in this article. Reductions in PTSD symptoms were observed across conditions. No significant between-group differences were observed in either clinical or process variables between conditions. The feasibility and acceptability of group psychotherapy for PTSD delivered via CVT is supported by the results of this study.

Price, M., Kuhn, E., Hoffman, J., Ruzek, J., & Acierno, R. (in press). **Validation of the PTSD Checklist (PCL) administered via mobile device.** *Journal of Traumatic Stress*. This article reported findings of an investigation of administering the PCL to trauma-exposed individuals (*N* = 153) via a mobile device compared to paper and pencil administration. Participants completed the PCL both via a mobile app and on paper. Results indicated that reported PTSD symptoms did not differ between modality of assessment administration. The authors concluded that valid results can be obtained by self-report measures that are administered through mobile apps.

Reger, G. M., Hoffman, J., Riggs, D., Rothbaum, B. O., Ruzek, J., Holloway, K. M., et al. (2013). **The "PE Coach" smartphone application: An innovative approach to improving implementation, fidelity, and homework adherence during prolonged exposure.** *Psychological Services, 10*, 342-349. doi:10.1037/a0032774 The PE Coach, a mobile app designed to be used to augment PE treatment, is described in this article. The functions of PE Coach involve a range of capabilities for use during and after PE, including the ability to audio record sessions onto the patient's device, construct the in vivo hierarchy, complete homework exercises, review homework adherence, schedule sessions, provide reminders and notifications, and present a visual display of symptom improvement and habituation to items on the in vivo hierarchy at the conclusion of treatment. The authors note that PE Coach may improve convenience, provider implementation and adherence, and patient compliance with treatment.

Rizvi, S. L., Dimeff, L. A., Skutch, J., Carroll, D., & Linehan, M. M. (2011). **A pilot study of the DBT Coach: An interactive mobile phone application for individuals with borderline personality disorder and substance use disorder.** *Behavior Therapy, 42*, 589-600. doi:10.1016/j.beth.2011.01.003 The goal of this study was to develop and test the feasibility of an app designed specifically to enhance generalization of a specific Dialectical Behavior Therapy (DBT) skill (opposite action), DBT Coach, among individuals with borderline personality disorder and

ADDITIONAL CITATIONS *continued*

comorbid substance use disorders. Participants were 22 individuals who were enrolled in DBT treatment program were provided with and instructed to use the DBT Coach as needed for 10 to 14 days. Results demonstrated high ratings of helpfulness and usability and decreases in emotion intensity, urges to use substances, depression and general distress, thus indicating that apps may be a useful tool in the treatment of substance use disorders.

Ruggiero, K. J., Resnick, H. S., Paul, L. A., Gros, K., McCauley, J. L., Acierno, R., et al. (2012). **Randomized controlled trial of an internet-based intervention using random-digit-dial recruitment: The Disaster Recovery web project.** *Contemporary Clinical Trials, 33*, 237-246. doi:10.1016/j.cct.2011.10.001 This article describes a unique study design intended to evaluate a highly individualized online intervention with a disaster-affected population-based sample. The authors discuss challenges to developing and evaluating online interventions that target post-disaster mental health problems and provide implications for future research and practice.

Wagner, B., Brand, J., Schulz, W., & Knaevelsrud, C. (2012). **Online working alliance predicts treatment outcome for posttraumatic stress symptoms in Arab war-traumatized patients.** *Depression and Anxiety, 29*, 646-651. doi:10.1002/da.21962 This trial assessed the quality of the working alliance and its relationship with treatment outcomes of an online CBT intervention conducted with Arabic-speaking traumatized patients in Iraq (N = 55). High ratings of therapeutic alliance, which remained stable through treatment, were found early in treatment and working alliance predicted treatment outcomes for PTSD symptoms. The authors conclude that it is possible to establish a stable online therapeutic relationship in instable settings and regions of conflict where individuals experience ongoing exposure to human right violations through war and dictatorships.

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Biomarkers for Treatment and Diagnosis

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Introduction

We appear to have reached a watershed in the development of biologically based interventions for the prevention and treatment of PTSD. Over the past 25 years, great strides have been made in the characterization of biological characteristics of PTSD (Pitman et al., 2012), but there remain few biologically oriented treatments for PTSD with proven efficacy, either as stand-alone pharmacotherapies or as augmentation for otherwise generally effective exposure-based cognitive therapies such as Prolonged Exposure (PE) or Cognitive Processing Therapy (CPT). Phamacological agents tested in PTSD have typically shown large effect sizes in at least some small scale preliminary studies, but considerably smaller effects when tested against placebo in large multisite trials. Even the two United State (US) Food and Drug Administration (FDA)-approved medications for PTSD (the serotonin-selective reuptake inhibitors, sertraline and paroxetine), showed only moderate effect sizes in four large FDA registrational trials conducted in general PTSD populations (Friedman and Davidson, 2014). Although there may be many reasons for the limited success in this area of PTSD treatment development, a primary reason may be the 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. However, rapidly evolving molecular, neuroimaging, psychophysiology, and data analytic strategies embedded in new multimodal study designs may afford new opportunities to capitalize on this earned insight—in the service of developing individually based precision biotherapies for PTSD and PTSD-related comorbid conditions. The following brief bibliography has therefore been assembled to guide clinical and basic scientists through the accumulated translational knowledge base of biological factors related to PTSD risk and constituting potential PTSD treatment targets or outcome variables. The list has been limited in accordance with space and is by no means exhaustive; rather, it is intended to highlight the discovery of critical biological factors and emergence of concepts that have advanced PTSD investigations to the current vantage point.

Neuroendocrine Systems

Monoamine and Peptide Transmitters

A pharmacological challenge study by Southwick et al. (1993) was among the most influential early studies to define the molecular underpinnings of autonomic nervous system hyperreactivity associated with PTSD (Pitman et al., 1987). In this study, administration of the noradrenergic alpha-2 receptor antagonist, yohimbine, induced marked noradrenergic system hyperreactivity in association with heightend cardiovascular and PTSD symptom responses in male Vietnam Veterans. Excessive PTSD-related noradrenergic system reactivity has been replicated in both men and women and constitutes the most consistent biological abnormality in PTSD to date. However, subsequent work by Southwick et al. (1997) demonstrated that PTSD symptoms were uniquely exacerbated by yohimbine-induced norardrenergic system activation in only one-third of the cohort of Vietnam Veterans, whereas a serotonin type-2A (5HT2A) receptor agonist (meta-chlorophenylpiperazine or mCPP) activated PTSD symptoms in another third, and both the noradrenergic and serotonergic system probes

Continued on page 2

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Continued from cover

activated symptoms in yet another third. This study thus clearly demonstrated subpopulation variability in the neurobiological systems that mediate PTSD symptoms, and supported the idea that treatments for PTSD may need to be individually targeted. Consistent with these findings, Raskind et al. (2007), demonstrated salutary effects of a selective noradrenergic alpha-1 receptor antagonist on sleep quality and nightmares in 71% of a cohort of Veterans with PTSD. Current work is exploring the utility of alpha-1 blockers for treatment of daytime PTSD symptoms. Future work will hopefully make use of already identified genetic, epigenetic, and clinical biomarkers of noaradrenergic hyperreactivity to aid in pre-treatment matching between such interventions and likely responders.

Marked decreases in resting plasma neuropeptide Y (NPY) levels and blunted NPY responses to yohimbine were also found in the aforementioned cohort of Vietnam Veterans with yohimbine-induced noradrenergic hyperreactivity (Rasmusson et al., 2000). NPY levels correlated positively with bodyweight and inversely with norardrenergic, cardiovascular, and PTSD symptom responses to yohimbine. As NPY is colocalized with norepinephrine in sympathetic neurons, and with multiple other neurotransmitters in systems distributed throughout the brain and periphery, this study introduced the possibility that abnormalities in one broad-impact neurobiological factor may result in multiple comorbid stress-related medical and psychiatric conditions (e.g., Rasmusson et al., 2010; Scioli et al., 2014). Subsequent work by Sah et al. (2009) confirmed decreased cerebrospinal fluid (CSF) NPY levels in men with PTSD. In contrast, work by Morgan et al. (2000) has shown a positive relationship between peak plasma NPY levels and military performance among active duty personnel participating in intensely stressful survival school exercises, a negative relationship between NPY and dissociation during peak stress, and a negative relationship between dissociation and performance—thus demonstrating NPY's reciprocal role in stress resilience. Work by Yehuda et al. (2006 and 2014) has further defined NPY as a predictor of PTSD recovery. The influence on NPY synthesis of sex steroids, genetic factors (Karvonen et al., 2001; Zhou et al., 2008; Zhang et al., 2012), and epigenetic processes now suggests that dysregulation of this system may arise from a variety of individually-variable processes—which in turn may serve as individualized targets for interventions aimed at reducing the risk for PTSD and PTSD-related medical comorbidities.

Corticotropin-releasing factor (CRF) is another peptide dysregulated in PTSD. Bremner et al. (1997) demonstrated increased CRF levels in the CSF of male Veterans with PTSD, a finding replicated in other male PTSD cohorts (e.g., Baker et al., 1999), but not yet studied in women. CRF in this compartment is thought to reflect extrahypothalamic CRF, which mediates increases in fear and anxiety-related behavior, in part by antagonizing effects of NPY. Subsequent attempts to pharmacologically target the CRF system in the treatment of PTSD have failed due to liver toxicity, but efforts in this area of treatment development continue.

Most recently, animal work has shown a role for endocannabinoids in stress adaptation and fear extinction, leading Neumeister et al. (2013) to conduct a positron emission tomography (PET) investigation of cannabinoid type 1 (CB1) receptors in PTSD. Elevated brain cannabinoid CB1 receptor availability was found in the PTSD group, particularly in women. The PTSD group also had lower plasma levels of cortisol and the endocannabinoid, anandamide. A subsequent study by Hill et al. (2013) has demonstrated low levels of the endocannabinoid 2-arachidonoylglycerol (2-AG) in a small cohort of individuals with PTSD exposed to the 9/11 World Trade Center attack. Therefore, although basic research suggests that direct cannabinoid receptor agonists are unlikely to be useful in reducing PTSD, these studies suggest that indirect strategies to upregulate endocannabinoid system function may have value.

Steroids

Study of the glucocorticoid system in PTSD has yielded variable results, which continue to be reinterpreted as scientific experience with the complex features of this system accumulates. Yehuda et al. (1995) conducted the first study to demonstrate alterations in glucocorticoid receptor number and function in association with trauma exposure and/or PTSD, and introduced the concept of glucocorticoid receptor supersensitivity. Work over time, however, has demonstrated variability in tests of glucocorticoid feedback among PTSD populations, as well as variability in resting cortisol levels and responses to provocation. To more definitively define the function of the glucocorticoid system in PTSD, Shalev et al. (2008) undertook a large prospective study of individuals presenting to an acute care setting in the aftermath of acute trauma—and demonstrated no predictive relationship between cortisol levels and PTSD risk, although a relationship was found between high adrenocorticotropin (ACTH) levels and PTSD risk in women. However, using a machine learning approach in the same cohort, Galatzer-Levy et al. (2014) most recently demonstrated a link between low cortisol levels and PTSD risk, but only among study participants with a history of childhood trauma. In support of the relevance of early childhood trauma to adult endocrine profiles, work by Klengel et al. (2013) has elegantly demonstrated the presence of a childhood developmental window for epigenetic dysregulation of an FKBP5 gene which increases the risk for stress-related PTSD—leading to deficient function of the glucocorticoid receptor. Individuals so affected have increased and prolonged cortisol responses to stress and increased risk for peritraumatic stress reactions, as well as increased risk for PTSD and depression as adults. This phenomenon thus may account for studies finding increased ACTH and/or cortisol levels in cohorts of women with PTSD, comorbid depression, and high rates of childhood trauma. An increase in expression of FKBP5 during cognitive behavioral treatment has been shown to predict treatment efficacy.

Most recently, the variability in glucocorticoid system function in PTSD has been embraced as a predictor of treatment outcome. Yehuda et al. (2014) measured selected stress system biomarkers before and after evidence-based PE therapy and a Minimal Attention (MA) condition in male and female Veterans with PTSD. Higher bedtime salivary cortisol levels, possession of BCL1 glucocorticoid receptor genotypes associated with increased glucocorticoid receptor sensitivity, and higher plasma NPY levels predicted PTSD remission across both conditions. Higher NPY levels at baseline were also associated with better global mental health after treatment. In addition, glucocorticoid receptor sensitivity decreased, while 24-hour cortisol levels increased

across treatment in responders. In non-responders, 24-hour urinary cortisol levels decreased, while glucocorticoid receptor sensitivity increased across treatment. This is one of the first studies to simultaneously investigate the relationship between more than one system of biomarkers and treatment outcome, while characterizing functional interactions between biomarkers within systems. It will be important in future studies to consider many more systems and their functional interactions to more fully understand the mechanisms that influence PTSD risk and recovery at the individual level.

Dysregulation of other steroid systems also plays a role in PTSD risk and severity. Rasmusson et al. (2006) first demonstrated a deficit in progesterone metabolites that potently and positively modulate the inhibitory effects of gamma-amino-butyric acid (GABA) at GABAA receptors in women with PTSD. Low CSF levels of allopregnanolone and its equipotent stereoisomer, pregnanolone (apparently related to an enzymatic block in allopregnanolone synthesis) correlated strongly with the severity of PTSD re-experiencing and depression symptoms. Animal research has shown that SSRIs at low doses reduce PTSD-like symptoms by increasing levels of allopregnanolone, suggesting that allopregnanolone synthesis deficits in PTSD patients may contribute to SSRI treatment resistance. Development of pharmacotherapies targeting such deficits are thus of interest.

Alterations in dehydroepiandrosteroine (DHEA), which facilitates excitatory n-methyl-D-aspartate (NMDA) receptor function and antagonizes GABAA receptors, also have been found in PTSD. Increased DHEA/cortisol levels at peak stress or in reaction to maximum adrenal activation, or increased levels of DHEAS (the more potent sulfated metabolite of DHEA stored in tissues for use during stress) have been found to predict military stress resilience in men (Morgan et al., 2003), lower PTSD symptom burden and depression in women (Rasmusson et al., 2004), and greater improvement in PTSD symptoms over time (Yehuda et al., 2006). However, a lower resting ratio of DHEA to cortisol has been associated both with childhood trauma (Yehuda et al., 2006) and with lower PTSD symptom severity after treatment (Yehuda et al., 2014). This suggests the importance of assessing childhood trauma, as well as distinguishing between resting and stress reactive ratios of DHEA to cortisol when using this metric as a biopredictor. As observed by Rasmusson et al. (2004), the ratio of DHEA to cortisol increased in response to maximum adrenal gland activation among trauma-exposed individual with and without PTSD, but decreased among non-traumatized individuals. Thus a lower resting DHEA to cortisol ratio may reflect less sensitivity to mild environmental stress among individuals with less severe PTSD. A higher DHEA/allopregnanolone ratio in CSF has been linked to greater re-experiencing and negative mood symptoms in women with PTSD (Rasmusson et al., 2006), suggesting that the balance of excitatory to inhibitory neurotransmission may be critical to PTSD symptom pathogenesis.

Genetics

Molecular genomics studies are multiplying and promise to contribute significantly to our understanding of mechanisms underlying PTSD risk. For example, epigenetic studies investigate functionally relevant changes to deoxyribonucleic acid (DNA) that do not involve a change in the nucleotide sequence and that may result from environmental influences. Epigenetic mechanisms include methylation of individual nucleotides and histone modifications (e.g., acetylation) that alter gene expression without altering the underlying DNA sequence. Uddin et al. (2010) conducted the first epigenetics study demonstrating differences in DNA methylation profiles between PTSD affected and unaffected groups. Using samples from the Detroit Neighborhood Health Study, the investigators found that PTSD was associated with altered immunologial function as indicated by decreased methylation of immune system genes in association with increased titers of antibodies to an infectious agent with high community prevalence. This work is consistent with a growing number of studies showing alterations in inflammatory factors in PTSD (e.g. Gill et al., 2008), suggesting the potential for future work in this area to help explain the high comorbidity between PTSD and multiple negative physical health sequelae of traumatic stress.

Ressler et al. (2011) conducted the first study demonstrating sex differences in a genetic risk factor for PTSD. A single nucleotide polymorphism (SNP) in a putative estrogen response element within the promoter for a gene (ADCYAP1R1) encoding the pituitary adenylate cyclase-activating polypeptide (PACAP) receptor (PAC1) predicted PTSD diagnosis and symptoms in females only. This finding may partially explain the higher prevalence of PTSD among females. Furthermore, considering the link between testosterone conversion to estrogen and aggression in males, it may be important to consider the role of such an estrogen dependent gene in PTSD even in male subpopulations. A subsequent study (Gillespie et al., 2013) demonstrated increased risk for PTSD in men with an apparent loss-of-function polymorphism in the gene coding for 5α-reductase-2, which converts testosterone to its more potent metabolite, 5α-dihydrotestosterone (5α-DHT), which is, in turn, metabolized to an inhibitory GABAergic neuroactive steroid (3α-diol). 5α-DHT may also serve to upregulate genes for enzymes that produce other resilience-related factors such as NPY or allopregnanolone. Yehuda et al. (2009) has shown that a reduction in the activity of 5α-reductase predicts poor outcome in response to a brief series of prolonged exposure therapy sessions.

Logue et al. (2013) conducted the first genome-wide association study (GWAS) in PTSD and established the retinoid-related orphan receptor alpha (RORA) gene as a PTSD risk locus. RORA is a nuclear hormone receptor involved in the protection of neurons and glia from oxidative stress, and RORA dysfunction is associated with reductions in grey and white matter integrity. RORA is also involved in brain development and regulation of circadian rhythms and steroid hormones. In a GWAS by Wolf et al. (2014), the ADCY8 and DPP6 genes were implicated in the new DSM-5 dissociative subtype of PTSD. ADCY8 is integral to long-term potentiation and synaptic plasticity, while DPP6 is critical for integration of synaptic inputs and neuronal excitation. Thus both are critical to sensory integration and cognitive processing of experience.

Psychophysiology Studies

Many studies have demonstrated increased reactivity to trauma-related cues and unconditioned noxious stimuli in PTSD (e.g., Pitman et al., 1987; Orr et al., 2003). They have also

demonstrated a variety of PTSD-related abnormalities in fear conditioning paradigms—including diminished extinction retention (Milad et al., 2009) and failure to inhibit learned fear in the context of learned safety signals (e.g., Jovanovic et al., 2013). Objective and subjective studies of PTSD-related sleep disturbances have also revealed a variety of sleep architecture abnormalities (Woodward et al., 2000; Richards et al., 2013; Kobayashi and Mellman, 2012). Objective and subjective sleep deficits in PTSD have been mapped onto abnormal nighttime peripheral noradrenergic indices and brain GABA and glutamate levels, respectively (Mellman et al., 1995 and Meyerhoff et al., 2014).

Brain Imaging

Bremner et al (1995) provided the first evidence of decreased hippocampal volume in PTSD, a brain region related to memory and fear extinction. Several studies, but not all, have replicated this finding in PTSD, depression, and various other psychiatric disorders. Gray matter reductions in PTSD have also been demonstrated in other brain regions (e.g. anterior cingulate). These findings are consistent with a hypothetical model in which stress dysregulates hypothalamic-pituitary-adrenal (HPA) axis and glial function, leading to increased glutamate excitotoxicity, and subsequent gray matter reduction. Supporting this model, pilot studies have shown normalization of hippocampal structure and function following treatment (Levy-Gigi et al., 2013; reviewed by Thomaes et al. 2014). A subsequent elegant twin study by Gilbertson et al. (2002) has provided strong evidence for small hippocampus size as a predisposing factor for PTSD, rather than a consequence. More recent work has presented a more complex picture wherein altered brain structures constitute both vulnerabilities to and outcomes of posttraumatic stress (Sekiguchi et al. 2013).

Reduced prefrontal cortex, but increased amygdala, activation in response to emotional processing (see Phan et al., 2002), has been repeatedly—but not consistently—demonstrated in PTSD. Etkin et al. (2007) therefore undertook a meta-analysis and confirmed these abnormalities. The specificity of the prefrontal impairment to PTSD was also demonstrated, supporting a PTSD model of reduced top-down control combined with increased bottom-up emotional sensitization. In contrast, in the dissociative subtype of PTSD, Lanius et al. (2012) found an increase in limbic inhibition by the midline prefrontal cortex.

Shin et al. (2011) used the Vietnam Twin Registry to confirm previous work suggesting that enhanced resting metabolic activity in the dorsal anterior and medial cingulate cortices (dACC/MCC) constitutes a familial risk factor, rather than state marker for PTSD. In this study, Shin et al. demonstrated that combat-exposed Veterans with PTSD and their unexposed co-twins had significantly greater activation in the dorsal anterior cingulate and a larger response time difference scores on the Multi-Source Interference Task, as compared to combat Veterans without PTSD and their co-twins.

Finally, a proof-of-concept study by Bryant et al. (2008) demonstrated the possible utility of imaging biomarkers in predicting treatment response. Other PTSD studies have shown that gray matter abnormalities predict poor response to cognitive behavior therapy (CBT) and eye movement desensitization and reprocessing (EMDR) therapy. In depression, brain structural deficits have been related to poor response to serotonergic drugs, but enhanced response to glutamatergic antidepressants, suggesting the presence of a subpopulation of patients with possible glutamate-based abnormalities leading to structural deficits and treatment resistance to serotonergic drugs (Abdallah et al. 2014).

Summary

A survey of the extant literature supports roles for a variety of interacting stress responsive factors in the pathogenesis of PTSD as well as the medical and other psychiatric features with which PTSD is commonly comorbid. Some factors such as adoption of nicotine or alcohol abuse on a casual basis or with the intention of self-treating stress-related symptoms may alter neuroendocrine profiles in directions that mimic the effects of naturally acquired PTSD risk factors (e.g. Cagetti et al., 2004; Koenen et al., 2005). Understanding and addressing the epigenetic or more direct regulatory effects of such environmental risk factors thus will be as important as revealing interactive genetic PTSD risk factors—so that individualized interventions can be appropriately targeted. Indeed, understanding bottom up individual points of malfunction in particular stress systems will be critical to the differential diagnosis and targeting of effective individualized treatments. For example, parsing out how epigenetic changes in the function of healthy genes mimic the effects of less healthy gene polymorphisms will strengthen our capacity to identify key pathogenetic pathways to PTSD as well as enable the targeted use of promising epigenetic treatments ranging from the exercise of particular brain circuits to exercise itself to the employment of epigenetics based pharmaceutical strategies. In support of these efforts, the emergence of fully translational study designs, and use of cutting edge data analytic strategies that embrace the real complexities of biological systems and allow for both direct testing of hypotheses as well as discovery within a common large dataset hold great promise. The related redesign of treatment trials to identify and enroll individuals possessing biological deficits to which particular treatments are matched or to enable identification of signals from true responder subpopulations can then speed development of more effective interventions for PTSD prevention and treatment.

FEATURED ARTICLES

Bremner, J.D., Randall, P., Scott, T.M., Bronen, R.A., Seibyl, J.P., Southwick, S.M., et al. (1995). **MRI-based measurement of hippocampal volume in patients with combat-related posttraumatic stress disorder.** *American Journal of Psychiatry, 152*, 973-981. *Objective:* Studies in nonhuman primates suggest that high levels of cortisol associated with stress have neurotoxic effects on the hippocampus, a brain structure involved in memory. The authors previously showed that patients with combat-related PTSD had deficits in short-term memory. The purpose of this study was to compare the hippocampal volume of patients with PTSD to that of subjects without psychiatric disorder. *Method:* Magnetic resonance imaging was used to measure the volume of the hippocampus in 26 Vietnam combat Veterans with PTSD and 22 comparison subjects selected to be

similar to the patients in age, sex, race, years of education, socioeconomic status, body size, and years of alcohol abuse. *Results:* The PTSD patients had a statistically significant 8% smaller right hippocampal volume relative to that of the comparison subjects, but there was no difference in the volume of other brain regions (caudate and temporal lobe). Deficits in short-term verbal memory as measured with the Wechsler Memory Scale were associated with smaller right hippocampal volume in the PTSD patients only. *Conclusions:* These findings are consistent with a smaller right hippocampal volume in PTSD that is associated with functional deficits in verbal memory.

Bremner, J.D., Licinio, J., Darnell, A., Krystal, J.H., Owens, M.J., Southwick, S.M., et al. (1997). **Elevated CSF corticotropin-releasing factor concentrations in posttraumatic stress disorder.** *The American Journal of Psychiatry, 154*, 624–629. *Objective:* Corticotropin-releasing factor (CRF) and somatostatin both play important roles in mediating responses to acute and chronic stress. The purpose of this study was to measure CSF concentrations of CRF and somatostatin in patients with chronic combat-related PTSD and comparison subjects. *Method:* Lumbar punctures for collection of CSF were performed in Vietnam combat Veterans with PTSD (*N* = 11) and comparison subjects (*N* = 17). CSF concentrations of CRF and somatostatin were compared between the two groups. *Results:* CSF concentrations of CRF were higher in the PTSD patients than in the comparison subjects (mean = 29.0 picograms per milliliter [pg/ml], SD = 7.8, versus mean = 21.9 pg/ml, SD = 6.0). This group difference remained significant after covariance for age. CSF somatostatin concentrations in PTSD patients were higher than those of the comparison subjects (mean = 19.9 pg/ml, SD = 5.4, versus mean = 13.7 pg/ml, SD = 8.0). However, co-varying for age reduced the level of significance. *Conclusions:* Higher CSF CRF concentrations in patients with PTSD may reflect alterations in stress-related neurotransmitter systems. The higher CSF CRF concentrations may play a role in disturbances of arousal in patients with PTSD.

Bryant, R.A., Felmingham, K., Kemp, A., Das, P., Hughes, G., Peduto, A., et al. (2008). **Amygdala and ventral anterior cingulate activation predicts treatment response to cognitive behaviour therapy for post-traumatic stress disorder.** *Psychological Medicine, 38*, 555-561. doi:10.1017/S0033291707002231 *Background:* Although CBT is the treatment of choice for PTSD, approximately half of patients do not respond to CBT. No studies have investigated the capacity for neural responses during fear processing to predict treatment response in PTSD. *Method:* Functional magnetic resonance imaging (fMRI) responses of the brain were examined in individuals with PTSD (*n*=14). fMRI was examined in response to fearful and neutral facial expressions presented rapidly in a backwards masking paradigm adapted for a 1.5 T scanner. Patients then received eight sessions of CBT that comprised education, imaginal and *in vivo* exposure, and cognitive therapy. Treatment response was assessed 6 months after therapy completion. *Results:* Seven patients were treatment responders (defined as a reduction of 50% of pretreatment scores) and seven were non-responders. Poor improvement after treatment was associated with greater bilateral amygdala and ventral anterior cingulate activation in response to masked fearful faces. *Conclusions:* Excessive fear responses in response to fear-eliciting stimuli may be a key factor in limiting responses to CBT for PTSD. This excessive amygdala response to fear may reflect difficulty in managing anxiety reactions elicited during CBT, and this factor may limit optimal response to therapy.

Etkin, A., & Wager, T.D. (2007). **Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia.** *American Journal of Psychiatry, 164*, 1476-1488. doi:10.1176/appi.ajp.2007.07030504 *Objective:* The study of human anxiety disorders has benefited greatly from functional neuroimaging approaches. Individual studies, however, vary greatly in their findings. The authors searched for common and disorder-specific functional neurobiological deficits in several anxiety disorders. The authors also compared these deficits to the neural systems engaged during anticipatory anxiety in healthy subjects. *Method:* Functional magnetic resonance imaging and positron emission tomography studies of PTSD, social anxiety disorder, specific phobia, and fear conditioning in healthy individuals were compared by quantitative meta-analysis. Included studies compared negative emotional processing to baseline, neutral, or positive emotion conditions. *Results:* Patients with any of the three disorders consistently showed greater activity than matched comparison subjects in the amygdala and insula, structures linked to negative emotional responses. A similar pattern was observed during fear conditioning in healthy subjects. Hyperactivation in the amygdala and insula were, of interest, more frequently observed in social anxiety disorder and specific phobia than in PTSD. By contrast, only patients with PTSD showed hypoactivation in the dorsal and rostral anterior cingulate cortices and the ventromedial prefrontal cortex—structures linked to the experience and regulation of emotion. *Conclusions:* This meta-analysis allowed us to synthesize often disparate findings from individual studies and thereby provide neuroimaging evidence for common brain mechanisms in anxiety disorders and normal fear. Effects unique to PTSD furthermore suggested a mechanism for the emotional dysregulation symptoms in PTSD that extend beyond an exaggerated fear response. Therefore, these findings help refine our understanding of anxiety disorders and their interrelationships.

Gilbertson, M.W., Shenton, M.E., Ciszewski, A., Kasai, K., Lasko, N.B., Orr, S.P., et al. (2002). **Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma.** *Nature Neuroscience, 5*, 1242-1247. doi:10.1038/nn958 In animals, exposure to severe stress can damage the hippocampus. Recent human studies show smaller hippocampal volume in individuals with the stress-related psychiatric condition PTSD. Does this represent the neurotoxic effect of trauma, or is smaller hippocampal volume a pre-existing condition that renders the brain more vulnerable to the development of pathological stress responses? In monozygotic twins discordant for trauma exposure, we found evidence that smaller hippocampi indeed constitute a risk factor for the development of stress-related psychopathology. Disorder severity in PTSD patients who were exposed to trauma was negatively correlated with the hippocampal

volume of both the patients and the patients' trauma-unexposed identical co-twin. Furthermore, severe PTSD twin pairs—both the trauma-exposed and unexposed members—had significantly smaller hippocampi than non-PTSD pairs.

Gillespie, C.F., Almli, L.M., Smith, A.K., Bradley, B., Kerley, K., Crain, D.F., et al. (2013). **Sex dependent influence of a functional polymorphism in steroid 5-alpha-reductase type 2 (SRD5A2) on post-traumatic stress symptoms.** *American Journal of Medical Genetics. Part B, Neuropsychiatric Genetics: 162B*, 283-292. doi:10.1002/ajmg.b.32147 A non-synonymous, SNP in the gene coding for steroid 5-α-reductase type 2 *(SRD5A2)* is associated with reduced conversion of testosterone to DHT. Because *SRD5A2* participates in the regulation of testosterone and cortisol metabolism, hormones shown to be dysregulated in patients with PTSD, we examined whether the V89L variant (rs523349) influences risk for. Study participants ($N = 1,443$) were traumatized African-American patients of low socioeconomic status with high rates of lifetime trauma exposure recruited from the primary care clinics of a large, urban hospital. PTSD symptoms were measured with the post-traumatic stress symptom scale (PSS). Subjects were genotyped for the V89L variant (rs523349) of *SRD5A2*. We initially found a significant sex-dependent effect of genotype in male but not female subjects on symptoms. Associations with PTSD symptoms were confirmed using a separate internal replication sample with identical methods of data analysis, followed by pooled analysis of the combined samples ($N = 1,443$, sex × genotype interaction $p < 0.002$; males: $n = 536$, $p < 0.001$). These data support the hypothesis that functional variation within *SRD5A2* influences, in a sex-specific way, the severity of post-traumatic stress symptoms and risk for diagnosis of PTSD.

Jovanovic, T., Sakoman, A.J., Kozaric-Kovacic, D., Mestrovic, A.H., Duncan, E.J., Davis, M., et al. (2013). **Acute stress disorder versus chronic posttraumatic stress disorder: Inhibition of fear as a function of time since trauma.** *Depression & Anxiety. 30*, 217-224. doi:10.1002/da.21991 *Background:* Previous work has shown that inhibition of fear is impaired in PTSD resulting from both civilian and combat trauma. The purpose of the present study was to investigate the inhibition of learned fear in traumatized individuals diagnosed with either acute stress disorder (ASD) or PTSD. This is the first study to use a conditioned inhibition paradigm with traumatized individuals within a month of trauma exposure. We hypothesized that impaired fear inhibition would be evident in PTSD, but not ASD. *Method:* Using established translational, psychophysiological methods including fear-potentiated startle, and skin conductance, we examined fear acquisition, stimulus discrimination, and the transfer of learned safety in a Croatian population with ASD or PTSD. This cross-sectional study included three age-matched groups: healthy non-trauma controls ($n = 27$), a group with chronic PTSD (10 or more years since trauma exposure, $n = 24$), and a group with ASD (30 days or less since trauma exposure, $n = 27$). *Results:* The presence of trauma-related psychopathology, whether acute or chronic, was associated with an impaired ability to transfer learned safety based on fear-potentiated startle measures, while healthy control subjects showed significant fear inhibition in the presence of the safety cue compared to the danger cue, $F(1,26) = 12.64$, $p = .001$. *Conclusions:* These data expand our previously observed findings of PTSD-associated fear inhibition deficits by demonstrating that trauma-related impairments in safety learning are evident within 30 days of trauma exposure.

Klengel, T., Mehta, D., Anacker, C., Rex-Haffner, M., Pruessner, J.C., Pariante, C.M., et al. (2013). **Allele-specific FKBP5 DNA demethylation mediates gene-childhood trauma interactions.** *Nature Neuroscience, 16*, 33-41. doi:10.1038/nn.3275 Although the fact that genetic predisposition and environmental exposures interact to shape development and function of the human brain and, ultimately, the risk of psychiatric disorders has drawn wide interest, the corresponding molecular mechanisms have not yet been elucidated. We found that a functional polymorphism altering chromatin interaction between the transcription start site and long-range enhancers in the FK506 binding protein 5 (*FKBP5*) gene, an important regulator of the stress hormone system, increased the risk of developing stress-related psychiatric disorders in adulthood by allele-specific, childhood trauma–dependent DNA demethylation in functional glucocorticoid response elements of *FKBP5*. This demethylation was linked to increased stress-dependent gene transcription followed by a long-term dysregulation of the stress hormone system and a global effect on the function of immune cells and brain areas associated with stress regulation. This identification of molecular mechanisms of genotype-directed long-term environmental reactivity will be useful for designing more effective treatment strategies for stress-related disorders.

Koenen, K.C., Hitsman, B., Lyons, M.J., Niaura, R., McCaffery, J., Goldberg, J., et al. (2005). **A twin registry study of the relationship between posttraumatic stress disorder and nicotine dependence in men.** *Archives of General Psychiatry, 62*, 1258-1265. doi:10.1001/archpsyc.62.11 *Context:* Recent studies indicate a strong association between PTSD and nicotine dependence (ND). However, the explanation for the association remains unclear. *Objective:* To test competing explanations for the association between PTSD and ND. *Design, Setting, and Participants:* Analysis of data on 6744 members of the Vietnam Era Twin Registry, a national registry of all male-male twin pairs who served in the military during the Vietnam era interviewed in 1991-1992. *Main Outcome Measures:* Risk of PTSD and ND using the Diagnostic Interview Schedule for the *DSM-III-R*. *Results:* The prevalence of ND was elevated among trauma-exposed individuals (52.0%) and those with PTSD (71.7%) compared with unexposed individuals (40.5%). This association was significant for ND and for trauma without PTSD (odds ratio, 1.31; 95% confidence interval [CI], 1.18-1.45) and for PTSD (odds ratio, 2.34; 95% CI, 1.92-2.84) and was not entirely explained by shared risk factors. Shared genetic effects explained 63% of the PTSD-ND association; the remaining covariance was explained by individual-specific environmental effects. Using survival analysis with time-dependent covariates, ND was associated with a substantially increased risk of PTSD among trauma-exposed men (hazard ratio, 1.98; 95% CI, 1.61-2.42). Trauma (hazard ratio, 1.49; 95% CI, 1.35-1.64) and PTSD (hazard ratio, 1.36; 95% CI, 1.14-1.61) were less strongly

but significantly associated with increased risk of ND onset after controlling for shared risk factors. *Conclusions:* Most of the PTSD-ND association is explained by shared genetic effects. However, there is a substantial, robust PTSD-ND association not explained by shared risk factors. Multiple explanations for the association were supported; however, the strongest association was consistent with preexisting ND increasing the risk of PTSD onset. These data suggest that male Veterans with a history of ND may be at increased risk for PTSD. Further research on the biological mechanisms underlying PTSD-ND comorbidity is needed.

Logue, M.W., Baldwin, C., Guffanti, G., Melista, E., Wolf, E.J., Reardon, A.F., et al. (2013). **A genome-wide association study of post-traumatic stress disorder identifies the retinoid-related orphan receptor alpha (RORA) gene as a significant risk locus.** *Molecular Psychiatry, 18*, 937-942. doi:10.1038/mp.2012.113 We describe the results of the first GWAS of PTSD performed using trauma-exposed white non-Hispanic participants from a cohort of Veterans and their intimate partners (295 cases and 196 controls). Several SNPs yielded evidence of association. One SNP (rs8042149), located in the RORA, reached genome-wide significance. Nominally significant associations were observed for other RORA SNPs in two African-American replication samples-one from the veteran cohort (43 cases and 41 controls) and another independent cohort (100 cases and 421 controls). However, only the associated SNP from the veteran African-American replication sample survived gene-level multiple-testing correction. RORA has been implicated in prior GWAS studies of psychiatric disorders and is known to have an important role in neuroprotection and other behaviorally relevant processes. This study represents an important step toward identifying the genetic underpinnings of PTSD.

Meyerhoff, D.J., Mon, A., Metzler, T., & Neylan, T.C. (2014). **Cortical gamma-aminobutyric acid and glutamate in posttraumatic stress disorder and their relationships to self-reported sleep quality.** *Sleep. 37*, 893-900. doi:10.5665/sleep.3654 *Study Objectives:* To test if PTSD is associated with low brain GABA levels and if reduced GABA is mediated by poor sleep quality. *Design:* Laboratory study using *in vivo* proton magnetic resonance spectroscopy (1H MRS) and behavioral testing. *Setting:* VA Medical Center Research Service, Psychiatry and Radiology. *Patients Or Participants:* Twenty-seven patients with PTSD (PTSD+) and 18 trauma-exposed controls without PTSD (PTSD-), recruited from US Army reservists, Army National Guard, and mental health clinics. *Interventions:* None. *Measurements And Results:* 1H MRS at 4 Tesla yielded spectra from three cortical brain regions. In parieto-occipital and temporal cortices, PTSD+ had lower GABA concentrations than PTSD-. As expected, PTSD+ had higher depressive and anxiety symptom scores and a higher Insomnia Severity Index (ISI) score. Higher ISI correlated with lower GABA and higher glutamate levels in parieto-occipital cortex and tended to correlate with lower GABA in the anterior cingulate. The relationship between parieto-occipital GABA and PTSD diagnosis was fully mediated through insomnia severity. Lower N-acetylaspartate and glutamate concentrations in the anterior cingulate cortex correlated with higher arousal scores, whereas depressive and anxiety symptoms did generally not influence metabolite concentrations. *Conclusions:* Low brain GABA concentration in PTSD is consistent with most findings in panic and social anxiety disorders. Low GABA associated with poor sleep quality is consistent with the hyperarousal theory of both primary insomnia and PTSD. Our data demonstrate that poor sleep quality mediates low parieto-occipital GABA in PTSD. The findings have implications for PTSD treatment approaches.

Milad, M.R., Pitman, R.K., Ellis, C.B., Gold, A.L., Shin, L.M., Lasko, N.B., et al. (2009). **Neurobiological basis of failure to recall extinction memory in posttraumatic stress disorder.** *Biological Psychiatry, 66*, 1075-1082. doi:10.1016/j.biopsych.2009.06.026 *Background:* A clinical characteristic of PTSD is persistently elevated fear responses to stimuli associated with the traumatic event. The objective herein is to determine whether extinction of fear responses is impaired in PTSD and whether such impairment is related to dysfunctional activation of brain regions known to be involved in fear extinction, viz., amygdala, hippocampus, ventromedial prefrontal cortex (vmPFC), and dACC. *Methods:* Sixteen individuals diagnosed with PTSD and 15 trauma-exposed non-PTSD control subjects underwent a 2-day fear conditioning and extinction protocol in a 3-T functional magnetic resonance imaging scanner. Conditioning and extinction training were conducted on Day 1. Extinction recall (or extinction memory) test was conducted on Day 2 (extinguished conditioned stimuli presented in the absence of shock). Skin conductance response (SCR) was scored throughout the experiment as an index of the conditioned response. *Results:* The SCR data revealed no significant differences between groups during acquisition and extinction of conditioned fear on Day 1. On Day 2, however, PTSD subjects showed impaired recall of extinction memory. Analysis of functional magnetic resonance imaging data showed greater amygdala activation in the PTSD group during Day 1 extinction learning. During extinction recall, lesser activation in hippocampus and vmPFC and greater activation in dACC were observed in the PTSD group. The magnitude of extinction memory across all subjects was correlated with activation of hippocampus and vmPFC during extinction recall testing. *Conclusions:*These findings support the hypothesis that fear extinction is impaired in PTSD. They further suggest that dysfunctional activation in brain structures that mediate fear extinction learning, and especially its recall, underlie this impairment.

Morgan, C.A., Wang, S., Southwick, S.M., Rasmusson, A., Hazlett, G., Hauger, R.L., et al. (2000). **Plasma neuropeptide-Y concentrations in humans exposed to military survival training.** *Biological Psychiatry, 47*, 902-909. doi:10.1016/S0006-3223(99)00239-5 *Background:* NPY is present in extensive neuronal systems of the brain and is present in high concentrations in cell bodies and terminals in the amygdala. Preclinical studies have shown that injections of NPY into the central nucleus of the amygdala function as a central anxiolytic and buffer against the effects of stress. The objective of this study was to assess plasma NPY immunoreactivity in healthy soldiers participating in high intensity military training at the US Army survival school. The Army survival school provides a means of observing individuals under high levels of physical, environmental, and psychological stress, and consequently is considered a reasonable analogue to stress

incurred as a result of war or other catastrophic experiences. *Methods:* Plasma levels of NPY were assessed at baseline (prior to initiation of training), and 24 hours after the conclusion of survival training in 49 subjects, and at baseline and during the Prisoner of War (POW) experience (immediately after exposure to a military interrogation) in 21 additional subjects. *Results:* Plasma NPY levels were significantly increased compared to baseline following interrogations and were significantly higher in Special Forces soldiers, compared to non-Special Forces soldiers. NPY elicited by interrogation stress was significantly correlated to the subjects' behavior during interrogations and tended to be negatively correlated to symptoms of reported dissociation. Twenty-four hours after the conclusion of survival training, NPY had returned to baseline in Special Forces soldiers, but remained significantly lower than baseline values in non–Special Forces soldiers. NPY was positively correlated with both cortisol and behavioral performance under stress. NPY was negatively related to psychological symptoms of dissociation. *Conclusions:* These results provide evidence that uncontrollable stress significantly increases plasma NPY in humans, and when extended, produces a significant depletion of plasma NPY. Stress-induced alterations of plasma NPY were significantly different in Special Forces soldiers compared to non-Special Forces soldiers. These data support the idea that NPY may be involved in the enhanced stress resilience seen in humans.

Neumeister, A., Normandin, M.D., Pietrzak, R.H., Piomelli, D., Zheng, M.Q., Gujarro-Anton, A., et al. (2013). **Elevated brain cannabinoid CB1 receptor availability in post-traumatic stress disorder: A positron emission tomography study.** *Molecular Psychiatry, 18*, 1034-1040. doi:10.1038/mp.2013.61 Endocannabinoids and their attending CB1 receptor have been implicated in animal models of PTSD. However, their specific role has not been studied in people with PTSD. Herein, we present an *in vivo* imaging study using PET and the CB1-selective radioligand [(11)C]OMAR in individuals with PTSD, and healthy controls with lifetime histories of trauma (trauma-exposed controls (TC)) and those without such histories (healthy controls (HC)). Untreated individuals with PTSD (N = 25) with non-combat trauma histories, and TC (N = 12) and HC (N = 23) participated in a magnetic resonance imaging scan and a resting PET scan with the CB1 receptor antagonist radiotracer [(11)C]OMAR, which measures the volume of distribution (VT) linearly related to CB1 receptor availability. Peripheral levels of anandamide, 2-arachidonoylglycerol, oleoylethanolamide, palmitoylethanolamide and cortisol were also assessed. In the PTSD group, relative to the HC and TC groups, we found elevated brain-wide [(11)C]OMAR VT values ($F(2,53)=7.96$, p = 0.001; 19.5% and 14.5% higher, respectively), which were most pronounced in women ($F(1,53)=5.52$, p = 0.023). Anandamide concentrations were reduced in the PTSD relative to the TC (53.1% lower) and HC (58.2% lower) groups. Cortisol levels were lower in the PTSD and TC groups relative to the HC group. Three biomarkers examined collectively—OMAR VT, anandamide and cortisol—correctly classified nearly 85% of PTSD cases. These results suggest that abnormal CB1 receptor-mediated anandamide signaling is implicated in the etiology of PTSD, and provide a promising neurobiological model to develop novel, evidence-based pharmacotherapies for this disorder.

Pitman, R.K., Orr, S.P., Forgue, D.F., deJong, J.B., & Claiborn, J. M. (1987). **Psychophysiologic assessment of posttraumatic stress disorder imagery in Vietnam combat Veterans.** *Archives of General Psychiatry, 44*, 970-975. doi:10.1001/archpsyc.1987.01800230050009 This study used psychophysiologic techniques to assess emotional arousal during imagery of psychologically traumatic experiences. All subjects were medication-free Vietnam combat Veterans, classified on the basis of *DSM-III-R* criteria into groups with PTSD (n =18) and no mental disorder (control, n =15), which did not differ in extent of combat or in the judged severity of the traumatic experiences reported. "Scripts" describing each subject's combat experiences as well as other experiences were read to them in the laboratory, and they were instructed to imagine the events the scripts portrayed, while heart rate, skin conductance, and frontalis electromyogram were recorded. The PTSD subjects' physiologic responses to their combat scripts were markedly higher than the controls'. The combined physiologic variables identified PTSD subjects with a specificity of 100% and a sensitivity of 61%. The results demonstrate exaggerated physiologic arousal during recollection of traumatic experiences in PTSD.

Pitman, R K., Rasmusson, A.M., Koenen, K.C., Shin, L.M., Orr, S.P., Gilbertson, M.W., et al. (2012). **Biological studies of post-traumatic stress disorder.** *Nature Reviews Neuroscience, 13*, 769-787. doi:10.1038/nrn3339 PTSD is the only major mental disorder for which a cause is considered to be known: that is, an event that involves threat to the physical integrity of oneself or others and induces a response of intense fear, helplessness or horror. Although PTSD is still largely regarded as a psychological phenomenon, over the past three decades the growth of the biological PTSD literature has been explosive, and thousands of references now exist. Ultimately, the impact of an environmental event, such as a psychological trauma, must be understood at organic, cellular and molecular levels. This Review attempts to present the current state of this understanding on the basis of psychophysiological, structural and functional neuroimaging, and endocrinological, genetic and molecular biological studies in humans and in animal models.

Raskind, M.A., Peskind, E.R., Hoff, D.J., Hart, K.L., Holmes, H.A., Warren, D., et al. (2007). **A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat Veterans with post-traumatic stress disorder.** *Biological Psychiatry, 61*, 928-934. doi:10.1016/j.biopsych.2006.06.032 *Background:* Excessive brain responsiveness to norepinephrine appears to contribute to PTSD, particularly at night. Prazosin, a brain active alpha-1 adrenergic receptor antagonist, significantly reduced trauma nightmares and sleep disturbance in 10 Vietnam War combat Veterans in a previous placebo-controlled crossover study. The current parallel group trial in a larger sample of Veterans evaluated prazosin effects on trauma nightmares, sleep quality, global clinical status, dream characteristics, and comorbid depression. *Methods:* Forty Veterans (mean age 56 ± 9) with chronic PTSD and distressing trauma nightmares and sleep disturbance were randomized to evening prazosin (13.3 ± 3 milligrams per day [mg/day]) or placebo for 8 weeks. *Results:* In the evaluable sample (n = 34), primary outcome

measures demonstrated that prazosin was significantly superior to placebo for reducing trauma nightmares and improving sleep quality and global clinical status with large effect sizes. Prazosin shifted dream characteristics from those typical of trauma-related nightmares toward those typical of normal dreams. Blood pressure changes from baseline to end study did not differ significantly between prazosin and placebo. *Conclusions:* Prazosin is an effective and well-tolerated treatment for trauma nightmares, sleep disturbance and global clinical status in Veterans with chronic PTSD.

Rasmusson, A.M., Hauger, R.L., Morgan C.A., Bremner, J.D., Charney, D.S., & Southwick, S.M. (2000). **Low baseline and yohimbine-stimulated plasma neuropeptide Y (NPY) levels in combat-related PTSD.** *Biological Psychiatry, 47*, 526-539. doi:10.1016/s0006-3223(99)00185-7 *Background:* Consistent with many studies demonstrating enhanced reactivity of the sympathetic nervous system in PTSD, the administration of yohimbine, a noradrenergic α2-antagonist, has been shown to increase core symptoms of PTSD and to induce greater increases in plasma 3-methyl-4-hydroxy-phenyl-glycol (MHPG) in subjects with PTSD compared with healthy control subjects. In turn, NPY has been shown to inhibit the release of norepinephrine from sympathetic noradrenergic neurons. *Methods:* In the following study, plasma NPY responses to yohimbine and placebo were measured in a subgroup of 18 subjects with PTSD and 8 healthy control subjects who participated in the previous study of the effect of yohimbine on plasma MHPG. *Results:* The PTSD subjects had lower baseline plasma NPY and blunted yohimbine-stimulated increases in plasma NPY compared with the healthy control subjects. Within the PTSD group, baseline plasma NPY levels correlated negatively with combat exposure scale scores, baseline PTSD and panic symptoms, and yohimbine-stimulated increases in MHPG and systolic blood pressure. *Conclusions:* This study suggests that combat stress-induced decreases in plasma NPY may mediate, in part, the noradrenergic system hyperreactivity observed in combat-related PTSD. The persistence of this decrease in plasma NPY may contribute to symptoms of hyperarousal and the expression of exaggerated alarm reactions, anxiety reactions, or both in combat Veterans with PTSD long after war.

Rasmusson, A.M., Pinna, G., Paliwal, P., Weisman, D., Gottschalk, C., Charney D., et al. (2006). **Decreased cerebrospinal fluid allopregnanolone levels in women with posttraumatic stress disorder.** *Biological Psychiatry, 60*, 704-713. doi:10.1016/j.biopsych.2006.03.026 *Background:* Alterations in the γ-amino-butyric acid (GABA) neurotransmitter system have been identified in some populations with PTSD. *Methods:* To further investigate factors of relevance to GABAergic neurotransmission in PTSD, we measured CSF levels of allopregnanolone and pregnanolone combined (ALLO: congeners that potently and positively modulate effects of GABA at the GABAA receptor), 5LOdihydroprogesterone (5ydroprogesterone (5ners that potentallopregnanolone), DHEA (a negative modulator of GABAA receptor function), and progesterone with gas chromatography, mass spectrometry in premenopausal women with (n = 9) and without (n = 10) PTSD. Subjects were free of psychotropic medications, alcohol, and illicit drugs; all were in the follicular phase of the menstrual cycle except three healthy and four PTSD subjects receiving oral contraceptives. *Results:* There were no group differences in progesterone, 5α-DHP, or DHEA levels. The PTSD group ALLO levels were < 39% of healthy group levels. The ALLO/DHEA ratio correlated negatively with PTSD re-experiencing symptoms (n = re werp < 008; trend) and with Profile of Mood State depression/dejection scores (n = 008; trp < 0008). *Conclusion:* Low CSF ALLO levels in premenopausal women with PTSD might contribute to an imbalance in inhibitory versus excitatory neurotransmission, resulting in increased PTSD re-experiencing and depressive symptoms.

Rasmusson, A.M., Vasek, J., Lipschitz, D.S., Vojvoda, D., Mustone, M.E., Shi, Q., Gudmundsen, G., et al. (2004). **An increased capacity for adrenal DHEA release is associated with decreased avoidance and negative mood symptoms in women with PTSD.** *Neuropsychopharmacology, 29*,1546-1557. doi:10.1038/sj.npp.1300432 We recently found increased adrenal cortisol responses to ACTH1-24 and increased pituitary ACTH and adrenal cortisol responses to corticotropin-releasing factor in premenopausal women with chronic PTSD compared to healthy non-traumatized subjects. This pattern of HPA hyper-reactivity has been previously seen in healthy individuals treated with the antiglucocorticoid mifepristone. We therefore investigated whether endogenous plasma levels of antiglucocorticoids such as DHEA and progesterone were increased in premenopausal women with PTSD at baseline or in response to adrenal activation by ACTH1-24. The study revealed that DHEA responses to 250 microg ACTH1-24 were increased in 13 PTSD subjects compared to 13 healthy non-traumatized subjects, while DHEA levels were generally increased in the PTSD subjects compared to seven healthy traumatized subjects. Cortisol responses to ACTH1-24 were also higher in the women with PTSD, while progesterone levels and responses were not different among the three groups. In addition, among the PTSD subjects, the peak change in DHEA in response to ACTH1-24 was negatively correlated with the total Clinician Administered PTSD Scale score, while the peak DHEA to cortisol ratio was inversely associated with negative mood symptoms measured by the Profile of Mood States scale. This work suggests that an increased capacity for DHEA release in response to extreme adrenal activation may influence the pattern of HPA axis adaptation to extreme stress, as well as mitigate the severity of PTSD and negative mood symptoms in premenopausal women with PTSD.

Ressler, K.J., Mercer, K.B., Bradley, B., Jovanovic, T., Mahan, A., Kerley, K., et al. (2011). **Post-traumatic stress disorder is associated with PACAP and the PAC1 receptor.** *Nature, 470*, 492-497. doi:10.1038/nature09856 PACAP is known to broadly regulate the cellular stress response. In contrast, it is unclear if the PACAP-PAC1 receptor pathway has a role in human psychological stress responses, such as PTSD. Here we find, in heavily traumatized subjects, a sex-specific association of PACAP blood levels with fear physiology, PTSD diagnosis and symptoms in females. We examined 44 SNPs spanning the PACAP (encoded by ADCYAP1) and PAC1 (encoded by ADCYAP1R1) genes, demonstrating a sex-specific association with PTSD. A single SNP in a putative oestrogen response

element within ADCYAP1R1, rs2267735, predicts PTSD diagnosis and symptoms in females only. This SNP also associates with fear discrimination and with ADCYAP1R1 messenger RNA expression in human brain. Methylation of ADCYAP1R1 in peripheral blood is also associated with PTSD. Complementing these human data, ADCYAP1R1 mRNA is induced with fear conditioning or oestrogen replacement in rodent models. These data suggest that perturbations in the PACAP-PAC1 pathway are involved in abnormal stress responses underlying PTSD. These sex-specific effects may occur via oestrogen regulation of ADCYAP1R1. PACAP levels and ADCYAP1R1 SNPs may serve as useful biomarkers to further our mechanistic understanding of PTSD.

Shalev, A.Y., Videlock, E.J., Peleg, T., Segman R., Pitman, R.K., & Yehuda, R. (2008). **Stress hormones and post-traumatic stress disorder in civilian trauma victims: A longitudinal study. Part I: HPA axis responses.** *International Journal of Neuropsychopharmacology, 11*, 365-372. doi:10.1017/S1461145707008127 The aim of the study was to evaluate the association between PTSD and HPA axis responses to the triggering trauma. A companion paper evaluates the adrenergic response and interactions between the two. We measured plasma and saliva cortisol, hourly urinary excretion of cortisol, plasma levels of ACTH, and the leukocyte glucocorticoid receptor (GR) density of 155 non-injured survivors of traumatic events (91 males and 64 females; 125 road traffic accidents, 19 terrorist attacks, 11 others). Measurements were taken during survivors' admissions to an emergency room (ER) of a general hospital; in the mornings; and 10 days, 1 month, and 5 months later. Symptoms of peritraumatic dissociation, PTSD, and depression were assessed on each follow-up session. The clinician-administered PTSD scale (CAPS) conferred a diagnosis of PTSD at 5 months. Survivors with (n =31) and without (n = 124) PTSD at 5 months had similar levels of hormones at all times. Plasma cortisol levels decreased with time in both groups. Female subjects had lower ACTH levels than males. PTSD in females was associated with higher levels of ACTH. In unselected cohorts of trauma survivors, PTSD is not preceded by a detectable abnormality of peripheral HPA axis hormones.

Shin, L.M., Bush, G., Milad, M.R., Lasko, N.B., Brohawn, K.H., Hughes, K.C., et al. (2011). **Exaggerated activation of dorsal anterior cingulate cortex during cognitive interference: A monozygotic twin study of posttraumatic stress disorder.** *American Journal of Psychiatry, 168*, 979-985. doi:10.1176/appi.ajp.2011.09121812 *Objective:* Neuroimaging studies have revealed functional abnormalities in the anterior cingulate cortex in PTSD. The goal of this study was to determine whether hyperresponsivity of the dorsal anterior cingulate in PTSD is an acquired characteristic or a familial risk factor. *Method:* Using a case-control twin design, the authors studied combat-exposed Veterans with PTSD (N = 12) and their identical combat-unexposed co-twins (N = 12), as well as combat-exposed Veterans without PTSD (N = 14) and their identical combat-unexposed co-twins (N = 14). Participants underwent functional MRI during completion of the Multi-Source Interference Task, which reliably activates the dorsal anterior cingulate. *Results:* Combat-exposed Veterans with PTSD and their unexposed co-twins had significantly greater activation in the dorsal anterior cingulate and tended to have larger response time difference scores, as compared to combat-exposed Veterans without PTSD and their co-twins. Dorsal anterior cingulate activation in the exposed twins was positively correlated with their PTSD symptom severity. Dorsal anterior cingulate activation in the unexposed twins was positively correlated with their combat-exposed co-twins' PTSD symptom severity, but not with depression or alcohol use severity in the combat-exposed co-twins. *Conclusions:* Hyperresponsivity in the dorsal anterior cingulate appears to be a familial risk factor for the development of PTSD following psychological trauma.

Southwick, S.M., Krystal, J.H., Bremner, J.D., Morgan, C.A., Nicolaou, A.L., Nagy, L.M., et al. (1997). **Noradrenergic and serotonergic function in posttraumatic stress disorder.** *Archives of General Psychiatry, 54*, 749-758. doi:10.1001/archpsyc.1997.01830200083012 *Background:* Yohimbine hydrochloride produces marked behavioral and cardiovascular effects in combat Veterans with PTSD. In the present study, yohimbine was used as a probe of noradrenergic activity, and meta-chlorophenylpiperazine (m-CPP) as a probe of serotonergic activity. To our knowledge, this is the first study to describe the behavioral and cardiovascular effects of meta-CPP in patients with PTSD, and to compare these effects with those of yohimbine. *Method:* Twenty-six patients with PTSD and 14 healthy subjects each received an intravenous infusion of yohimbine hydrochloride (0.4 mg/kg), m-CPP (1.0 mg/kg), or saline solution on 3 separate test days in a randomized balanced order and in double-blind fashion. Behavioral and cardiovascular measurements were determined at multiple times. *Results:* Eleven (42%) of the patients with PTSD experienced yohimbine-induced panic attacks and had significantly greater increases compared with controls in anxiety, panic, and PTSD symptoms, but not in cardiovascular measurements. Eight patients (31%) with PTSD experienced m-CPP-induced panic attacks and had significantly greater increases compared with controls in anxiety, panic, and PTSD symptoms, and in standing diastolic blood pressure. Yohimbine-induced panic attacks tended to occur in different patients from m-CPPinduced panic attacks. *Conclusion:* These data suggest the presence of two neurobiological subgroups of patients with PTSD, one with a sensitized noradrenergic system, and the other with a sensitized serotonergic system.

Southwick, S.M., Krystal, J.H., Morgan, C.A., Johnson, D., Nagy, L.M., Nicolaou, A., et al. (1993). **Abnormal noradrenergic function in posttraumatic stress disorder.** *Archives of General Psychiatry, 50*, 266-274. doi:10.1001/archpsyc.1993.01820160036003 To evaluate possible abnormal noradrenergic neuronal regulation in patients with PTSD, the behavioral, biochemical, and cardiovascular effects of intravenous yohimbine hydrochloride (0.4 mg/kg) were determined in 18 healthy male subjects and 20 male patients with PTSD. A subgroup of patients with PTSD were observed to experience yohimbine-induced panic attacks (70% [14/20]) and flashbacks (40% [8/20]), and they had larger yohimbine-induced increases in plasma 3-methoxy-4-hydroxyphenylglycol levels, sitting systolic blood pressure, and heart rate than those in healthy subjects. In addition, in the patients with PTSD,

yohimbine induced significant increases in core PTSD symptoms, such as intrusive traumatic thoughts, emotional numbing, and grief. These data were consistent with a large body of preclinical data that indicated that uncontrollable stress produces substantial increases in noradrenergic neuronal function. We discuss the implications of these abnormalities in noradrenergic functional regulation in relation to the long-term neurobiological sequelae of severe uncontrollable stress and the pathophysiological relationship between PTSD and other anxiety disorders, such as panic disorder.

Uddin, M., Aiello, A.E., Wildman, D.E., Koenen, K.C., Pawelec, G., de Los Santos, R., et al. (2010). **Epigenetic and immune function profiles associated with posttraumatic stress disorder.** *Proceedings of the National Academy of Sciences of the United States of America, 107*, 9470-9475. doi:10.1073/pnas.0910794107 The biologic underpinnings of PTSD have not been fully elucidated. Previous work suggests that alterations in the immune system are characteristic of the disorder. Identifying the biologic mechanisms by which such alterations occur could provide fundamental insights into the etiology and treatment of PTSD. Here we identify specific epigenetic profiles underlying immune system changes associated with PTSD. Using blood samples (n = 100) obtained from an ongoing, prospective epidemiologic study in Detroit, the Detroit Neighborhood Health Study, we applied methylation microarrays to assay CpG sites from more than 14,000 genes among 23 PTSD-affected and 77 PTSD-unaffected individuals. We show that immune system functions are significantly overrepresented among the annotations associated with genes uniquely unmethylated among those with PTSD. We further demonstrate that genes whose methylation levels are significantly and negatively correlated with traumatic burden show a similar strong signal of immune function among the PTSD affected. The observed epigenetic variability in immune function by PTSD is corroborated using an independent biologic marker of immune response to infection, CMV, a typically latent herpesvirus whose activity was significantly higher among those with PTSD. This report of peripheral epigenomic and CMV profiles associated with mental illness suggests a biologic model of PTSD etiology in which an externally experienced traumatic event induces downstream alterations in immune function by reducing methylation levels of immune-related genes.

Wolf, E.J., Rasmusson, A.M., Mitchell, K.S., Logue, M.W., Baldwin, C.T., & Miller, M.W. (2014). **A genome-wide association study of clinical symptoms of dissociation in a trauma-exposed sample.** *Depression and Anxiety, 31*, 352-360. doi:10.1002/da.22260 *Background:* Recent work suggests that a subset of individuals with PTSD exhibit marked dissociative symptoms, as defined by derealization and depersonalization. A dissociative subtype of PTSD was added to the diagnostic criteria listed in the *Diagnostic and Statistical Manual of Mental Disorders*, Version 5 (*DSM-5*) to capture this presentation of PTSD. This study examined genetic polymorphisms for association with the symptoms that define the dissociative subtype of PTSD using a genome-wide approach. *Methods:* The sample comprised 484 white, non-Hispanic, trauma-exposed Veterans and their partners who were assessed for lifetime PTSD and dissociation using a structured clinical interview. The prevalence of PTSD was 60.5%. SNPs from across the genome were obtained from a 2.5 million SNP array. *Results:* Ten SNPs evidenced suggestive association with dissociation ($P < 10^{-5}$). No SNPs met genome-wide significance criteria ($P < 5 \times 10^{-8}$). The peak SNP was rs263232 ($\beta = 1.4$, $P = 6.12 \times 10^{-7}$), located in the adenylyl cyclase 8 (*ADCY8*) gene; a second SNP in the suggestive range was rs71534169 ($\beta = 1.63$, $P = 3.79 \times 10^{-6}$), located in the dipeptidyl-peptidase 6 (*DPP6*) gene. *Conclusions: ADCY8* is integral for long-term potentiation and synaptic plasticity and is implicated in fear-related learning and memory and long-term memory consolidation. *DPP6* is critical for synaptic integration and excitation. These genes may exert effects on basic sensory integration and cognitive processes that underlie dissociative phenomena.

Yehuda, R., Boisoneau, D., Lowy, M.T., & Giller, E.L. (1995). **Dose-response changes in plasma cortisol and lymphocyte glucocorticoid receptors following dexamethasone administration in combat Veterans with and without posttraumatic stress disorder.** *Archives of General Psychiatry, 52*, 583-593. doi:10.1001/archpsyc.1995.03950190065010 *Background:* Our previous studies have suggested that combat Veterans with PTSD have alterations in hypothalamic-pituitary-adrenal axis functioning that are different from the well-documented biological changes observed in major depressive disorder and following exposure to stress. *Methods:* In the present study, we examined cortisol and lymphocyte glucocorticoid receptor number before and after the administration of 0.50 and 0.25 mg of dexamethasone in 14 combat Veterans with PTSD, 12 combat Veterans without PTSD, and 14 non-psychiatric healthy men. All subjects were medication free at the time of testing and none met diagnostic criteria for major depression or substance dependence. *Results:* Combat Veterans with PTSD suppressed cortisol to a greater extent than did combat Veterans without PTSD and normal controls in response to both doses of dexamethasone. Differences in cortisol suppression could not be attributed to substance dependence history or differences in dexamethasone bioavailability. Combat Veterans with PTSD showed a larger number of baseline glucocorticoid receptors compared with normal men. Combat Veterans without PTSD also had a larger number of baseline glucocorticoid receptors compared with normal men and in fact were comparable to combat Veterans with PTSD on this measure. However, only Veterans with PTSD showed a decrease in lymphocyte glucocorticoid receptor number following dexamethasone administration. *Conclusion:* The data support the hypothesis of an enhanced negative feedback sensitivity of the hypothalamic-pituitary-adrenal axis in PTSD.

Yehuda, R., Pratchett, L.C., Elmes, M.W., Lehrner, A., Daskalakis, N.P., Koch, E., et al. (2014). **Glucocorticoid-related predictors and correlates of post-traumatic stress disorder treatment response in combat Veterans.** *Interface Focus, 4*, 20140048. doi:10.1098/rsfs.2014.0048 The identification of biomarkers for PTSD and resilience/recovery is critical for advancing knowledge about pathophysiology and treatment in trauma-exposed persons. This study examined a series of glucocorticoid-related biomarkers prior to and in response to psychotherapy. Fifty-two male and female Veterans with PTSD were randomized 2 : 1 to receive either prolonged exposure (PE) therapy or a weekly MA

FEATURED ARTICLES *continued*

intervention for 12 consecutive weeks. Psychological and biological assessments were obtained prior to and following treatment and after a 12-week naturalistic follow-up. Response was defined dichotomously as no longer meeting criteria for PTSD at post-treatment based on the Clinician Administered PTSD Scale for DSM-IV (CAPS). Clinical improvement on the CAPS was apparent for both PE and MA, with no significant difference according to treatment condition. Biomarkers predictive of treatment gains included the BCLI polymorphism of the glucocorticoid receptor gene. Additional predictors of treatment response were higher bedtime salivary cortisol and 24 h urinary cortisol excretion. Pre-treatment plasma dehydroepiandrosterone/cortisol ratio and NPY levels were predictors of reductions in PTSD symptoms, and, for NPY only, of other secondary outcomes as well, including anxiety and depression ratings. Glucocorticoid sensitivity changed in association with symptom change, reflecting clinical state. It is possible to distinguish prognostic and state biomarkers of PTSD using a longitudinal approach in the context of treatment. Identified markers may also be relevant to understanding mechanisms of action of symptom reduction.

ADDITIONAL CITATIONS

Abdallah, C.G., Salas, R., Jackowski, A., Baldwin, P., Sato, J.R., & Mathew, S.J. (in press). **Hippocampal volume and the rapid antidepressant effect of ketamine.** *Journal of Psychopharmacology*. doi:10.1177/0269881114544776 Although smaller hippocampal volumes predict poor treatment responses to monoaminergic antidepressants, this study showed that smaller hippocampal volume predicted enhanced responses to the glutamate-antagonist, ketamine, in depressed patients.

Baker, D.G., West, S.A., Nicholson, W.E., Ekhator, N.N., Kasckow, J.W., Hill, K.K. et al. (1999). **Serial CSF corticotropin-releasing hormone levels and adrenocortical activity in combat Veterans with posttraumatic stress disorder.** *American Journal of Psychiatry, 156*, 585-588. This study replicated findings of increased CSF CRF levels in males with PTSD; the study also found a relationship between low levels of urinary cortisol and severity of PTSD symptoms.

Cagetti, E., Pinna, G., Guidotti, A., Baicy, K., & Olsen, R.W. (2004). **Chronic intermittent ethanol (CIE) administration in rats decreases levels of neurosteroids in hippocampus, accompanied by altered behavioral responses to neurosteroids and memory function.** *Neuropharmacology, 46*, 570-579. doi:10.1016/j.neuropharm.2003.10.001 This study demonstrated deficits in the conversion of the allopregnanolone precursor (3α-dihydroprogesterone) to allopregnanolone by the enzyme 3α-hydroxysteroid dehydrogenase in model of binge alcohol consumption in male rodents, a pattern of findings similar to that demonstrated in women with PTSD without current substance abuse—suggesting convergence between environmental and intrinsic biological PTSD risk factors.

ADDITIONAL CITATIONS *continued*

Friedman, M.J., & Davidson, J.R.T (2014). **Pharmacotherapy for PTSD. In M.J. Friedman, T.M. Keane, & P.A. Resick (Eds.),** *Handbook of PTSD, science and practice (2nd ed.)*. (pp. 482-501). New York: Guilford Publications. This exhaustive review of pharmacotherapy studies in PTSD suggests the importance of developing medications that prevent or treat PTSD by targeting specific pathophysiological abnormalities associated with the disorder or sub-phenotypes of the disorder.

Galatzer-Levy, I.R., Karstoft, K.I., Statnikov, A., & Shalev, A.Y. (2014). **Quantitative forecasting of PTSD from early trauma responses: A Machine Learning application.** *Journal of Psychiatric Research. 59*, 68-76. doi:10.1016/j.jpsychires.2014.08.017 This study illustrates the advantage over data analytic techniques that rely on *a priori* hypothesis testing of new machine learning techniques that "learn from the data."

Gill, J., Vythilingam, M., & Page, G.G. (2008). **Low cortisol, high DHEA, and high levels of stimulated TNF-α, and IL-6 in women with PTSD.** *Journal of Traumatic Stress, 21*, 530-539. doi:10.1002/jts.20372 Consistent with other studies suggesting that an increase in DHEA constitutes a protective adaptation to trauma, women with PTSD in this study had higher DHEA levels than trauma-exposed and non-exposed controls, but women with comorbid PTSD and major depression had lower morning DHEA levels, as well as lower DHEA/cortisol ratios and increased IL-6 levels.

Hill, M.N., Bierer, L.M., Makotkine, I., Golier, J.A., Galea, S., McEwen, B.S., et al. (2013). **Reductions in circulating endocannabinoid levels in individuals with post-traumatic stress disorder following exposure to the World Trade Center attacks.** *Psychoneuroendocrinology, 38*, 2952-2961. doi:10.1016/j.psyneuen.2013.08.004 This study in individuals selected for their proximity to the World Trade Center attack found low blood levels of the endocannabinoid 2-AG, but not anandamide among participants with lifetime PTSD compared to those with no PTSD.

Karvonen, M.K., Valkonen, V.P., Lakka, T.A., Salonen, R., Koulu, M., Pesonen, U., et al. (2001). **Leucine7 to proline7 polymorphism in the preproneuropeptide Y is associated with the progression of carotid atherosclerosis, blood pressure and serum lipids in Finnish men.** *Atherosclerosis, 159*, 145-151. doi:10.1016/S0021-9150(01)00468-3 This seminal study found associations between a gene polymorphism conferring increases in NPY release during stress—thought to confer neuropsychological resilience to stress—and risk for long-term physical health consequences, pointing to future challenges in development of strategies to enhance both short- and long-term mental and physical health.

Kobayashi, I., & Mellman, T.A. (2012). **Gender differences in sleep during the aftermath of trauma and the development of posttraumatic stress disorder.** *Behavioral Sleep Medicine, 10*, 180–190. doi:10.1080/15402002.2011.654296 This first study to examine gender differences in sleep architecture in the aftermath of trauma found that women who developed PTSD had more sleep awakenings than men, and that women who developed PTSD exhibited less sleep than women who did not.

ADDITIONAL CITATIONS *continued*

Kuo, L.E., Kitlinska, J.B., Tilan, J.U., Li, L., Baker, S.B., Johnson, M.D., et al. (2007). **Neuropeptide Y acts directly in the periphery on fat tissue and mediates stress-induced obesity and metabolic syndrome.** *Nature Medicine, 13*, 803-811. doi:10.1038/nm1611 This high-profile study demonstrated that stress reduced weight in rodents, but stress combined with a high fat/high sugar diet markedly increased centripetal obesity and other stigmata of metabolic syndrome, mediated by actions of NPY at NPY-Y_2 receptors in abdominal fat—phenomena reversed by the local or systemic injection of an NPY-Y_2 receptor antagonist or local glucocorticoid antagonist.

Lanius, R.A., Brand, B., Vermetten, E., Frewen, P.A., Spiegel, D. (2012). **The dissociative subtype of posttraumatic stress disorder: Rationale, clinical and neurobiological evidence, and implications.** *Depression & Anxiety. 29*, 701-708. doi:10.1002/da.21889 This review presents up-to-date evidence characterizing the neurobiological underpinnings and treatment outcomes related to the dissociative subtype of PTSD-characterized primarily by depersonalization and derealization symptoms in addition to other PTSD symptoms.

Levy-Gigi, E., Szabo, C., Kelemen, O., & Keri, S. (2013). **Association among clinical response, hippocampal volume, and FKBP5 gene expression in individuals with posttraumatic stress disorder receiving cognitive behavioral therapy.** *Biological Psychiatry, 74*, 793-800. doi:10.1016/j.biopsych.2013.05.017 This study demonstrated reduced pretreatment FKBP5 gene expression and hippocampal volume in PTSD, abnormalities that normalized in association with positive response to CBT.

Mellman, T.A., Kumar, A., Kulick-Bell, R., Kumar, M., & Nolan, B. (1995). **Nocturnal/daytime urine noradrenergic measures and sleep in combat-related PTSD.** *Biological Psychiatry, 38*, 174-179. doi:10.1016/0006-3223(94)00238-X This polysomnography study in unmedicated participants who also collected urine over 24 hours for norepinephrine and MHPG in three 8-hour epochs, demonstrated “non-diminished” nighttime noradrenergic activity in individuals with PTSD that correlated negatively with sleep disturbance.

Morgan, C.A., Rasmusson, A.M., Winters, B., Hauger, R.L., Morgan, J., Hazlett, G., et al. (2003). **Trauma exposure rather than posttraumatic stress disorder is associated with reduced baseline plasma neuropeptide-Y levels.** *Biological Psychiatry 54*, 1087-1091. doi:10.1016/S0006-3223(03)00433-5 This paper reported data from two studies: one of male Vietnam Veterans with PTSD and one of male active duty participants in survival training, to demonstrate the relationship between trauma exposure and reductions in plasma NPY.

Orr, S.P., Metzger, L.J., Lasko, N.B., Macklin, M.L., Hu, F.B., Shalev, A.Y., et al. (2003). **Physiologic responses to sudden, loud tones in monozygotic twins discordant for combat exposure: Association with posttraumatic stress disorder.** *Archives of General Psychiatry, 60*, 283-288. doi:10.1001/archpsyc.60.3.283 This study in Vietnam combat Veterans and their non-combat exposed monozygotic twins showed that greater heart rate responses to sudden loud tones was an acquired trait related to PTSD rather than to combat exposure, and was not a familial vulnerability factor.

Phan, K.L., Wager, T., Taylor, S.F., & Liberzon, I. (2002). **Functional neuroanatomy of emotion: A meta-analysis of emotion activation studies in PET and fMRI.** *Neuroimage, 16*, 331-348. doi:10.1006/nimg.2002.1087 This meta-analysis compiled PET and fMRI data in healthy subjects to determine the neuroanatomical correlates of positive and negative emotions, including disgust, sadness, happiness, anger, and fear.

Rasmusson, A.M., Schnurr, P.P., Zukowska, Z., Scioli, E., & Forman, D.E. (2010). **Adaptation to extreme stress: Post-traumatic stress disorder, neuropeptide Y, and metabolic syndrome.** *Experimental Biology and Medicine, 235*, 1150-1162. doi:10.1258/ebm.2010.009334 This review focused on the link between alterations in NPY system functioning, PTSD, and metabolic syndrome—as new studies emerged linking trauma exposure and PTSD to risk for metabolic syndrome as well as to cardiovascular system dysfunction.

Richards, A., Metzler, T.J., Ruoff, L.M., Inslicht, S.S., Rao, M., Talbot, L.S., et al. (2013). **Sex differences in objective measures of sleep in post-traumatic stress disorder and healthy control subjects.** *Journal of Sleep Research, 22*, 679-687. doi10.1111/jsr.12064 This laboratory electroencephalography (EEG) study in 83 unmedicated men and women with and without PTSD revealed differences in sleep architecture related both to gender and PTSD severity.

Sah, R., Ekhator, N.N., Strawn, J.R., Sallee, F.R., Baker, D.G., Horn, P.S., et al. (2009). **Low cerebrospinal fluid neuropeptide Y concentrations in posttraumatic stress disorder.** *Biological Psychiatry, 66*, 705-707. doi:10.1016/j.biopsych.2009.04.037 This study was the first to find low NPY levels in the cerebrospinal fluid of male Veterans with PTSD, replicating findings of low NPY in plasma.

Scioli-Salter, E.R., Forman, D.E., Otis, J.D., Gregor, K., Valovski, I., & Rasmusson, A.M. (in press). **The shared neuroanatomy and neurobiology of comorbid chronic pain & PTSD: Therapeutic implications.** *Clinical Journal of Pain.* doi:10.1097/AJP.0000000000000115 This review provided details regarding shared neuroanatomic and multiple neurobiological substrates accounting for the high rates of comorbidity between chronic pain and PTSD, implicating the NPY, GABAergic neuroactive steroid, opiate and endocannabinoid systems.

Sekiguchi, A., Sugiura, M., Taki, Y., Kotozaki, Y., Nouchi, R., Takeuchi, H., et al. (2013). **Brain structural changes as vulnerability factors and acquired signs of post-earthquake stress.** *Molecular Psychiatry, 18*, 618-623. doi:10.1038/mp.2012.51 This elegant longitudinal study showed that reduced gray matter volume in the anterior cingulate cortex prior to trauma predicted PTSD development, while orbitofrontal cortex gray matter volume decreased following trauma among those who developed PTSD—highlighting the interplay between factors that confer PTSD vulnerability and the effects of persistent traumatic stress.

ADDITIONAL CITATIONS *continued*

Thomaes, K., Dorrepaal, E., Draijer, N., Jansma, E.P., Veltman, D.J., van Balkom, A.J. (2014). **Can pharmacological and psychological treatment change brain structure and function in PTSD? A systematic review.** *Journal of Psychiatric Research, 50*, 1-15. doi:10.1016/j.jpsychires.2013.11.002 This review suggested that pharmacotherapy, but not psychotherapy, was associated with increases in hippocampal volume, while both treatment modalities changed regional brain activation—in some cases, in the direction of normalization.

Woodward, S.H., Arsenault, N.J., Murray, C. & Bliwise, D.L. (2000). **Laboratory sleep correlates of nightmare complaint in PTSD inpatients.** *Biological Psychiatry, 48*, 1081-1087. doi:10.1016/S0006-3223(00)00917-3 In this polysomnography study of 63 unmedicated male Veterans, increased wake-after-sleep-onset was specifically associated with complaints of trauma-related nightmares, which were found to occur outside of normal REM sleep.

Yehuda, R., Brand, S.R., Golier, J.A., & Yang, R.K. (2006). **Clinical correlates of DHEA associated with post-traumatic stress disorder.** *Acta Psychiatrica Scandinavica, 114*, 187-193. doi:10.1111/j.1600-0447.2006.00801.x This study found that a higher plasma DHEA/cortisol ratio measured at baseline predicted greater PTSD recovery over time among male Vietnam combat Veterans.

Yehuda, R., Bierer, L.M. Sarapas, C., Makotkine, I., Andrew, R., & Seckl, J.R. (2009). **Cortisol metabolic predictors of response to psychotherapy for symptoms of PTSD in survivors of the World Trade Center attacks on September 11, 2001.** *Psychoneuroendocrinology, 34*, 1304-1313. doi:10.1016/j.psyneuen.2009.03.018 This study found reductions in the endocannabinoid 2-AG, but not anandamide (AEA) among individuals in close proximity to the World Trade Center attacks who had a lifetime history of PTSD compared to those with no PTSD.

Zhang, K., Rao, F., Miramontes-Gonzalez, J.P., Hightower, C.M., Vaught, B., Chen, Y., et al. (2012). **Neuropeptide Y (NPY) genetic variation in the human promoter alters glucocorticoid signaling, yielding increased NPY secretion and stress responses.** *Journal of the American College of Cardiology, 60*, 1678-1689. doi:10.1016/j.jacc.2012.06.042 This study used multiple techniques to show relationships between one common NPY gene promoter polymorphism that confers increased NPY release and resistance to glucocorticoid regulatory restraint and increases in blood pressure and cardiovascular resistance in association with decreases in cardiac output.

Zhou, Z., Zhu, G., Hariri, A.R., Enoch, M.A., Scott, D., Sinha, R., et al. (2008). **Genetic variation in human NPY expression affects stress response and emotion.** *Nature, 452*, 997-1001. doi:10.1038/nature06858 This elegant study demonstrated the relationship between loss-of-function NPY polymorphisms and susceptibility to amygdala hyperreactivity and negative emotional reactions.