

First-line Psychotherapies for Military-Related PTSD

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Two well-established first-line cognitive-behavioral psychotherapies for posttraumatic stress disorder (PTSD), prolonged exposure therapy (PE) and cognitive processing therapy (CPT), are used in the US Department of Veterans Affairs (VA) and US Department of Defense (DoD) based chiefly on good outcomes in randomized clinical trials (RCTs) with civilians. PE and CPT are manualized (ie, protocolized in a session-by-session manner) trauma-focused therapies that are based on processing the emotional and cognitive aspects of the traumatic event. Consequently, these treatments are emotionally demanding for patients because PTSD is characterized by a strong motivation to avoid talking about the trauma and rekindling negative emotions associated with it. The prominence of PE and CPT in treating individuals with military-related PTSD has been increasingly challenged in recent years because RCTs of veterans and military personnel have yielded mixed results, with patients often not obtaining clinically meaningful symptom improvement. These findings have led to questions about the extent to which these therapies should be prioritized and how military-related PTSD is best conceptualized, namely as a disorder that can be reliably managed by brief (approximately 12 session) monotherapies or as a highly complex and multiform condition requiring more individualized and comprehensive intervention.

A review of the psychotherapy for military-related PTSD literature in 2015 includes 4 RCTs examining PE and 5 examining CPT. These studies showed that while PE and CPT, on average, reduced PTSD with large effects (Cohen *d* range [the difference between 2 mean PTSD severity scores divided by the pooled SD; a *d* of 0.20 indicates a small effect size; a *d* of 0.50, a medium effect size; and a *d* of 0.80, a large effect size], 0.78-1.10), the outcomes were heterogeneous. Nonresponse rates were high and the benefit of PE and CPT relative to non-trauma-focused treatments was small.¹ Since that review, several high-quality clinical trials have been published that are some of the largest and most concerted efforts to date to study military-related PTSD treatment. These newer studies are summarized in this update.

In contrast to prior investigations, the more recent trials of PTSD treatment have had a greater emphasis on combat exposure instead of sexual trauma, used active comparison groups, and examined active duty personnel treated in garrison, rather than only veterans.

Three trials conducted as part of the South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR) consortium evaluated the efficacy of PE or CPT among 746 in-garrison active-duty personnel. In a setting where there was substantial need for PTSD care but limited resources to provide it, the trials examined group-delivered CPT compared with a group-delivered non-trauma-focused treatment (present-centered therapy [PCT], which focuses on symptom management and problem-solving)²; group-delivered vs individually delivered CPT³; and massed (10 sessions over 2 weeks) vs spaced (10 sessions over 8 weeks) versions of individually delivered PE, with spaced PCT as a control condition⁴ (Supplement). Two other major

DoD-funded trials include a comparison of PE plus placebo, sertraline hydrochloride, and PE plus sertraline hydrochloride⁵ and a non-inferiority trial of PE vs transcendental meditation (a meditation practice involving repetition of a mantra).⁶

In all these trials, active treatments (PE, CPT, PCT, sertraline, and transcendental meditation) were not significantly different in all direct comparisons of clinician-administered primary PTSD outcomes. Neither PE nor CPT (individual or group) demonstrated clear superiority over non-trauma-focused PCT, a finding consistent with prior trials in civilians and veterans. PE plus placebo, sertraline hydrochloride, and PE plus sertraline hydrochloride were comparably efficacious,⁵ and transcendental meditation was found to be noninferior to PE.⁶ Individually administered CPT significantly outperformed group-delivered CPT.³ Although outcomes were statistically comparable across the disparate treatments, notable differences were observed in treatment dropout, particularly for PCT vs other conditions, with individuals receiving PCT demonstrating less dropout. With the exception of massed PE, rates of treatment noncompletion for trauma-focused therapies and transcendental meditation ranged from 25% to 48%, compared with 12% dropout for those receiving individual or group PCT.¹⁻⁶ Massed PE, likely because it could deliver a full dose of treatment during a shorter time period, showed comparable rates of noncompletion as PCT (14%).

Across trials, all active treatments, on average, reduced PTSD symptoms, often with moderate to large effect sizes, although outcomes were heterogeneous at the individual level and treatment nonresponse rates were high. An analysis of individual-level metadata combined from the 3 STRONG STAR trials found that overall only 31% of patients recovered or improved in all of these trials; symptom change was in part explained by individuals' baseline symptom severity, which was a proxy for case complexity.⁷ About half of the participants who received PE plus placebo in the PE vs sertraline trial demonstrated clinically meaningful change,⁵ while 42% of patients who received PE compared with 61% of patients who underwent transcendental meditation showed clinically significant improvement.⁶ Even when PTSD symptoms improved following treatment, they often persisted to some degree at or above diagnostic thresholds for PTSD, indicating that patients got better but rarely got well. Approximately 60% of patients continued to be diagnosed with PTSD in the 2 trials that reported this outcome.^{3,4} Treatment outcomes may have been less than optimal because of the complexity of military-related PTSD resulting from the extended and intense nature of deployment trauma that involves exposure not only to life-threatening events, but also to morally compromising experiences and traumatic losses.

Overall, these new findings suggest that first-line psychotherapies do not effectively manage military-related PTSD in large proportions of patients and do not outperform non-trauma-focused interventions. This is consistent with outcomes from prior RCTs of civilian- and military-related PTSD. The finding of no significant difference across mechanistically distinct treatments raises theoretical challenges for leading models of PTSD that are based on extinction

learning and cognitive theories that argue that trauma processing is essential for recovery. Perhaps several concurrent therapeutic approaches are necessary to result in effective treatment. It also raises important practical questions, particularly the value of emotionally demanding therapies, such as PE and CPT, relative to comparably efficacious and more tolerable interventions, such as PCT, transcendental meditation, and sertraline.

The high nonresponse, underresponse, and dropout rates in these studies suggest a mismatch between the typically highly complex clinical reality of managing military-related PTSD and one-size-fits-all treatment approaches rolled out in VA and DoD health care settings. Manualized short-term monotherapies widely disseminated across the VA and DoD, particularly PE and CPT, are not effective for between one-half and two-thirds of patients, and more long-term personalized approaches that draw on the wider array of different trauma-focused and non-trauma-focused therapeutic techniques available in the trauma field are needed. Notably, the most recent VA and DoD PTSD clinical practice guideline recommends individual manualized trauma-focused psychotherapy (such as PE and CPT) as first-line intervention, ahead of medication and non-trauma-focused psychotherapies. These guidelines

may no longer be relevant because they were published in 2017, predating most of the trials summarized in this article.⁸

In addition to training clinicians in empirically supported first- and second-line therapies, greater attention should be paid to managing nonresponse to treatment (eg, switching treatments when there are early signs of nonresponse), addressing posttreatment residual symptoms, and identifying patients with complex presentations who likely require individualized treatment. Research also needs to shift from confirmatory trials to studies that explore flexible, multifaceted, and long-term evidence-informed modular or combination treatments, including biological therapies (eg, ketamine or transcranial magnetic stimulation), and that examine matching of patients to treatments. Effectiveness studies are necessary to examine how these interventions perform in practice because a more phased, flexible, and expanded application within the context of an established therapeutic relationship may yield better outcomes (eg, through improved retention). More broadly, recent PTSD treatment trials show that military-related PTSD is a complex and heterogeneous condition and that managing it with a single course of trauma-focused monotherapy is not well tolerated by many patients and has limited efficacy.

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Published Online: January 30, 2020.
doi:10.1001/jama.2019.20825

Conflict of Interest Disclosures: None reported.

Disclaimer: The views of this article are those of the authors and do not represent an official position of the US Department of Veterans Affairs or the listed institutions.

Additional Contributions: The authors would like to thank Charles Hoge, MD (Walter Reed Army Institute of Research, Silver Spring), for his critical

review, edits, and input on the manuscript. He was not compensated for his contributions. We also thank Jessica Carney, BA, VA Boston Healthcare System, for assistance with literature review.

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