Chapter

Assessment and Treatment of Combat-Related Posttraumatic Stress Disorder: Results from STRONG STAR and the Consortium to Alleviate PTSD

Alan L. Peterson, Barbara L. Niles, Stacey Young-McCaughan and Terence M. Keane

Abstract

Extensive research has been conducted since 11 September 2001 to develop and evaluate evidence-based treatments for combat-related posttraumatic stress disorder (PTSD) in active duty United States military personnel treated in the combat theater and in garrison. This chapter reviews the results of 20 PTSD clinical trials funded by the United States Department of Defense and Department of Veterans Affairs on the treatment of combat-related PTSD. All of the studies were conducted under the leadership and management of two research consortia: the South Texas Research Organizational Network Guiding Studies on Trauma and Resilience (STRONG STAR) Consortium and the Consortium to Alleviate PTSD.

Keywords: posttraumatic stress disorder, PTSD, acute stress disorder, combat and operational stress reactions

1. Introduction

Posttraumatic stress disorder (PTSD) is a common psychiatric disorder that occurs in about 7% of the adult population after exposure to a significant traumatic event [1, 2]. Combat-related PTSD occurs as a result of exposure to military combat or other traumas experienced during military deployments. The rate of combat-related PTSD in active duty military personnel and veterans who have deployed to a combat theater of operations is about double the rate of PTSD seen in civilians. [3–6]. Prior to the terrorist attacks on the United States on September 11, 2001, most research on PTSD had been conducted with civilian and veteran populations, with a striking absence of clinical trials conducted in active duty military populations with combat-related PTSD. The need for such studies was acute because, although there are many similarities in the assessment and treatment of PTSD in civilian, veteran, and military samples, active duty personnel represent a distinct population with specific characteristics and needs. In the early- and mid-2000s, it was unclear whether methods and treatments developed for civilians would successfully translate to military personnel returning from warzones.

Combat-related PTSD in service members differs from PTSD in other populations. As compared to most civilian populations [7–9], considerable research suggests that combat-related PTSD in service members and veterans is more difficult to treat and results in a smaller percentage of patients achieving significant reductions in symptoms [10–13]. In addition, the types of traumatic events experienced in warzones are often different than for civilians [14–16] and the frequency, intensity, and duration of trauma exposure are often greater.

There are also several factors that distinguish PTSD in active duty military populations from PTSD in veteran populations and that may affect treatment and assessment. Veterans have completed their military service, are not at risk for additional combat deployments, and may receive disability compensation for their PTSD symptoms and diagnoses. Active duty military personnel with PTSD who wish to continue their military careers are faced with unique obstacles and challenges. Many service members actively avoid seeking treatment for PTSD because of the negative stigma associated with mental health treatment and concerns that a PTSD diagnosis might affect career advancement and lead to a premature discharge. Notably, U.S. military personnel who complete a minimum of 20 years of active duty service are eligible to retire at a relatively young age with a sizeable lifelong retirement pension that is often more than half of their active duty base pay in addition to other retirement benefits such a lifetime medical coverage. With few exceptions, military personnel who serve less than 20 years active service receive no military pension or benefits. As a result, there is a strong desire and incentive for many military personnel to serve on active duty for at least 20 years to be eligible for full military retirement benefits, and many are reluctant to seek care that may jeopardize this.

Assessment of PTSD relies on accurate report of symptoms, and the particular circumstances of active duty service members who do seek out treatment may impact how symptoms are reported. Many on active duty have a strong desire to be treated into remission so they can remain fully fit to continue their military service. However, there are undoubtedly some service members who actively seek a diagnosis of PTSD that will lead to separation from active duty and some compensation through a military medical disability. Despite considerable clinical and research efforts, the ability to distinguish between service members seeking continued active duty service versus those who seek a medical separation has remained difficult, and the current method is to simply ask service members their career intentions. In either instance, the service member's future career objective is challenging, but critical for the clinician to assess.

To address the lack of research on combat-related PTSD in active duty military personnel, the U.S. Congress allocated funding to Department of Defense (DoD) in 2007 through the Congressionally Directed Medical Research Programs to establish a Multidisciplinary PTSD Research Consortium. After a competitive peer-reviewed process, the STRONG STAR (South Texas Research Organizational Network Guiding Studies on Trauma And Resilience) Consortium was awarded DoD research funding in 2008 to establish a nationwide PTSD research consortium. STRONG STAR is a multidisciplinary and multi-institutional research consortium focused on the detection, diagnosis, prevention, and treatment of combat PTSD and related conditions (e.g., traumatic brain injury, sleep disorders, chronic pain, substance use disorders, suicide, etc.) in active-duty military personnel and veterans, www.STRONGSTAR.org.

The initial STRONG STAR funding supported 14 research projects and 4 research cores. STRONG STAR investigators subsequently secured additional investigator-initiated, peer-reviewed research funding through the DoD, the Department

of Veterans Affairs (VA), the National Institutes of Health, and private organizations to support over 40 additional STRONG STAR-affiliated projects. In 2013, STRONG STAR investigators partnered with the VA's National Center for PTSD and were selected for joint funding by the DoD and VA to establish the Consortium to Alleviate PTSD (CAP). The CAP extended the STRONG STAR Consortium with 11 additional research projects: www.ConsortiumToAlleviatePTSD.org.

This chapter first reviews the assessment measures used to assess PTSD in the STRONG STAR and CAP studies. Next, the results of 20 STRONG STAR and CAP PTSD clinical trials evaluating a variety of treatments for combat-related PTSD in active duty military personnel and veterans are summarized.

2. The assessment of PTSD in military populations

2.1 Clinician-Administered PTSD Scale for *DSM-5*

The Clinician-Administered PTSD Scale for *DSM-5* (CAPS-5) [17, 18] is the gold-standard structured clinical diagnostic interview for assessing PTSD. The CAPS-5 is a 30-item structured clinical interview designed to be administered by a trained clinical interviewer and requires about 45–60 minutes to administer. Administration of the CAPS-5 requires the initial identification of a *DSM-5* Criterion A index traumatic event. It uses a 5-point ordinal rating scale to assess symptom the severity of the 20 PTSD symptoms included in the *DSM-5*. The CAPS-5 score can range from 0–80 with higher scores representing greater symptom severity. However, a diagnosis of PTSD is made only if the individual is experiencing ≥1 intrusion, ≥1 avoidance, ≥2 negative cognitions and mood, and ≥ 2 arousal and reactivity symptom all at a severity rating of ≥2. The CAPS-5 has strong inter-rater reliability (N = 78; *Cohen's kappa* = .90), and the correlation of severity scores between raters is excellent (r = .98) [19].

2.2 PTSD Checklist for *DSM-5*

The PTSD Checklist for *DSM-5* (PCL-5) [20] is a self-report measure of the 20 PTSD symptoms included in the *DSM-5*. Similar to the CAPS-5, it uses a 5-point ordinal rating scale to measure symptom severity with a range from 0–80. The PCL-5 can be scored in several ways, and interpretation should be made by a clinician. Initial research suggests that total scores between 31 and 33 on the PCL-5 are indicative of probable PTSD. A provisional diagnosis of PTSD can be made by summing each of the five *DSM-5* symptoms clusters with items endorsed as a 2 (Moderately) or higher and then following the *DSM-5* diagnostic guidelines. The PCL-5 has excellent psychometric characteristics for screening and as a secondary indicator of PTSD symptom severity [21, 22].

2.3 Primary Care PTSD Screen for *DSM-5*

The Primary Care PTSD Screen for *DSM-5* (PC-PTSD-5) [23] is a 5-item measure to screen for PTSD symptoms and was designed to be administered in primary care settings. The measure begins with one item to evaluate previous exposure to a potentially traumatic event. It then includes five additional yes-no items related to key PTSD symptoms. Validation studies suggest that a cut-off point of 3 on the PC-PTSD-5 is optimally sensitive for probable PTSD. Individuals who screen positive should be further evaluated with the PCL-5 or CAPS-5.

2.4 Assessment of trauma types in military personnel

Due to the unique aspects of combat- or deployment-related PTSD, the STRONG STAR investigators developed a scheme for categorizing traumatic military events [14–16]. The categorization of Criterion-A event descriptions is completed by CAPS-5 trained diagnostic interviewers. The traumatic military events are then categorized into six types of military-related Criterion-A events including (1) life-threat to self, (2) life-threat to others, (3) traumatic loss, (4) exposure to the aftermath of violence, (5) moral injury by self, and (6) moral injury by others. Research is ongoing to determine if different military trauma types respond differently to evidence-based treatments for combat-related PTSD.

2.5 The use of common data elements for PTSD research

A recent development to standardize the assessment and outcome measures that are used in PTSD research is to administer what are called *Common Data Elements*, or *CDEs* [24]. When different measures are used across studies, it makes it difficult to interpret the findings. The use of CDEs helps allow for the comparison of findings across different research studies. A major benefit of research studies conducted as part of the STRONG STAR Consortium and the Consortium to Alleviate PTSD is the use of CDEs for PTSD research [19]. This strategy also increases the possible use of future metanalytic strategies to understand the impact of various psychotherapeutic approaches in the treatment of PTSD.

3. The treatment of combat-related PTSD in military populations

At the time of the initial funding of the STRONG STAR Consortium by the DoD in 2008, no clinical trials existed to evaluate any form of treatment for combat-related PTSD in active duty military forces. Precious few randomized trials for PTSD treatment in veterans were in the published scientific literature. As a result, STRONG STAR investigators evaluated the published literature on the treatment of PTSD in civilian and veteran populations to help guide the initial studies of combat-related PTSD in active duty military personnel. The 2008 publication by the Institute of Medicine [3] titled the *Treatment of Posttraumatic Stress Disorder: An Assessment of the Evidence* provided an excellent state-of-the science review of the research literature at the time. That IOM committee report reviewed 52 psychotherapy studies and 37 pharmacotherapy studies and concluded, *"The committee finds that the evidence is sufficient to conclude the efficacy of exposure therapies in the treatment of PTSD"* [3].

Two cognitive-behavioral treatments were highlighted as the treatments with the strongest scientific support for their efficacy—Prolonged Exposure (PE) [25, 26] and Cognitive Processing Therapy (CPT) [27–29]. As a result, PE and CPT were the two treatments identified as leading candidates to be evaluated in randomized clinical trials in active duty military populations with combat-related PTSD.

Prolonged Exposure [30, 31] is a cognitive-behavioral therapy that includes four primary components: (1) imaginal exposure, or the repeated revisiting of the trauma memories, (2) in vivo exposure, or repeated exposure to avoided situations, (3) psychoeducation about common reactions to trauma, and (4) relaxed breathing. The standard treatment program includes 10 to 12 individual treatment sessions of 90 minutes each conducted once or twice a week.

Cognitive Processing Therapy is another cognitive-behavioral therapy that is usually delivered in 12 treatment sessions over the course of 6 weeks, with each

session lasting 1 hour [32]. CPT begins with psychoeducation about PTSD symptoms and making connections between events, thoughts, and feelings. Patients write an "impact statement" in which they describe why they think the traumatic event happened and how the event has affected their view of themselves, others, and the world. Throughout CPT, unhelpful cognitions are identified and challenged through Socratic questioning until more helpful and accurate beliefs can replace distorted cognitions. The final five sessions of CPT focus on cognitions related to safety, trust, power, esteem, and intimacy.

A summary of the STRONG STAR and CAP clinical trials is provided in **Table 1**.

3.1 Treating combat-related PTSD in the combat theater

The first clinical case series to report on the treatment of combat-related PTSD in the combat theater [33, 34] used a modified version of Prolonged Exposure [25] that was adapted for the deployed environment. The results showed that PE could be safely and effectively delivered in the deployed environment to allow service members to return to combat duties and complete their deployments. The promising results from this case series led to the funding of a larger nonrandomized clinical trial as part of the STRONG STAR Consortium to evaluate the use of PE and CPT in Iraq and Afghanistan for the treatment of 12 service members with combat-related PTSD [35]. All patients were treated by military behavioral health providers deployed to the combat theater using modified versions of PE (n = 6) or CPT (n = 6). Because this study was conducted prior to the publication of the PCL-5, the PTSD Checklist-Military Version (PCL-M) was used [36, 37], which was based on *DSM-IV* criteria and asks about symptoms in response to "stressful military experiences." The results showed that both treatments demonstrated clinically significant change in PTSD symptoms on the PCL-M.

Despite the small sample size (N = 12), this prospective, nonrandomized trial is the largest study to date to evaluate the treatment of combat-related PTSD in the deployed combat theater. Previous military operational guidelines limited the use of trauma-focused treatments such as PE and CPT and recommended not treating PTSD until military service members returned from their deployments [38]. These recent findings should be considered in future military guidelines on the treatment of combat operational stress reactions and combat-related PTSD in the military combat theater.

3.2 Treating combat-related PTSD in military personnel in garrison

3.2.1 Prolonged Exposure Therapy

The first study to evaluate the efficacy of PE for the treatment of combat-related PTSD in active duty military personnel treated in garrison (i.e., at their non-deployed, home duty location) included 366 active duty US Army soldiers treated at Fort Hood, in Killeen, Texas. The study [39] was a 4-armed RCT to evaluate: (1) the standard delivery format of PE, which was referred to as Spaced PE (n = 109; 10 weekly 90-minute PE sessions); (2) a non-trauma focused active comparison condition called Present Centered Therapy (PCT; n = 107; 10 weekly 90-minute PCT sessions); (3) a compressed, daily format of PE called Massed PE (n = 110; 10 daily 90-minute PE sessions over 2 weeks); and a minimal-contact control condition (n = 40) involving brief, weekly phone calls from therapists to be used as a comparison condition for the Massed PE arm. The results demonstrated significant reductions in PTSD symptoms in all three active treatment arms. The Massed PE format had equivalent efficacy as the Spaced PE arm, although there were fewer dropouts

Principal Investigator/ DoD Award Number	Project Title	Interventions	Project Description	Research Participants
Jeffrey Cigrang W81XWH-08-02-0109	Brief Cognitive-Behavioral Treatment of Combat-Related PTSD in Primary Care Settings: A Pilot Study	Prolonged Exposure for Primary Care	Nonrandomized pilot clinical trial of brief cognitive-behavioral therapy (CBT) for PTSD in primary care	*N* = 24 Active Duty Military
Jeffrey Cigrang W81XWH-08-02-0109	Brief Cognitive-Behavioral Treatment of Combat-Related PTSD in Primary Care Settings: A Randomized Controlled Trial	Prolonged Exposure for Primary Care	RCT of brief cognitive-behavioral therapy for PTSD in primary care vs. wait list	*N* = 67 Active Duty Military
Edna Foa W81XWH-08-02-0111	Prolonged Exposure for PTSD in OIF/OEF Personnel: Massed versus Spaced Trials	Prolonged Exposure; Present-Centered Therapy	Four-armed RCT of spaced (weekly) PE, massed (daily) PE, present-centered therapy (PCT), or a minimal-contact control condition	*N* = 366 Active Duty Military
Edna Foa W81XWH-15-1-0555	60- Versus 90-Minute Prolonged Exposure for PTSD: A Randomized Control Trial in Active Duty Military Personnel	Prolonged Exposure	Two-armed RCT noninferiority trial	*N* = 140 Active Duty Military
Peter Fox W81XWH-13-2-0065	Image-guided, Robotically Delivered TMS for PTSD	Transcranial Magnetic Stimulation	Double-blind RCT of image-guided, robotically delivered transcranial magnetic stimulation versus sham	*N* = 119 (*n* = 114 Active Duty Military; *n* = 5 Veterans)
Steffany Fredman W81XWH-13-2-0065	Multi-Couple Group Intervention for PTSD	Cognitive-Behavioral Conjoint Therapy	Non-randomized clinical trial of abbreviated, intensive, multi-couple group Cognitive Behavioral Conjoint Therapy for PTSD	*N* = 24 Couples (*n* = 17 Active Duty Military; *n* = 7 Veterans

Principal Investigator/ DoD Award Number	Project Title	Interventions	Project Description	Research Participants
John Krystal W81XWH-13-2-0065	Ketamine for Antidepressant-Resistant PTSD	Ketamine	RCT of 0.2 mg/kg ketamine, 0.5 mg/kg ketamine, or saline placebo delivered twice per week for 4 weeks	*N* = 156 (*n* = 54 Active Duty Military; *n* = 102 Veterans)
Brian Marx W81XWH-16-2-0003	Decreasing Suicide Risk among Service Members with Posttraumatic Stress Using Written Exposure Therapy	Written Exposure Therapy for Suicide	Recruitment in Progress	Recruitment target *N* = 140 Active Duty Military
Donald McGeary W81XWH-13-2-0065	RCT of Cognitive Behavioral Therapy for PTS and Headache	Cognitive Behavior Therapy for Headache Cognitive Processing Therapy	RCT of CBT for headaches, CPT, Treatment as Usual	*N* = 193 (*n* = 3 Active Duty Military; *n* = 69 Veterans)
Carmen McLean W81XWH-14-1-0008	A Randomized Clinical Trial of Internet-Delivered PE for PTSD	Prolonged Exposure; Present-Centered Therapy	Two-armed RCT of Web-PE versus PCT	*N* = 40 (37 Active Duty Military; 3 Veterans)
Carmen McLean W81XWH-14-1-0008	A Nonrandomized Trial of Internet-Delivered PE for PTSD	Prolonged Exposure	Open clinical trial of Web-PE	*N* = 34 (2 Active Duty Military; 32 Veterans)
Candice Monson W81XWH-08-02-0115	Individual Prolonged Exposure versus Couples' Cognitive-Behavioral Therapy for Combat-Related PTSD	Cognitive Behavioral Conjoint Therapy; Prolonged Exposure	Two-armed RCT of Cognitive Behavioral Conjoint Therapy versus PE	*N* = 116 (58 Active Duty Military; 58 Military Spouses)
Alan Peterson W81XWH-08-02-0109	Outcomes of PE and CPT for Combat Operational Stress Reactions in Deployed Settings	Prolonged Exposure; Cognitive Processing Therapy	Nonrandomized clinical trial of PE and CPT delivered during a military deployment	*N* = 12 Active Duty Military
Alan Peterson W81XWH-12-2-0073	Clinical Effectiveness Trial of In-Home CPT for Combat-Related PTSD	Cognitive Processing Therapy	Three-armed RCT of In-Office, Telebehavioral Health, and In-Home CPT	*N* = 120 (*n* = 24 Active Duty Military; *n* = 96 Veterans

Principal Investigator/ DoD Award Number	Project Title	Interventions	Project Description	Research Participants
Alan Peterson W81XWH-13-2-0065	Project Remission: Maximizing Outcomes with Intensive PTSD Treatment	Prolonged Exposure	RCT of 15 daily Massed-PE or Intensive Outpatient Program-PE sessions over 3 weeks	*N* = 234 (*n* = 145 Active Duty Military; *n* = 144 Veterans)
Patricia Resick W81XWH-08-02-0116	Group Cognitive Processing Therapy versus Group Present Centered Therapy for Combat-Related PTSD	Cognitive Processing Therapy; Present-Centered Therapy	Two-armed RCT of group CPT versus group PCT	*N* = 108 Active Duty Military
Patricia Resick W81XWH-08-02-0116	Individual versus Group Cognitive Processing Therapy for Combat-Related PTSD	Cognitive Processing Therapy	Two-armed RCT of individually delivered CPT versus group-delivered CPT	*N* = 268 Active Duty Military
Patricia Resick W81XWH-13-02-0012 Alan Peterson W81XWH-13-02-0013	Variable-Length CPT for Combat-Related PTSD	Cognitive Processing Therapy	Non-randomized clinical trial of variable-lengths of CPT	*N* = 130
Denise Sloan W81XWH-15-1-0391	Brief Treatment for PTSD: Enhancing Treatment Engagement and Retention	Written Exposure Therapy	Two-armed RCT comparing WET versus CPT	*N* = 170 Active Duty Military
Daniel Taylor W81XWH-13-2-0065	Treatment of Comorbid Sleep Disorders and PTSD	Cognitive Processing Therapy; Cognitive-Behavioral Therapy for Insomnia	RCT of CPT, CPT followed by CBT-I, or CBT-I followed by CPT	*N* = 94 (*n* = 87 Active Duty Military; *n* = 7 Veterans)

Notes: CBTi = Cognitive-Behavioral Therapy for Insomnia; CPT = Cognitive Processing Therapy; CAP = Consortium to Alleviate PTSD; DoD = Department of Defense; PTSD = posttraumatic stress disorder; PCT = Present-Centered Therapy; PE = Prolonged Exposure; RCT = randomized clinical trial; STRONG STAR = South Texas Research Organizational Network Guiding Studies on Trauma and Resilience; WET = Written Exposure Therapy.

Table 1.
Summary of STRONG STAR and CAP PTSD clinical trials.

from treatment with the Massed PE format (13.6%) as compared to the Spaced PE format (24.8%), and there were fewer adverse events with the Massed PE format (25.3%) as compared to the Spaced PE format (54.1%). These results provide strong support for the compressed, Massed PE treatment format for active duty military personnel; with close coordination with military leadership, it is much easier to schedule and complete a full dose of treatment over a 2-week period as compared to weekly treatment formats that often require 3–4 months to complete.

The promising findings from the Massed PE arm of the study by Foa, McLean, and colleagues [39] led to the funding of a Consortium to Alleviate PTSD (CAP) project to further enhance the Massed PE treatment and to compare it to an Intensive Outpatient Program based on PE (IOP PE). The CAP study [40] randomized 234 active duty service members and veterans to either 15 sessions of daily Massed PE or IOP PE treatment over a 3-week period. The IOP PE arm included eight enhancements to the Massed PE protocol that targeted many of the unique aspects of combat-related PTSD. The enhancements included (1) a team-based treatment approach, rather than relying on one therapist; (2) completion of daily homework assignments at the clinic; (3) 15- to 30-minute, in-person feedback sessions after daily homework assignments; (4) active involvement of the spouse or other support person for in vivo exposures; (5) targeting the patients' top three most distressing traumas during imaginal exposure; (6) starting imaginal exposure with the least distressing trauma and progressing to the most distressing trauma; (7) a brief review of all other potentially traumatic events that occurred during previous deployments; and (8) the completion of three posttreatment booster sessions. The final results of this study have not yet been published, but preliminary results [41] indicate that both treatments resulted in large reductions in PTSD symptoms at the conclusion of treatment, but only those randomized to the IOP PE maintained the large treatment gains over the 6-month follow-up period. The reduction of PTSD symptoms and maintenance of treatment gains with the IOP PE arm are among the strongest treatment outcomes to date for combat-related PTSD.

Another adaptation of the standard, weekly, 90-minute outpatient format for PE was a series of STRONG STAR studies designed to adapt PE for use in military primary care clinics. The first project was a pilot study (N = 24) to develop and test an abbreviated PE protocol adapted for primary care (called PE for Primary Care) consisting of four to six 30-minute treatment sessions conducted by a behavioral health consultant embedded in an integrated primary care clinic. The results showed that PTSD severity was significantly reduced and 50% of the patients no longer met criteria for PTSD after treatment [42, 43].

The results of the pilot project were then used in a subsequent RCT in which 67 service members were randomized to receive the PE for Primary Care treatment or a minimal contact control condition followed by treatment after 6 weeks [44]. The results indicated that the immediate treatment group had large reductions in PTSD severity as compared to the minimal contact control. Similar improvements were found in the delayed treatment group when they received the PE for Primary Care treatment, and the treatment benefits persisted through the 6-month follow-up point for all participants. These finding suggest that an abbreviated version of PE delivered in integrated primary care clinics is effective for the treatment of PTSD and may help reduce barriers and stigma found in specialty care settings.

Another adaptation of the standard outpatient PE protocol was the development of a web-based version of PE [45] to help improve accessibility of effective and efficient evidence-based treatments for PTSD. Web-PE was first compared to in-person Present-Centered Therapy in an RCT with 40 military personnel with PTSD at Fort Hood, Texas. Due to recruitment challenges in the RCT, the efficacy of the Web-PE treatment was then evaluated in an open trial with 34 service members and veterans recruited nationwide. The results of the RCT showed that both Web-PE and PCT significantly reduced interviewer-assessed and self-reported symptoms of PTSD, with no significant differences between the groups and a medium effect size for Web-PE [46]. The open trial of Web-PE showed significant reductions in self-reported PTSD symptoms with a large effect size. These results suggest that Web-PE is a potential alternative to standard, in-person PE, although the benefits

in reducing PTSD symptoms are likely to be greater in patients who are specifically seeking a web-based treatment.

A significant limitation of the outpatient version of PE for the treatment of military personnel in garrison is that delivering the standard 90-minute PE sessions is difficult in many military mental health settings. To address this challenge, an RCT was conducted to evaluate the efficacy of 60-minute versus 90-minute PE sessions [47]. The preliminary results indicate that the shorter sessions possess equal efficacy, thereby increasing the potential feasibility of using the 60-minute format in military mental health settings [48].

3.2.2 Cognitive Processing Therapy

The first study to evaluate the efficacy of CPT for the treatment of combat-related PTSD in active duty military personnel treated in garrison included 108 active duty US Army soldiers treated at Fort Hood, in Killeen, Texas [49]. The study was an RCT to compare group CPT to group Present-Centered Therapy (PCT). Participants were randomized to attend twice weekly 90-minute group treatments of CPT or PCT. The results indicated that both treatments resulted in large reductions in both clinician-administered and self-report measures of PTSD symptoms, but the group CPT treatment resulted in larger reductions [49].

As a follow-on study to the group CPT versus group PCT, another RCT (N = 268) was conducted at Fort Hood to compare CPT delivered in a group format to CPT delivered in an individual format [50]. The study was designed as a noninferiority trial and hypothesized that group CPT would function as well as individual CPT in reducing symptoms. If proved true, group CPT would be more efficient to deliver to a larger proportion of active duty military patients with the need for fewer therapists. The results, however, did not support this hypothesis. Individual CPT was found to be significantly more effective in reducing PTSD symptoms compared to group CPT. The findings suggest that the effective treatment of PTSD with CPT requires a focus on the specific traumas and related cognitions that are unique to individual patients. However, even among those receiving individual CPT, approximately one-half still had clinically significant PTSD symptoms, indicating that additional improvements are needed for existing treatments.

To address these concerns, a study was conducted modeled after a study conducted with civilians that demonstrated treatment outcomes could be improved by varying the number of CPT sessions based on patient response to treatment. The study was conducted using a nonrandomized, within-group design treating 127 active duty military personnel [51]. Patients received variable-length CPT which could end before 12 sessions or extend up to 24 sessions over 18 weeks if patient and therapist agreed a good end state had been reached (PCL-5 $\leq$ 19). The results indicated that the variable-length CPT outcomes were superior to the previous fixed-length CPT studies conducted with military personnel in proportion to diagnostic remission on the CAPS-5 (65% vs. 40%) and clinically significant symptom improvement on the PCL-5 (76% vs. 46%) [52].

Another method to address some of the potential limitations of the standard CPT protocol is to evaluate different delivery settings for CPT. To evaluate these factors, an RCT was conducted to determine if CPT delivered face-to-face in a patient's home (In-Home CPT) or by telehealth to their home (Telehealth CPT) would result in increased acceptability, fewer dropouts, and better outcomes for service members and veterans than standard In-Office CPT [53]. This study used an equipoise stratified randomization design in which participants could opt out of one delivery modality and still be randomized to one of the other two.

The results showed that 57% of participants declined one of the treatment arms (In-Home = 30%; In-Office = 16%; Telehealth = 11%). However, dropout from treatment was lowest when therapy was delivered In-Home (21%) as compared to Telehealth (33%) and In-Office (44%) [54]. Significant reductions in PTSD symptoms occurred across all three treatments, and a remarkable 56% of participants no longer met diagnostic criteria for PTSD at the end of treatment. Treatment outcomes were better when patients received more treatment, and improvements were considerably better when CPT was delivered In-Home or by Telehealth. An additional advantage of the Telehealth CPT is that it reduced the average patient and therapist time commitment by 50% as compared to the In-Office or In-Home treatments. CPT delivered by telehealth is also an efficient and effective treatment modality for PTSD in active duty military. This is an important scientific observation considering recent limitations to in-person care resulting from the COVID-19 pandemic.

Although CPT was designed for the treatment of PTSD related to sexual assault in civilians, there is increasing evidence that it may also be helpful for PTSD that is comorbid with other deployment-related disorders such as posttraumatic headache and insomnia. One CAP 3-armed RCT (N = 193) compared CPT, Cognitive-Behavioral Therapy for Headache, and treatment as usual for veterans and active duty service members with comorbid posttraumatic and PTSD symptoms [55]. The results indicated that, compared to treatment as usual, both CPT and Cognitive-Behavioral Therapy for Headache reduced PTSD symptoms on the PCL-5, but only Cognitive-Behavioral Therapy for Headache reduced headache disability symptoms [56].

Furthermore, one CAP study evaluated the sequencing of treatment for comorbid PTSD and insomnia [57] in military service members and veterans (*N* = 94). The RCT compared (1) 18 sessions of CPT alone, (2) 12 session of CPT followed by 6 sessions of Cognitive-Behavioral Therapy for Insomnia (CBT-I), or (3) 6 sessions of CBT-I followed by 12 sessions of CPT. The preliminary results [58] suggest that treatment sequencing matters and that there are greater reductions in PTSD symptoms when CPT is used first and is followed by CBT-I. Conversely, improved outcomes for insomnia occur when CBT-I is used first and followed by CPT.

3.2.3 Cognitive-Behavioral Conjoint Therapy

Cognitive-Behavioral Conjoint Therapy (CBCT) [59] is a couples-based, 15-session, weekly treatment program to address both PTSD symptoms and relationship functioning. Despite previous research to support the efficacy of CBCT in civilian and veteran couples, the first RCT with active duty military couples comparing CBCT to PE failed to replicate previous results [60]. One of the primary challenges in conducting CBCT with military couples was that the military work environment made it very difficult for both spouses to attend the proposed 15 treatment sessions, resulting in a high dropout rate. To address these challenges, the treatment protocol was redesigned as an abbreviated, intensive, multi-couple group version of CBCT in which the entire treatment protocol was delivered as a 2-day weekend retreat [61]. The results of a nonrandomized clinical trial (N = 24 couples) that included an active duty service member or veteran who had previously deployed found significant reductions in both clinician-rated and self-reported PTSD symptoms as well as significant improvements in relationship satisfaction. However, the results are limited by the nonrandomized design used for this pilot project. Additional research is needed comparing the abbreviated, intensive, multi-couple group version of CBCT to an active comparison intervention.

3.2.4 Written Exposure Therapy

One of the more recent developments to improve treatment efficacy and efficiency for PTSD and decrease dropout rates is a 5-session treatment called Written Exposure Therapy (WET) [62]. After almost 20 years of research with civilian and veteran populations to investigate imaginal exposure in a written form, the first RCT to treat service members in garrison was a 2-armed noninferiority RCT (N = 170) comparing WET to CPT [63]. The results indicated that the 5-session WET protocol was equally effective as the 12-session CPT protocol. However, dropouts from treatment were significantly less for WET (24%) as compared to CPT (45%). The results demonstrate that WET is an efficient method to treat combat-related PTSD and results in fewer dropouts from treatment and may well represent an important treatment improvement from a public health perspective (i.e., fewer sessions needed and fewer dropouts).

The results of this initial WET study provided support for a follow-on study to evaluate a modified version of WET targeting co-morbid PTSD symptoms and suicidal ideations (WET-S) for service members hospitalized on a military psychiatric inpatient facility. Crisis Response Planning was added to the standard WET protocol to address the suicidal ideations. Recruitment is ongoing for this study, but preliminary results appear quite promising [64].

3.2.5 Medications and devices for the treatment of PTSD in military personnel

Although exposure-based cognitive-behavioral treatments have the largest number of studies supporting the efficacy in treating PTSD, other approaches exist and are promising. One CAP study was a double-blind RCT (N = 119) comparing 20 sessions of image-guided, robotically delivered transcranial magnetic stimulation (irTMS) to a sham TMS in service members and veterans hospitalized in a private psychiatric facility in San Antonio, Texas [65]. The treatment for PTSD was delivered to the right dorsolateral prefrontal cortex, an area related to the neural circuitry for stress and anxiety disorders. The preliminary results indicated that there were greater PCL-5 score reductions for active irTMS than for sham at every assessment time point.

Another CAP study was the largest RCT to date to evaluate ketamine for antidepressant-resistant PTSD in 156 service members and veterans randomized to 0.2 mg/kg ketamine, 0.5 mg/kg ketamine, or saline placebo delivered twice per week for 4 weeks [66]. The preliminary results indicated that there were no statistically significant differences in reductions in PTSD among any of the treatment arms; however, there were significant reductions in depression with the higher dose of ketamine. More data analyses are ongoing to more fully understand the impact of ketamine treatment for combat-related PTSD.

4. Summary and conclusions

Over the past decade, the STRONG STAR Consortium and the Consortium to Alleviate PTSD successfully completed 20 clinical trials to evaluate various treatment interventions for combat-related PTSD in active duty military personnel. These studies documented that combat-related PTSD can be effectively treated in military personnel, with up to 80% having significant reductions in their PTSD symptoms and about one-half no longer meeting diagnostic criteria for PTSD at the end of treatment. Importantly, a clinical case series demonstrated that trauma-focused treatments to address combat operational stress reactions and

combat-related PTSD can be successfully delivered in the military combat theater [33, 34]. Several studies presented above successfully adapted PE for military populations in various ways to improve access, reduce dropout, and enhance outcomes. These include shortening the time between sessions [39, 40], reducing the number of sessions [42–44], providing web-based treatment [46], reducing the length of sessions [47], and conducting intensive weekend retreats for couples [61]. Similarly, a variable length CPT protocol successfully treated active duty military with improved outcomes [51] and demonstrated efficacy in multiple in-person or telehealth settings [54]. A study showing individually delivered CPT to be more efficacious than CPT delivered in a group format [50] has important implications for health care delivery in both military and VA facilities. Studies of the treatment of comorbid posttraumatic headache [56] and insomnia [58] showed that CPT can be successfully paired with other treatments to improve outcomes. A pilot study of conjoint treatment for military couples using a weekend retreat format shows great promise for reducing PTSD symptoms as well as enhancing relationship satisfaction [59]. Finally, WET, a 5-session written exposure treatment, has been shown to treat service members in garrison as successfully as a 12-session CPT but with lower dropout [63]. Despite these important advances, there remains a critical need for research to further improve upon the assessment, diagnosis, treatment, and prevention of PTSD and comorbid conditions in service members and veterans.

Findings from multiple clinical trials have now demonstrated combat-related PTSD can be effectively treated in active duty service members and veterans, but there are additional challenges in the treatment of these populations as compared to many civilian traumas. The assessment and treatment approaches for these conditions must be adapted and tailored for the unique aspects of combat-related traumas and for PTSD that is complicated by one or more of the most common comorbid conditions including TBI, sleep disorders, substance use disorders, chronic pain, and risk for suicide. Clinical trials are also needed to further evaluate the combination of cognitive-behavioral therapies with medications and medical devices. In addition, brief interventions that can be administered soon after trauma exposure in far-forward combat locations need to be evaluated as methods to prevent the onset of chronic PTSD.

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Author details

Alan L. Peterson[1,2,3*], Barbara L. Niles[4,5], Stacey Young-McCaughan[1,2] and Terence M. Keane[4,5]

1 University of Texas Health Science Center at San Antonio, San Antonio, Texas, USA

2 South Texas Veterans Health Care System, San Antonio, Texas, USA

3 University of Texas at San Antonio, San Antonio, Texas, USA

4 National Center for PTSD, VA Boston Healthcare System, Boston, Massachusetts, USA

5 Boston University School of Medicine, Boston, Massachusetts, USA

*Address all correspondence to: petersona3@uthscsa.edu

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