Supplementary Online Content

Foa EB, McLean CP, Zang Y, et al; STRONG STAR Consortium. Effect of prolonged exposure therapy delivered over 2 weeks vs 8 weeks vs present-centered therapy on PTSD symptom severity in military personnel: a randomized clinical trial. *JAMA*. doi:10.1001/jama.2017.21242

Study Protocol and Statistical Analysis Plan

Brooke Army Medical Center (BAMC)
PROTOCOL FOR CLINICAL INVESTIGATION -- HUMAN

1.0 Title: Prolonged Exposure (PE) for PTSD among OIF/OEF Personnel: Massed vs. Spaced Trials

2.0 Study Personnel: See P01-Core Application-HSR-Part A

Medical Monitor: See P01-Core Application-HSR-Part A

3.0 Location(s): See P01-Core Application-HSR-Part A

4.0 Research Plan

4.1 Purpose: The purpose of this study to improve the efficiency of treatment for posttraumatic stress disorder (PTSD) with prolonged exposure (PE), an efficacious treatment for PTSD typically administered in once- or twice-weekly sessions, by evaluating whether massing 10 PE sessions in 2 weeks (massed trials; PE-M) is more efficacious than Minimal Contact (MC) control, and retains the efficacy of treatment compared to 10 PE sessions spaced over 8 weeks (spaced trials; PE-S), and to evaluate for the first time the efficacy of the 10 PE sessions delivered in 8 weeks in an active duty population by comparing it to an active comparison condition, Present-Centered Therapy (PCT).

4.2 Hypotheses/Research Questions:

Research Question 1: Will prolonged exposure delivered in massed sessions (PE-M) be an efficacious treatment for PTSD among military personnel recently returned from deployments in Afghanistan and Iraq compared to a wait list control group?

Research Question 2: Will prolonged exposure delivered in massed sessions (PE-M) be as efficacious as prolonged exposure delivered in spaced sessions (PE-S) 2-weeks and 12-weeks after the completion of each treatment (Weeks 4 and 14 for Group PE-M compared to Weeks 10 and 20 for Group PE-S)?

Research Question 3: Will prolonged exposure delivered in spaced sessions (PE-S) be an efficacious treatment for PTSD among military personnel recently returned from deployments in Afghanistan and Iraq compared to Present-Centered Therapy (PCT), immediately after and 12-weeks after the completion of treatment (Weeks 8 and 20)?

4.3. Significance: Estimates from epidemiological studies indicate between 10-20% of military personnel returning from Iraq and Afghanistan suffers from PTSD (Hoge et al., 2004). This highlights the need for developing treatments that are even more efficient than the methods currently proven efficacious in order to minimize the suffering endured by America's warriors. Exposure therapy is a well-studied and highly efficacious treatment approach for PTSD (Cahill et al., in press;) and prolonged exposure (PE) is the single most researched and best empirically supported exposure therapy protocol (Foa et al., 1991, 1999a, 2005; Resick et al., 2002; Rothbaum et al., 2005, 2006; Schnurr et al., 2007). In comparison to traditional "talk therapy", not only is exposure therapy highly efficacious but it is efficient as well. Treatment studies have repeatedly found clinically meaningful improvement utilizing 8-12 sessions of prolonged exposure administered once or twice weekly. If prolonged exposure delivered in massed sessions (i.e., 10 session delivered in two weeks) is at least as efficacious as prolonged

exposure delivered in a more standard fashion (10 sessions delivered over 8 weeks) then it would constitute an optimal treatment for OIE/OEF service personnel with PTSD by minimizing the time and inconvenience required by a longer treatment before their readjustment prior to continuing a military career or returning to civilian life.

4.4. Military Relevance: One of the most significant research gaps of PTSD in the Department of Defense (DoD) is in the development and validation of effective treatments for combat-related PTSD and related psychosocial health problems in active-duty military personnel. This research gap is highlighted in three recent reports: the Institute of Medicine (IOM; 2007) report on the treatment of PTSD; the Report of the DoD Task Force on Mental Health (DoD TFMH, 2007); and the Joint DoD/VA Conference on Post Deployment Mental Health (2005). Recent studies of Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF), and Operation New Dawn (OND) veterans suggest that 5 to 17% of U.S. military personnel returning from deployments have symptoms of PTSD, and as many as 25% report some psychological problem (Hoge et al., 2004, 2006, 2007; Milliken et al., 2007). The IOM report (2007) also highlighted the scant evidence exploring the unique aspects of treating combat-related PTSD in veterans, and it concluded that well-designed research is needed to answer the key questions regarding the efficacy of treatment modalities in combat veterans.

4.5 Background/ Review of Literature:

PTSD is an often chronic and debilitating condition that is associated with many co-morbid medical and psychiatric disorders. The wars in Iraq and Afghanistan have substantially increased the number of active duty personnel and veterans who are in need of care for military-related trauma, and in particular, treatment for PTSD. Current estimates of the number of returning OIF/OEF/OND military personnel who meet criteria for PTSD is between 10% and 20% (Hoge et al., 2004). To meet the current and growing demand for effective and efficient interventions for PTSD, and to prevent the development of long-term and costly chronic PTSD in OIF/OEF/OND veterans, it is important to investigate whether the existing empirically supported treatments can be effectively delivered in an even more efficient timeframe.

There is currently a large body of knowledge on how to treat PTSD effectively and efficiently using cognitive behavioral treatment (CBT). Prolonged Exposure (PE; Foa, Hembree, & Rothbaum, 2007; Foa & Rothbaum, 1998) was developed by the PI, Edna Foa, and colleagues in the Center for the Treatment & Study of Anxiety (CTSA), University of Pennsylvania. It has been found quite efficacious in reducing PTSD and related psychopathology with various types of trauma in PTSD centers around the world. Furthermore, PE has been identified in the joint VA-Department of Defense Clinical Practice Guideline for PTSD (VA-DoD Clinical Practice Guideline Working Group, 2003) as “strongly recommended” for use with veterans with PTSD, based on the strong empirical support for PE. The recent report issued by the United States Institute of Medicine (IOM, 2008) concluded that exposure therapy (which includes both prolonged exposure and cognitive processing therapy) was the only treatment for PTSD with sufficient evidence to support its recommendation as an effective treatment intervention.

PE is designed to help PTSD sufferers to emotionally process traumatic events by providing education about PTSD, repeated and prolonged imaginal exposure to trauma memories, and repeated in vivo confrontation with trauma-related situations the patient is avoiding. Studies have shown that in addition to greatly reducing PTSD symptom severity, PE also reduces depression and general anxiety, guilt, anger, and anxiety sensitivity, and that it improves social functioning. Results of follow-up assessments consistently indicate that most people maintain their treatment gains. A recently completed VA Cooperative Study (CSP 494; Schnurr et al.,

2007) in which 284 female veterans and active duty personnel were randomized to either PE or a manualized, present-centered therapy (PCT), again demonstrated that PE is an efficacious treatment in reducing PTSD and co-morbid symptoms. Additionally, PE was more efficacious in reducing PTSD than PCT.

Recent unpublished analyses of data from four PE studies (Foa et al., 1999, 2005; Resick et al., 2002; Rothbaum et al., 2005) found that 125 out of 135 (96%) female assault victims with chronic PTSD who completed PE had a post-treatment PTSD severity score that was significantly lower (i.e., a change greater than would be expected by measurement error alone) than their pre-treatment score, compared to only 36 out of 99 subjects completed wait list (WL) conditions. Using a similar definition of treatment response, Schnurr et al. (2007) found the 75% of female veterans with service-connected chronic PTSD who completed PE were responders; even among those who dropout from treatment, 64% were responders. Accordingly, it is expected the majority of subjects who receive PE will experience a significant reduction in PTSD severity along with anxiety, depression, and anger.

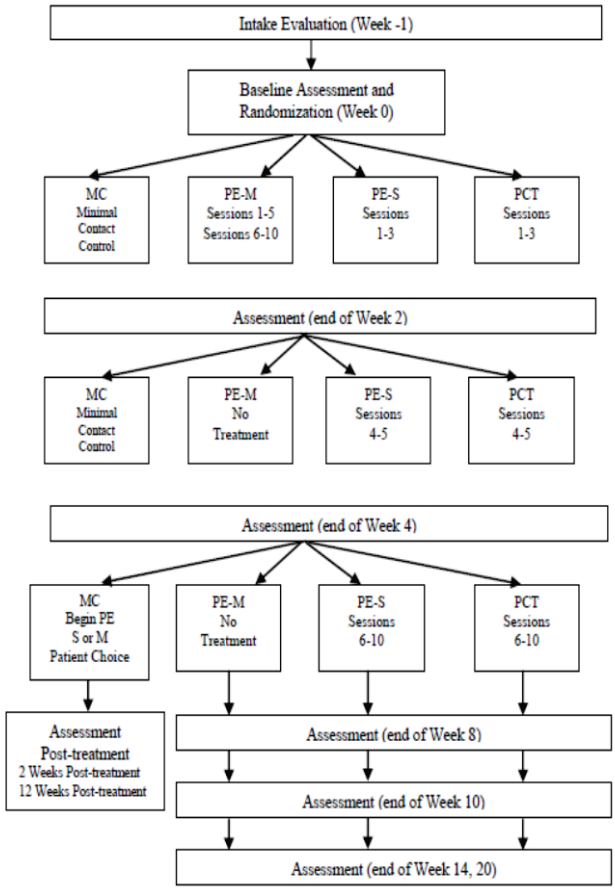
Currently, PE is most commonly administered in 9-12 sessions conducted once or twice weekly. Thus, treatment can last between 5-12 weeks, even longer when a patient misses appointments. Finding ways to speed recovery from trauma will reduce suffering, allow treatment to be administered more efficiently and, in a military sample, minimize the time required for readjustment prior to continuing a military career or returning to civilian life. Thus subjects' participation in this study will enhance our knowledge about the comparative efficiency of different ways of delivering PE.

4.6 Research Design and Methods:

Design

Military personnel returning from deployments in Afghanistan and Iraq diagnosed with PTSD and meeting other eligibility criteria will be assigned to one of four study conditions: Minimal Contact (MC) Control, 10 sessions of PE administered over 2-weeks (prolonged exposure–massed or PE-M), 10 sessions of PE administered over 8-weeks (prolonged exposure–spaced or PE-S), or Present Centered Therapy (PCT). A modified randomization procedure will be used; more participants will be assigned to one of the active treatment (n = 110 per treatment) than the Minimal Contact Control (n = 50).

Figure 1.



The design of this study is summarized in Figure 1. Eligibility and interest will be determined at an intake screening evaluation. Participants who consent to enroll in the study will return for a baseline evaluation (Week 0) and then undergo randomization to one of the four study conditions. The Week 0 assessment and all subsequent assessments will consist of a clinical interview administered by a trained independent evaluator (IE) blind to treatment condition. Participants will also complete a series of self-report measures.

Following randomization, participants in all four groups will be re-evaluated at Week 2 (immediately after group PE-M has completed treatment and groups PE-S and PCT have completed the first three treatments sessions) and Week 4 (two weeks after group PE-M has completed treatment and groups PE-S and PCT have completed first five treatment sessions). After the Week 4 assessment, participants assigned to MC will begin delayed treatment. MC participants will be given the choice of receiving PE-M, PE-S, or PCT. Additional assessments will occur for MC participants immediately upon completion of 10 sessions of PE and again two weeks later for clinical purposes (i.e., monitoring progress) and 12 weeks after completing treatment to assess maintenance of treatment gains. Groups PE-M, PE-S, and PCT will undergo additional assessments at Weeks 8, 10, 14, and 20 as well as at 6- and 9-months following treatment. To evaluate the acute efficacy of PE-S relative to PCT, the comparison of interest is PE-S vs PCT at Week 8. To evaluate the acute efficacy of PE-M relative to MC, the comparison of interest is PE-M at Week 4 vs. MC at Week 4. To evaluate the equivalency of PE-M with PE-S two weeks after completing treatment, the comparison of interest is PE-M at Week 4 vs. PE-S at Week 10. To evaluate the equivalency of PE-M with PE-S at follow-up, the

comparisons of interest are PE-M at Week 14 vs. PE-S at Week 20 (12-weeks after completing treatment). To evaluate the relative efficacy of PE-S versus PCT at follow-up, the comparisons of interest are PE-S vs. PCT at Week 20 (12-weeks after completing treatment) Treatments are described below in the Study Procedures section.

The *independent variable*, therefore, is the treatment condition (PE-S, PE-M, PCT, or MC) to which subjects are assigned. Equal randomization between all four groups will occur completing the MC cohort before the PE-S, PE-M, and PCT cohorts to answer the first research question as soon as possible, "Will prolonged exposure delivered in massed sessions (PE-M) be an efficacious treatment for PTSD among military personnel recently returned from deployments in Afghanistan and Iraq compared to a wait list control group?" Knowing the answer to this first research question will serve to minimize risk to subjects. If PE-M is efficacious as compared with MC, the study will continue; if PE-M is found to not be as efficacious as minimal contact the study design will need to be revised. Once the MC group is filled, an amendment will be submitted to the IRB removing this as a potential treatment. The *primary dependent variable* is PTSD symptom severity as measured by PSS-I administered by independent evaluators blind to study condition.

Training of Therapists: Therapists will be credentialed providers at the facility. Therapists will also be rigorously trained and carefully supervised. Drs. Foa and Lichner, from the University of Pennsylvania Center for the Treatment and Study of Anxiety, will provide oversight of PE training and supervision following procedures that have been used successfully with other joint research projects (e.g., the recently published multi-VA study CSP-494; Schnurr et al., 2007). Therapists will first undergo an intensive 4-day workshop on the administration of PE and then complete three training cases under intense supervision before treating study cases. Dr. Tracie Shea will provide oversight of training for the PCT condition, also following procedures that were successfully used in CSP 494 (Schnurr et al., 2007). Therapists will undergo a 2-day workshop on provision of PCT and then complete two training cases under intense supervision before treating study cases. Training and study cases will receive session-by-session supervision, but study cases will involve less intensive supervision than training cases. Three sessions of each study case will be evaluated for treatment fidelity. Any serious deviation from the protocol may be grounds for additional training or suspension of a therapist from seeing additional study cases at Dr. Foa's discretion.

Treatments: (See Appendix A for a copy PE-S, PE-M, and PCT Manuals).

Prolonged Exposure – Spaced (PE-S): PE is a manualized cognitive behavior therapy program and consists of psychoeducation about the nature of trauma, common reactions to trauma including PTSD, factors that maintain PTSD, and a rationale for treatment; training in controlled breathing as a coping skill for managing day-to-day stress; and two kinds of exposure, revisiting the traumatic memory: repeated recounting of the traumatic event and processing it (i.e., imaginal exposure plus discussion) and gradually approaching trauma-related reminders (i.e., in vivo exposure). Sessions are scheduled to last approximately 90 minutes. In Session 1 the therapist presents the overall rationale for the treatment program, asks the client questions about his or her trauma history as well as the current difficulties the person is experiencing, and teaches a breathing skill to help manage anxiety. In Session 2 common reactions to trauma are discussed, the rationale for in vivo, or real-life exposure, is discussed, and a hierarchical list of trauma-related safe or low-risk situations that the client has been avoiding is developed. In vivo exposure activities from this list are practiced between the therapy sessions from this session onward, beginning with the relatively easier ones and working up the list over time to the harder ones. Beginning in the 3rd session and continuing

through the 10th session, the client is asked to confront the memory of his or her trauma by revisiting it in imagination and recounting it aloud. After the revisiting, the therapist and client discuss the client's thoughts and feelings about the trauma with the aim of helping the client to develop a realistic perspective on the event(s). The therapy sessions are audio taped and given to the client to listen to between sessions as part of homework. Therapy sessions are also video recorded for purposes of supervision and treatment fidelity monitoring (see fidelity monitoring session below). In PE-S, the two educational and treatment planning sessions (Sessions 1 and 2) will occur during Week 1, followed by one treatment session per week during each of Weeks 2-7, and the final treatment session plus a wrap-up session in Week 8.

Prolonged Exposure – Massed (PE-M): PE-M will be implemented in identical fashion to PE-S with the exception that five sessions will be administered each week (Monday-Friday) for a total of 10 sessions administered in two weeks.

Present Centered Therapy (PCT): PCT is also a manualized therapy, and will provide a credible comparison therapy to control for nonspecific therapeutic factors so that observed effects of prolonged exposure can be attributed to its specific ingredients beyond the benefits of good therapy. Rather than focusing on trauma memories directly, PCT focuses on current life problems that may or may not be trauma- or PTSD-related. Sessions are scheduled to last approximately 90 minutes, just like PE, although the content of sessions differs significantly. Sessions 1 and 2 are introductory and include discussion of the treatment rationale and education about PTSD. Sessions 3 through 9 are focused on discussing and reviewing daily stresses and difficulties with which the patient struggles. Session 10 focuses on reviewing accomplishments made during therapy and making plans for the future. Therapists are prohibited from suggesting or giving instructions for exposure and from implementing cognitive restructuring. The therapist's role is to listen actively, help patients to identify daily stresses, and to discuss them in a supportive, empathic, and nondirective manner. In PCT, the two introductory and educational sessions (Sessions 1 and 2) will occur during Week 1, followed by one treatment session per week during each of Weeks 2-7, and the final two treatment sessions in Week 8. Therapy sessions will be video recorded for purposes of supervision and treatment fidelity monitoring (see fidelity monitoring session below).

Minimal Contact (MC): Participants assigned to MC will be asked to not work with another therapist or seek additional treatment for trauma-related difficulties during the 4-week MC period. They will be called once per week by the study therapist or independent evaluator in order to monitor their status and to provide support as needed. The calls will be limited to 10-15 minutes. MC participants will also be given contact information to use in case of worsening of symptoms or increasing distress. They will be seen in a face-to-face evaluation at Week 2, the midpoint of their 4-week waiting period, and will be assessed at that time. Immediately following the Week 4 assessment, MC subjects will be offered their choice of PE-S or PE-M, and will be offered immediate treatment. Individuals showing significant worsening of their psychiatric condition during the MC period will be discontinued early from the study after completing an end-point evaluation and provided either PE or PCT by the study team or a referral as deemed clinically appropriate.

Quality Control

Supervision: Therapist training procedures were described above. Training cases and randomized study cases will receive session-by-session supervision. Supervision of training cases will be more intensive than supervision of study cases. As described above, DVDs of training cases will be reviewed by the supervisor who will provide the therapist with verbal

feedback prior to the next session. Because the intensity of treatment in the PE-M condition (i.e., daily), it will not be feasible for supervisors to review DVDs of therapy sessions prior to the next session. Instead, supervision in the PE-M condition will be based on therapist report to the supervisor via daily (excluding weekends) telephone calls. In order to maintain comparability of the level of supervision between treatment conditions, supervision of PE-S will be limited to weekly telephone calls. Supervision calls typically last between 30-45 minutes. Participants' condition and response to treatment will be monitored throughout treatment by therapists and regularly discussed in supervision. The On-Site PI, will be available for consultation and intervention in event of concerns about the status or welfare of a study participant. See section below on Safeguards for Protecting Subjects for additional information about participant monitoring.

Assessment of Treatment Fidelity: Because supervisors will not be able to review therapy recordings, it will be important for quality assurance to assess treatment fidelity in an ongoing fashion so that any therapists demonstrating low fidelity to the treatment protocols can be identified as soon as possible and corrective action can be taken. Accordingly, upon completion of each study case, DVDs of all therapy sessions will be sent via Federal Express to the CTSA or uploaded to a secure STRONGSTAR data base, and a sample of 3 sessions from each case will be randomly selected for review and evaluation for treatment fidelity by the CTSA using previously developed procedures (e.g., Foa et al., 2005). The fidelity raters will be trained at a 4-day PE workshop. Any significant deviations from the study protocol will be brought to the attention of Dr. Foa and the therapist's supervisor for corrective action. Repeated significant deviations from the study protocol by a therapist may be grounds for requiring additional training or suspension of a therapist from seeing additional study cases at Dr. Foa's discretion.

Rules for Early Termination / Withdrawal of Participants: Participation in the study may be discontinued by the principal investigator if continued participation is considered a danger to a participant's welfare. Reasons for discontinuation include: 1) serious adverse event; 2) clinical worsening for any reason that is deemed to necessitate non-study psychological or psychiatric treatment; 3) exacerbation of PTSD, anxiety, or depressive symptoms that the participant cannot tolerate; or 4) discontinuation would be in the participant's best interest. Participants deemed candidates for discontinuation will be discussed in the weekly conference calls with the therapist and the supervisor and will be brought to the attention of the PI for final decision.

Participants who are discontinued from the study for any reason will be scheduled for a final evaluation within one week and given appropriate treatment referrals. If participants are discontinued due to a serious adverse event, they will continue to be followed clinically by the On-Site PI until the adverse event is resolved or becomes stable. If participants are discontinued for a medical or psychiatric reason, they will be given the opportunity to either complete the balance of their PE sessions or to receive a full course of PE treatment after the condition has resolved or stabilized and the endpoint assessment has been completed. The reason the participants are discontinued from the study and any referrals made will be documented. Participants will be told they will be contacted for follow-up whether or not they complete the trial.

4.7 Source of Research Material: See Appendix B for a summary of the assessments and timing of administration.

Source of Research Material	**Standard Care**
1. History of Head Injuries (that includes the DVBIC Screening Tool)	No
2.Automated Neuropsychological Assessment Metrics (ANAM®)	No

3.Deployment Risk and Resilience Inventory (DRRI) Combat Experience Sub-Scale, Aftermath-of-Battle Sub-Scale & Deployment Environment Sub-Scale	No
4.PTSD Symptom Scale – Interview (PSS-I)	No
5.PTSD CheckList – Stressor Specific (PCL-S) & PTSD CheckList – Version for proposed DSM-V (PCL-V)	No
6.Veterans Rand 12-Item Health Survey (VR-12)(Functional Impact)	No
7.Conflict Tactics Scale (revised) (CTS2) Psychological Aggression & Physical Assault Sub-Scales	No
8.State-Trait Anger Expression Inventory (STAXI)	No
9.Beck Depression Inventory (BDI)-II	No
10.Beck Anxiety Inventory	No
11.Beck Scale for Suicide Ideation (BSS)	No
12.Columbia-Suicide-Severity Rating Scale (C-SSRS)	No
13.Alcohol Use Disorders Identification Test (AUDIT)	No
14.Response to Stressful Experiences Scale (RSES)	No
15.Life Event Checklist (LEC)	No
16.PERI Life Events Checklist	No
17.Peri-Traumatic & Post-Traumatic Emotions	No
18.Demographics & Military Service Characteristics	No
19.Interpersonal Support Evaluation List (ISEL)	No
20.Trauma-Related Guilt Inventory (TRGI)	No
21.Walter Reed Army Institute of Research (WRAIR) Military Vertical & Horizontal Cohesion Scales	No
22.Post-Traumatic Cognitions Inventory (PTCI)	No
23.Credibility / Expectancy Questionnaire (CEQ)	No
24. Cognitive Emotions Regulation Questionnaire (CERQ)	No
25. Patient Health Questionnaire (PHQ)-15	No
26. Health Interview (Pre- & Post-Treatment)	No
27. Mini International Neuropsychiatric Interview (MINI), Modules C (Mania) & (Psychosis)	
28. American College of Rheumatology (ACR) Fibromyalgia Questionnaire	No
29. Self-Assessment of Sleep Questionnaire	No
30. Frequency of Nightmares Questionnaire	No
31. Snoring, Tired, Observed, Blood Pressure (STOP) Sleep Apnea Screen	No
32. Epworth Sleepiness Scale	No
33. Insomnia Severity Index	No
34. Beliefs in a Just World (BJW) Scale	No
35. PROMIS Sexual Function Profile	No

4.8 Instrumentation: See Appendix B for a summary of the assessments and timing of administration. For participants who have left military service $25 compensation will be offered for completion of the 6- and 9-month follow-up assessments (for a total of $50). Payment will only be offered to participants who have left military service to be in compliance with the recently published Department of Defense Instruction (DoDI) 3216.02: Protection of Human Subjects and Adherence to Ethical Standards in DoD-Supported Research, dated 20 October 2011.

One questionnaire, the American College of Rheumatology (ACR) Fibromyalgia Questionnaire, is being included in the questionnaire packet in support of another BAMC IRB-approved protocol, Prevalence of Fibromyalgia (FM) in Posttraumatic Stress Disorder (PTSD) (C.2011.145d, IRBNet 364862). Additionally, participants will be given the option of taking a questionnaire packet home to their spouse offering the spouse participation in C.2011.145d, IRBNet 364862. This packet includes a demographics form for spouses and the ACR

Fibromyalgia Questionnaire. As described in the informed consent document for the treatment study, Service Members are not required to take the packet home; neither is the Service Member's spouse required to complete the packet.

1. History of Head Injuries: Traumatic brain injury (TBI), in particular mild TBI is very difficult to assess and diagnose with an administered questionnaire or automated testing. Yet, it is imperative that some assessment for TBI be made to more fully assess TBI in the presence of PTSD and more fully evaluate response to PTSD treatment. In consultation with civilian and military experts in TBI, the STRONG STAR Assessment Core is administering a modified version of the Defense and Veterans Brain Injury Center (DVBIC) 3-Item Screening Tool (Schwab, Baker, Ivins, Sluss-Tiller, Lux & Warden, 2006; Schwab, Ivins, Cramer, Johnson, Sluss-Tiller, Kiley, Lux & Warden, 2006) to all participants. This instrument, initially called the Brief Traumatic Brain Injury Screen (BTBIS), was tested with 596 Soldiers returning from duty in Iraq and/or Afghanistan and responses compared with a Quarterly Survey administered to assess ballistic helmets, a Computerized Traumatic Brain Injury (TBI) Questionnaire, responses to the Neurobehavioral Symptom Inventory (that includes criteria for postconcussional syndrome or PCS) and an interview by a Masters' level psychologist or staff member trained and supervised by the psychologist (Schwab, Ivins, Cramer, Johnson, Sluss-Tiller, Kiley, Lux & Warden, 2006). The interview was used as the gold standard for the diagnosis of TBI in this sample. Testing indicated that the 3-Questions DVBIC Screening Tool has good concurrent validity in that it identified more self-reported TBIs than either the Quarterly Survey or the Computerized TBI Questionnaire. Furthermore, participants who reported TBI on the 3-Question Screen were more likely to report three or more post-concussive symptoms on the Neurobehavioral Symptom Inventory than those who denied TBI. As recommended by the DVBIC, for the STRONG STAR studies the 3-Question Screen is positive when the participant endorses an injury (question 1) and altered consciousness (question 2, items A-E) for the worst head injury sustained while deployed. The form was modified for this study to describe the worst injury; the original form does not recognize the possibility of multiple head injuries during deployment. Participants who are positive using this screen will then be further tested using the Automated Neuropsychological Assessment Metrics (ANAM). As the 3-Question Screen does not query head injuries prior to deployment, an additional four questions have been added to solicit information about each head injury sustained.

2. Automated Neuropsychological Assessment Metrics (ANAM). The ANAM is a computerized battery of neuropsychological tests originally developed within the Department of Defense in the early1990s to provide a standardized and valid method of testing to detect deficits in cognitive functioning in various clinical and military settings (Reeves, Winter, Bleiberg & Kane, 2007). The ANAM battery is a collection of tests that assess different basic functions or domains of cognition to include reaction time, processing speed (procedural reaction time), learning (code substitution), delayed memory (code substitution), working memory (mathematical processing), and spatial memory (matching). The test assesses both speed and accuracy. "Throughput" is the number of correct items within a certain time. Norms for military Service Members and college studies, both male and female ranging in age from 18 to 51 have been established. Test print-outs compare scores for the individual being tested to a preselected normative group. The ANAM has compared favorably to a variety of traditional neuropsychological measures including the math, running memory, code substitution delayed memory, logical reasoning, the Wechsler Adult Intelligence Scale (WAIS-III) Digits Backward and Digit Symbol, Trail Making Tests A&B, Paced Auditory Serial Addition Test (PASAT), the Controlled Oral Word Association Test, Animal Naming, and the Rivermead Behavioral memory Test Short (Cernich, Wilken & Kane, 2007). The

ANAM has been used to screen for impairment in various clinical populations including patients with multiple sclerosis, systemic lupus erythematosus, Parkinson's disease, Alzheimer's dementia, migraine headache, and acquired brain injury (Kane, Roebuck-Spencer, Short, Kabat & Wilken, 2007). In 22 individuals enrolled in a traumatic brain injury rehabilitation program, the ANAM was able to differentiate between participants marginally impaired, mildly impaired, and moderately impaired with 91% accuracy based upon their throughput scores (Levinson & Reeves, 1997 as cited in Kane, Roebuck-Spencer, Short, Kabat & Wilken, 2007). When the marginally and mildly impaired individuals were grouped together, the ANAM differentiated between these individuals and those moderately impaired with 100% accuracy. Testing in 25 individuals with migraine headaches demonstrated that the ANAM is sensitive to change with ANAM scores declining following migraine onset and improving following migraine treatment (Roebuck-Spencer, Sun, Cernich, Farmer & Bleiberg, 2007). Furthermore, the ANAM was able to discern differences in side effect profiles of various medications including antihistamines, desloratadine, transdermal nicotine, mianserin (Wilken, Sullivan, Lewandowski & Kane, 2007). While there is not a specific ANAM score that is indicative of no, mild, moderate, or severe traumatic brain injury, the STRONG STAR Consortium is administering the ANAM to provide additional descriptive data about the cognitive functioning of study participants based upon the recommendations of civilian and military experts in TBI and the STRONG STAR Consortium External Advisory Board and consistent with the assessment of TBI being used for the USAMRMC Congressionally Directed Medical Research Program (CDMRP) Psychological Health Research Program Multidisciplinary Research Consortium for TBI, Mission Connect.

3. Deployment Risk and Resilience Inventory (DRRI) Combat Experience, Aftermath-of-Battle, and Deployment Environment Sub-Scales: High- and low-intensity deployment stress exposure will be assessed using scales from the DRRI (King, King, Vogt, Knight, & Samper, 2006). The DRRI was developed and tested in three separate national samples of veterans of the first Gulf War. It has been revised and tested with OEF/OIF/OND returnees (Vogt et al., 2008). High intensity stressor exposures will be assessed using the DRRI Combat Experiences and Aftermath of Battle subscales. Responses to these scales are on a 5-point Likert scale. The total score is the sum of the item scores, where higher scores signify greater exposure to combat or exposure to the consequences of combat, respectively. In addition, low-intensity deployment stress will be assessed with the DRRI Deployment Environment subscale. Responses to this scale are on a 5-point Likert scale with anchors 1 (almost none of the time) to 5 (almost all of the time). The total score equals the sum of the item scores, where higher scores are indicative of a more difficult living and working environment. All three subscales have very good internal consistency (α = .85 to .89) and construct validity (Vogt, et al., 2008).

4. PTSD Symptom Scale, Interview Version (PSS-I): The PSS-I is a 20-minute, 17-item clinical interview that evaluates DSM-IV PTSD symptoms on a frequency/severity scale (Foa, Riggs, Dancu, & Rothbaum, 1993). The PSS-I is comparable to the gold standard employed in studies of veterans (the Clinician Administered PTSD Scale; CAPS) yet takes considerably less time to administer (Foa & Tolin, 2000). Each symptom is rated on a 4-point scale ranging from 0 (not at all) to 3 (very much). Subscale scores are calculated by summing items in each of the PTSD symptom clusters: re-experiencing, avoidance, and arousal. The scale has excellent internal consistency (α = .91), test-retest reliability (.80), and inter-rater reliability (kappa = .91). This measure will be administered by a blinded Independent Evaluator at each study site. At the end of the PSS-I, there are nine items from the CAPS that ask the Independent Evaluator to judge the extent to which various PTSD symptoms that do not specifically reference the index event are related to the index

event (1=definite, 2=probable, 3=unlikely). The items that do not specifically reference the index event are: loss of interest in free time activities, feelings of detachment, impairment in the range of emotions, change in future plans or hopes, difficulty in falling or staying asleep, irritability or outbursts of anger, difficulty concentrating, over alertness, jumpiness and ease of startle. This assessment of "relatedness" was added to assist the adjudication of caseness decisions but not to affect either the integrity or validity of the PSS-I instrument. The data will be used in data analysis to better understand the study outcomes.

5. PTSD CheckList – Stressor Specific (PCL-S) & PTSD CheckList – V (PCL-V): The PCL-S is a 17-item self-report measure based upon the PTSD CheckList – Miiltary (PCL-M; Weathers, Litz, Herman, Huska, & Keane, 1993) that evaluates how much participants have been bothered by PTSD symptoms in the past month as a result of the stressful life events identified by either the participant, or by the Independent Evaluator following administration of the PSS-I. Each item of the PCL-S is scored on a five-point scale ranging from 1 ("not at all") to 5 ("extremely"). The measure is divided into 3 subscales: Re-experiencing symptoms (items 1- 5); Avoidance/ Emotional Numbing symptoms (items 6- 12); and Hyper-arousal symptoms (items 12-17). This is the instrument recommended to assess post-traumatic stress in military members by the Veterans Affairs/Department of Defense (VA/DoD) Clinical Practice Guideline for the Management of Post-Traumatic Stress (Veterans Affairs Office of Performance and Quality & U. S. Army Medical Command Quality Management Directorate, 2004). A recent review of 21 studies testing 9,628 subjects, almost one-third of which (n=2,767) were military Veterans, reported overall internal consistency alpha coefficients between .85 and .96, test-retest reliability between .96 (at 2 to 3 days) and .68 (at 12 to 14 days), and convergent validity with the Clinician-Administered PTSD Scale (CAPS), Center for Epidemiological Studies – Depression (CESD), Mississippi Scale for Combat-Related PTSD, Impact of Event Scale (IES), and the National Women's Study PTSD Module (NWS-PTSD; Keen, Kutter, Niles & Krinsley, 2008). The 21 studies reviewed used PCL scores between 30 and 50 to determine a diagnosis of PTSD. In the most recent studies using the PCL-M to assess PTSD in Service Members injured in Iraq or Afghanistan (Grieger et al, 2006; Hoge et al, 2004, 2008; Smith et al, 2008) subjects were categorized as positive for PTSD if they reported at least one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms, each present at the level of moderate or higher during the past month, and if they received a total severity score of 50 or higher. At baseline and again following treatment, the PCL-V based upon the proposed DSM-V criteria for PTSD will be administered as well as the PCL-S so that when the results of this study are published the Research Team will be able to put the findings of the study in the context of the most current criteria of PTSD.

6. Veterans Rand 12-Item Health Survey (VR-12): Because a certain level of PTSD symptoms is an occupational hazard among Service Members redeployed for combat, it is critical to pay close attention to functional capacities as an important index of intervention efficacy. The Veterans SF-36 (VR-36) was adapted from the RAND SF-36 Version 1.0 questionnaire, and spans the range of health domains from physical to psychological health status. It includes two modifications. The first modification is an increase in the number of response choices for the role physical (RP) and role emotional (RE) items from a two point yes/no choice to a five-point likert scale (no, none of the time, yes, a little of the time, yes, some of the time, yes, most of the time, yes, all of the time). The second modification is the use of two items to assess health change, one focusing on physical health and one on emotional problems, in contrast to the one general change item in the RAND SF-36 (Kazis, Lee et al., 2004; Kazis, Miller, Clark et al 2004). The VR-36 has been widely used, distributed and documented in the Veterans Health Administration (VHA) with close to 2 million

questionnaires administered nationally in six national surveys since 1996. The changes to the survey have increased the overall precision of the instrument and the discriminant validity of the physical and mental component summary scales (Kazis, Nethercot, et al 2006). The VR-36 is comprised of 37 items and eight scales: physical functioning, role limitations due to physical problems, bodily pain, general health perceptions, energy/ vitality, social functioning, role limitations due to emotional problems, and mental health. Also, there are two summary scales: a physical component summary (PCS) and mental component summary (MCS). Higher scores indicate better health. Each summary is expressed as a T score, which facilitates comparisons between the VA patients and the general U.S. population. The PCS and MCS scores provide at least 90% of the reliable variance in the eight SF-36 concepts (Kazis & Wilson, 1998; Kazis, Wilson, et al., 1999). The Veterans SF-12 was developed from the Veterans SF-36 and adapted from the MOS SF-36. It includes fewer items for seven of the eight scales and provides 90% of the reliable variance in the two component summary measures using the Veterans SF-36. Using independent results from the Veterans Health Study and the 1996 National Survey of Ambulatory Care Patients, the results for the Veterans SF-12 corresponded very closely with the results for the Veterans SF-36 (average differences of 0.06 points between them for PCS and 0.31 points for MCS; Kazis et al., 1996; Kazis & Wilson, 1998).

7. Conflict Tactics Scale (revised) (CTS2) Physical Assault & Psychological Aggression Subscales: The CTS was designed to assess the use of reasoning, verbal aggression, and violence within the family (Straus, 1979) and over time has become the most widely used instrument to assess intimate partner violence (Straus & Douglas, 2004; Straus, Hamby, Boney-McCoy & Sugarman, 1996). The CTS (revised; CTS2) poses 39 questions to assess five tactics used when there is conflict in the relationships of dating, cohabitating, or marital couples, i. e., Physical Assault, Psychological Aggression, Negotiation, Injury, and Sexual Coercion (Straus, Hamby, Boney-McCoy & Sugarman, 1996). In 2004 a revised Conflict Tactics Scales (CTS2S) was developed shortening the instrument from 78 questions to 20 reducing the test administration time to three minutes (Straus & Douglas, 2004). For the STRONG STAR studies, only the Physical Assault and Psychological Aggression subscales (20 items) of the CTS2 will be used broadening the assessment of conflict to query interpersonal conflict among friends, colleagues, and acquaintances as well as the family as these subscales represent the content areas of most interest and are most relevant to the targeted populations. Testing in a sample of 317 undergraduate students from well-educated parents, the CTS2 demonstrated alpha reliabilities ranging from 0.79 to 0.95 (Straus, Hamby, Boney-McCoy & Sugarman, 1996). Furthermore, Straus et al (1996) felt that the instrument demonstrated construct and discriminate validity in that men were shown to be more likely to use coercion to obtain sex and more likely to have serious injury result from physical assault. Discriminate validity was demonstrated in that two of the subscales, negotiation and sexual coercion and negotiation and injury, were shown to not be correlated. Various versions of the CTS have been used in other studies of military personnel (Adler et al, 2008; McCarroll et al., 2000; Taft, Street, Marshall, Dowdall, & Riggs, 2007), but to assess conflict in the family and not wider affiliations as STRONG STAR intends to assess.

8. State-Trait Anger Expression Inventory (STAXI)*:* The STAXI (Spielberger, 1988), a 44-item scale that evaluates dimensions of anger, to assess participants' feelings of anger at a given moment. Only the 10 items related to the State-Anger (S-Anger) subscale will be used. Items in this subscale ask participants to indicate how much they are experiencing certain feelings and desires on a four-point scale ranging from 1 ("not at all") to 4 ("very much so"). Scores on all 10 items are summed to assess the overall intensity of anger felt at a

particular moment in time. We are only interested in the state items because they are the most likely to change with treatment. Internal consistency of the subscale was found to be strong (average α = .90), as was its convergent validity with measures of hostility and other personality scales (Spielberger, 1988).

9. Beck Depression Inventory (BDI-II): The BDI-II is one of the most widely used instruments for measuring the severity of depressive symptoms. It consists of 21 items that assess both affective and somatic symptoms related to depression and depressive disorders. Each item is composed of four statements that reflect symptom severity. The statements are scaled from 0 (no disturbance) to 3 (maximal disturbance). Scores on all items are summed to obtain a total severity score. Scores reflect minimal depressive symptoms (0-13), mild depressive symptoms (14-19), moderate depressive symptoms (20-28), or major depressive symptoms (29-63; Beck, Brown & Steer, 1997). The BDI has internal consistency of .91, and correlates strongly with other measures of depression (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961).

10. Beck Anxiety Inventory (BAI): The BAI will be used to assess anxiety symptomology. This is a 21-item measure that asks participants to rate the severity of their symptoms of anxiety within the past week on a four-point scale ranging from 0 ("not at all") to 3 ("severely"). Scores on all items are summed to obtain a general severity of anxiety score, indicating the presence of physical and/or psychological symptoms of anxiety. The BAI has been shown to have high internal consistency (α = .92) and test-retest reliability. It has also been shown to reliably discriminate between anxious and non-anxious diagnostic groups (Beck, Epstein, Brown & Steer, 1988).

11. Beck Scale for Suicide Ideation (BSSI): The BSSI (Beck & Steer 1991) will be used to assess current suicide ideation. The BSSI will be self-report. Instructions will instruct the participants to respond based on the past week. Current intent will be calculated using questions 11-19 on the BSSI. A person with 0 positives will be considered to have low intent, 1-3 positives will be considered moderate intent, and 3+ positives will be considered severe intent. Non-multiple attempters will be placed in one of these 3 categories. There will be no "low" category for multiple attempters. In a sample of 330 psychiatric inpatients, the BSSI was found to have a Cronbach's alpha coefficient of .95, indicating high internal consistency (Steer et al., 1993). The BSSI was also found to correlate with severity of anxiety, depression, and the BDI suicidal ideation item in this sample, suggesting strong concurrent validity.

12. Columbia-Suicide Severity Rating Scale (C-SSRS): The Columbia-Suicide Severity Rating Scale (C-SSRS; Posner, Oquendo, Gould, Stanley, & Davies, M., 2007) will be used to assess past suicide ideation. The C-SSRS will be administered by an Independent Evaluator, who will instruct the participants to answer the questions based on their entire lifetime of experience. Distinctions will be made between multiple and non-multiple attempters. In the Suicidal Behavior section of the C-SSRS, the participant will be considered a non-multiple attempter if they answered 0 or 1 for total number of attempts, and a multiple attempter if they answered 2 or more attempts.

13. Alcohol Use Disorders Identification Test (AUDIT): The AUDIT (Babor et al, 2001) will be used to identify people with hazardous or harmful patterns of alcohol consumption. The AUDIT is a 10-item screening measure, developed by the World Health Organization (WHO), with three subscales (alcohol consumption, drinking behavior, and alcohol-related

problems) that are scored on a 4-point scale for a highest possible total score of 40. Among those identified as using alcohol in a harmful manner, 92% had scores of 8 or more, though determining a cutoff score should be left up to the clinician, depending upon the population being studied. The AUDIT has good internal consistency (α = .80-.93) as well as sensitivity and specificity (Saunders, Aasland, Babor, De La Fuente & Grant, 1993).

14. Response to Stressful Experiences Scale (RSES). The RSES is a 22-item questionnaire developed by a team of experts at the National Center for PTSD to assess trait-related cognitive, emotional, and behavioral resilience (Johnson, et al., 2008). It asks participants to assess how well each statement describes them, both during and after stressful events in their lives. Responses are given on a 5-point scale, with anchors 0 (not at all like me) to 4 (exactly like me). Psychometric testing in 1,014 active duty, reserve and veteran groups showed that the instrument has sound internal consistency (coefficient alpha 0.91 to 0.93) as well as good test-retest reliability over 7-days (reliability correlation = 0.87). The instrument correlated positively with another measure of resilience, the Connor-Davidson Resilience Scale (coefficient alpha 0.61 to 0.81) as well as unit cohesion (coefficient = 0.38), and post-deployment support (coefficient 0.36 to 0.56). The instrument correlated negatively with psychological symptom distress as assessed with the Patient Health Questionnaire - 9 (coefficient = -0.51), posttraumatic stress as assessed with the PCL-M (coefficient -0.23 to -0.39), and overall mental health as assessed with the Minnesota Multiphasic Personality Inventory-2 Neuroticism (coefficient = -0.35) demonstrating concurrent validity. Factor analysis revealed a six-factor model of resilience including subscales for active coping, meaning-making, cognitive flexibility, spirituality, self-efficacy, and restoration.

15. Life Events Checklist (LEC): The LEC includes a list of 16 different potentially traumatic life events that that are commonly associated with PTSD symptoms and was designed to facilitate the diagnosis of PTSD (Gray, Litz, Hsu, & Lombardo, 2004). In this study, the LEC will also be used to identify the index event and focus of the PTSD treatment. For each potentially traumatic life event, respondents rate their experience of that event on a 5-point nominal scale (1 = happened to me, 2 = witnessed it, 3 = learned about it, 4 = not sure, and 5 = does not apply). However, for data entry purposes each nominal point will be scored separately, as either 0 (=not endorsed by participant) or 1 (=endorsed by participant). Three totals will be generated: number of events experienced, number of events witnessed, and number of events learned about. In a group of 108 undergraduate psychology students the instrument demonstrated good convergence with the Traumatic Life Events Questionnaire (TLEQ) (average kappa = 0.55) and correlated with the Posttraumatic Stress Disorder CheckList – Civilian (PCL-C) (reliability coefficients 0.34 to 0.48). The LEC demonstrated good test-retest reliability over 7-days (all kappa statistics except one for “caused serious injury / death of another” >0.52). In 131 combat veterans the LEC was related in the predicted directions with other measures of psychopathology known to be associated with potentially traumatic life events as assessed with the Posttraumatic Stress Disorder CheckList – Military (PCL-M), Clinician Administered PTSD Scale (CAPS), and the Mississippi Scale for Combat-Related PTSD. The STRONG STAR Consortium Assessment Core has added the two-item screen for military sexual trauma to the LEC that is used in the VA to assess for uninvited and unwanted sexual attention as well as sexual assault.

16. PERI Life Events Scale (Brief): The PERI Life Events Scale (Dohrenwend et al., 1978) is a 102-item measure, designed to assess the number and severity of low and moderate magnitude stressful life events that a person has experienced in the previous six months. In

order to minimize time burden, the 10 items most relevant to the military population to which the measure will be administered were selected by military subject matter experts. In some cases, the military experts combined items to adequately cover all of the major content areas of the original measure with the fewest number of items. This measure is intended to be a checklist; therefore, it is not expected to have high internal consistency (i.e., just because someone has one stressful event does not necessarily make it more likely that s/he would have another stressful event). The intent is to capture the most common, yet most stressful life events, which could affect treatment outcome.

17. Peri-Traumatic & Posttraumatic Emotions Questionnaire (PTEQ). The PTEQ is a self-report measure that has been adapted from various Trauma Interviews (Bernat, Ronfeldt, Calhoun & Arias, 1998; Kilpatrick, Resnick, Freedy, Pelcovitz, Resick, Roth & van der Kolk, 1998; Resick, Jordan, Girelli, Hutter & Marhoefer-Dvorak, 1988; Rizvi, Kaysen, Gutner, Griffen, & Resick, 2008). The PTEQ was developed by Dean Kilpatrick, Karen Calhoun and Patricia Resick from clinical interviews of rape victims in an attempt to understand why some people developed psychological problems after being raped while some people recovered (P.A. Resick, personal communication, February 15, 2010). Over time, as more research used the interview and asked questions about peri-traumatic emotions the interview has been further refined. Published studies have slightly different items and different names for the PTEQ (Bernat, Ronfeldt, Calhoun & Arias, 1998; Kilpatrick, Resnick, Freedy, Pelcovitz, Resick, Roth & van der Kolk, 1998; Resick, Jordan, Girelli, Hutter & Marhoefer-Dvorak, 1988; Rizvi, Kaysen, Gutner, Griffen, & Resick, 2008). In one study of 296 individuals (145 rape victims and 151 assault victims), the responses to a 29-item PTEQ were subjected to exploratory factor analysis revealing four factors: 1) Negative Affect (other than fear), 2) Fear, 3) Active Responding, and 4) Freeze Responses (Rizvi, Kaysen, Gutner, Griffen, & Resick, 2008). Responses indicative of a Freeze Response were associated with greater PTSD and depressive symptomatology while Fighting was associated with lower symptomatology. The questionnaire in its current form asks respondents to identify how much they felt to a series of 20 emotions (ranging from 0 = “not at all” to 4 = “all of the time”) during the time of their traumatic experience and how much they currently feel to the same 20 emotions. This 40-item version of the instrument will be used for the STRONG STAR studies; however a factor analysis and psychometric testing will be done as part of the Consortium's data analysis. One of the innovations of the STRONG STAR studies is to use the PTEQ during treatment for PTSD to assess when change in emotions occurs.

18. Demographics and Military Service Characteristics Form: The Demographics Form measures standard demographics (race, gender, age) and military service information (e.g., rank).

19. Interpersonal Support Evaluation List (ISEL): The ISEL (Cohen & Hoberman, 1983) measures multiple dimensions of perceived social support. This measure has been shown to have good internal consistency with alpha levels ranging in the general population from 0.88 to 0.90 (Cohen, Mermelstein, Kamarck, & Hoberman, 1985). The short form is a 12-item measure that asks participants about their relationships with other people in their lives. It covers three subscales: Appraisal (items 2, 3, 6, and 11), Belonging (items 1, 5, 7, and 9), and Tangible (items 3, 8, 10, and 12). Responses are given on a 4-point scale with anchors, 1 (definitely false) to 4 (definitely true). Scoring involves summing all items with the following items reverse coded: 1, 2, 7, 8, 11, and 12. Higher scores indicate more perceived social support.

20. Trauma Related Guilt Inventory (TRGI) (brief): The TRGI was developed to assess guilt feelings and attitudes about a specific traumatic event (Kubany, Haynes, Abueg, Manke, Brennan, Stahura, 1996). Often survivors of trauma experience guilt related to the trauma about things they did or did not do or feelings they had or did not have. A combat veteran may experience guilt about having provided first aid to some of his or her wounded colleagues but not others even though it was not possible to care for everyone. Or, an individual may experience survivor's guilt not understanding why he lived while others died. These feelings of guilt can be important in evaluating the various treatments for PTSD. The TRGI is scored into three scales (i. e., 4-item Global Guilt Scale, 6-item Distress Scale, and a 22-item Guilt Cognitions Scale) and 3 subscales (i. e., the Hindsight-Bias / Responsibility Subscale, the Wrongdoing Subscale, and the Lack of Justification Subscale). Psychometric testing has been conducted using almost 600 individuals including 357 university students, 163 women receiving counseling services in a battered women's program, and 74 Vietnam veterans. Internal consistency was high across all the testing samples. In the sample of Vietnam veterans the alpha coefficient ranged from 0.66 to 0.94. In the Vietnam veterans, the scores on the various scales and subscales were significantly correlated with the Posttraumatic CheckList – Military (PCL-M), the Mississippi Scale for Combat-Related Posttraumatic Stress Disorder, the Zung Self-Rating Depression Scale, the Guilt Inventory, and the Social Avoidance and Distress Scale with reliability coefficients ranging from 0.36 to 0.77 ($p<.05$). In a sample of 32 university students, the test-retest correlations after two days ranged from 0.74 to 0.83. An abbreviated 16-item version of the TRGI will be used in the STRONG STAR studies allowing only for the calculation of the three subscale scores. The Hindsight-Bias / Responsibility Subscale score = (sum of scores on Items 1, 5, 9, 14, 19, 23, and 26) divided by 7. The Wrongdoing Subscale score = (sum of scores on Items 3, 7, 11, 16, and 21) divided by 5. And, the Lack of Justification Subscale score = [sum of scores on Items 4 (R), 8 (R), 12 (R), and 17 (R)] divided by 4.

21. Walter Reed Army Institute of Research (WRAIR) Military Vertical & Horizontal Cohesion Scales: These cohesion scales are the gold standard method of evaluating attitudes about support from peers (horizontal) and leaders (vertical). They were developed by a team of researchers at the Walter Reed Army Institute of Research (WRAIR) and they are used extensively in research on service members' psychological health and wellness. Horizontal cohesion will be measured using a revised three-item cohesion scale. This scale has a Chronbach Alpha from .86 to .88 (Podsakoff & MacKenzie, 1994). Items assess the degree to which unit members are cooperative, can depend on one another, and stand up for one another. The wording was revised to match the military description of work group (i.e., unit). Agreement is rated on a 5-point scale (1 = strongly disagree to 5 = strongly agree). The vertical cohesion subscale was derived from the Unit Manning Research (see Vaitkus, 1994 for a complete overview) and consists of 12 items on a 5-point scale (1 = never to 5 = always). Items for the vertical cohesion scale were selected based on inter-item correlations greater than .50 as reported by Vaitkus (1994), and whether they had a consistent response options set, were not redundant, and related to Company-level ratings. Individuals will answer the questionnaire for the unit they are currently assigned to, rather than assigned to previously. Subscale scores for vertical and horizontal cohesion as well as a total cohesion score will be calculated.

22. Posttraumatic Cognitions Inventory (PTCI): The PTCI is a 36-item questionnaire that was developed to determine how an individual views the trauma and its sequelae in an attempt to understand both how PTSD develops and is maintained (Foa, Elhers, Clark, Tolin, & Orsillo, 1999). Using an emotional processing theory, Foa and her colleagues (1999) have suggested that PTSD is a consequence of disruptions in the normal processes of recovery

when an individual has excessively rigid concepts about self and world rendering the person vulnerable if a traumatic event occurs. Thus the PTCI was developed as a measure of trauma-related thoughts and beliefs. It is comprised of three subscales (Negative Cognitions about the Self, Negative Cognitions about the World, and Self-Blame). The measure was tested in almost 600 adult volunteers recruited from two university PTSD treatment clinics as well as a university community. Approximately 65% (n=392) of individuals reported having experienced a trauma in which their own life or that of another person was perceived to be in danger and their response at the time included intense terror, horror, or helplessness (Criterion A event). The remaining 35% (n=162) denied such a traumatic experience. Of those who had experienced a trauma, 170 had PTSD symptoms of at least moderate severity while the remaining 185 reported a low symptom severity. The three subscales of the PTCI demonstrated internal consistency with alpha coefficients ranging from 0.86 to 0.97. Convergent validity was demonstrated comparing the PTCI to appropriate subscales of the World Assumptions Scale and Personal Beliefs and Reactions Scale. Significant correlations between the appropriate subscales ranged from 0.20 to 0.85. The PTCI was able to differentiate individuals with and without PTSD demonstrating discriminate validity (sensitivity = 0.78, specificity = 0.93). Test–retest reliability for each of the three subscales at a 1-week interval ranged from 0.75 to 0.89 and for a 3-week interval ranged from 0.80 to 0.86.

23. Credibility/ Expectancy Questionnaire (CEQ): The CEQ is a 6-item measure that was designed to assess treatment expectancy and rationale credibility for use in clinical outcomes studies (Devilly & Borkovec, 2000). It has been expanded from a 5-item measure designed primarily to assess credibility (Borkovec & Nau, 1972), 4-items of which have been used by both Foa and Resick (P.A. Resick, personal communication, February 22, 2010; E.A. Hembree, personal communication, February 23, 2010; E. B. Foa, personal communication, February 25, 2010) with the name Expectancy of Therapeutic Outcomes (ETO). The 6-item CEQ assesses both whether the person cognitively understands how the therapy works (credibility) as well as whether the person affectively believes that the therapy will work for them personally (expectancy). The 6-item CEQ has been tested in 217 individuals including 68 male Vietnam veterans and 58 female spouses, 69 individuals diagnosed with general anxiety disorder who had received treatment, and 22 individuals who had received either Cognitive Based Therapy (CBT) or Eye Movement Desensitization and Reprocessing (EMDR) for the treatment of PTSD. The scale demonstrated high internal consistency (alpha coefficients ranged from 0.84 to 0.85). Test-retest reliability over a one-week period was found to be 0.82 for expectancy and 0.75 for credibility. The CEQ was able to differentiate between two treatment rationales in one study, one with and one without an encompassing theory while maintaining equivalence between three rationales in another study. Responses to four questions are scored using a 9-point Likert scale (1= not at all, 9= extremely). Responses to two of the questions are scored using an 11-point Likert Scale (0% to 100%). The combined responses are used to generate a score for credibility and another score for expectancy.

24. Cognitive Emotion Regulation Questionnaire (CERQ-short): The CERQ was designed to assess cognitive coping strategies people tend to use, or what someone thinks, after having experienced threatening or stressful events (Garnefski, Kraaij, & Spinhoven, 2001). The CERQ can be used to assess cognitive strategies that characterize the individual's style of responding to stressful events. Thirty six (36)-items are scored to produce nine subscales including: 1) Self-Blame, 2) Blaming Others, 3) Rumination, 4) Catastrophizing, 5) Positive Refocusing, 6) Planning, 7) Positive Reappraisal, 8) Putting into Perspective, and 9) Acceptance. The answer categories for each item range from 1 (almost never) to 5 (almost

always). Individual subscale scores are obtained by summing up the scores belonging to the particular subscale. The higher the subscale score, the more a specific cognitive strategy is used. Psychometric testing of the 36-item CERQ was conducted using a group of 547 secondary school students aged 12 to 16 attending a state school in the Netherlands. Internal consistency of the subscales ranged from 0.71 to 0.92. The CERQ was positively correlated with both depression and anxiety as assessed with the subscales of the Symptom Check List-90. Test-retest reliability for each of the subscales at five months ranged from 0.41 to 0.59. The CERQ-short form (Garnefski & Kraaij, 2006) is an 18-item questionnaire that produces the same 9 subscales as the 36-item questionnaire. A study of 611 adults from a general practitioner's office practice in the Netherlands indicated that the internal consistency of the 2-item subscales remained acceptably high (α = 0.67 to 0.81). In support of the validity of the CERQ-short, correlations with outcome measures were comparable to reported results with the original CERQ in that the Rumination, Self-Blame and Catastrophizing subscales were related to more depression and anxiety symptoms, while the Positive Reappraisal subscale was related to fewer symptoms (Garnefski & Kraajj, 2006).

25. Patient Health Questionnaire-15 (PHQ-15): The original PHQ (Spitzer, Kroenke, & Williams, 1999) was derived from the PRIME-MD and consisted of a three-page, self-administered questionnaire that asked about both somatic and psychological symptoms. The PHQ-15 (Pfizer Inc., 1999) is an abbreviated version of the original PHQ that asks about somatic symptoms and symptom clusters that account for more than 90% of physical complaints reported in an outpatient setting. The 15-item measure asks patients to report symptom severity on a scale ranging from 0 ("not bothered at all") to 2 ("bothered a lot"). Research on the psychometric characteristics of the PHQ-15 has found it to have excellent internal reliability (α = .80) and good convergent validity with scales such as the SF-12 and other measures of symptom severity and functionality (e.g., sick days, healthcare utilization and symptom-related difficulty) (Kroenke, Spitzer, & Williams, 2002).

26. Health Interview (Pre- & Post-Treatment): The original Health Care Utilization (HCU) is a 16-item questionnaire developed in 2000 for Dr. Patricia A. Resick's NIH grant, "Cognitive Processes in PTSD: Treatment II." The questionnaire was based on the 1999 Behavioral Risk Factor Surveillance System. The version that will be administered as part of the STRONG STAR Consortium has been modified to be of increased relevance to active-duty service personnel. The measure includes items regarding use of mental health services, current psychiatric medication, past psychiatric medication, hospitalization, and outpatient medical services, as well as items intended to assess changes in participants' military status.

27. Mini-International Neuropsychiatric Interview (MINI). The MINI is a short, structured diagnostic interview that was originally developed in 1990 by psychiatrists and clinicians in the United States and Europe to diagnose DSM-IV and ICD-10 psychiatric disorders (Sheehan, et al., 1998). Modules C (for Mania) and K (for Psychosis) will be used to assess, in a standardized way, for any evidence or schizophrenia, bipolar disorder, or other psychotic disorder that would exclude participants from treatment on this study.

28. American College of Rheumatology (ACR) Fibromyalgia Questionnaire (Wolfe et al, 2010). This is a landmark publication by top experts in the field of fibromyalgia diagnosis. The new criteria were validated in a multi-center study of 829 patients previously diagnosed with fibromyalgia and controls. Compared to the old criteria which required a tender point examination, this simpler clinical case definition correctly classified 88% of old-criteria patients, and obviates the need for physician examination and tender point determination.

In a follow-up study, Wolfe et. al. further modified the criteria to facilitate its use as a simple questionnaire rather than requiring a history taken by medical personnel (Wolfe et al, 2011). The intent of this latest tool is to allow its use in epidemiologic and clinical studies without requirement for an examiner. The modification replaced a physician-judged scale of somatic symptom severity with four questions, which resulted in loss of only 0.3% accuracy over the ACR 2010 criteria. It takes less than 3 minutes to complete the questionnaire.

It is not clear that trauma-related sleep disturbance is treated to the point of remission with cognitive behavioral therapy for PTSD such as PE. Therefore the following assessments of sleep will be administered to determine the effect of treatment for PTSD on sleep.

While many clinicians use the 24-question Pittsburg Sleep Quality Index (PSQI; Buysse et al., 1989) to assess for "disordered" sleep, the PSQI has not been validated to provide specific diagnostic data for nightmares, apnea, daytime sleepiness, or insomnia. Instead of using the PSQI, five sleep assessments (totaling 24 questions) will be administered to assess typical sleep durations and patterns on weekends and weekdays as well as to assess for specific sleep difficulties (i. e., nightmares, apnea, daytime sleepiness, and insomnia) often found in patients with PTSD and other behavioral health issues using established diagnostic criteria.

29. Self-Assessment of Sleep. The Self -Assessment of Sleep questionnaire was developed by a board-certified sleep specialist and one of the STRONG STAR investigators, Daniel Taylor PhD, to be a brief assessment of self-reported sleep quantity and sleep quality. Five items assess estimated total sleep times during the week and during weekends, self-reported hours of sleep needed to feel rested, overall sleep quality, and duration of current sleep pattern. Although there are no established psychometrics for this measure, combined with the other four measures of sleep the battery will provide the information needed to comprehensively assess sleep in study participants.

30. Frequency of Nightmares Questionnaire. The items assessing nightmare frequency and nightmare disturbance were selected from *The Trauma-Related Nightmare Survey* (TRNS; Davis, Wright, & Borntrager, 2001). Davis and Wright (2007) report adequate test-retest reliabilities over a 2-week period for frequency of nightmares (r = .64), and disturbance of nightmares (r = .63). Convergent validity was also found with daily behavioral records of nights with nightmares (r = .82) and the Modified PTSD Symptom Scale – Self-Report (MPSS-SR; Resick, Falsetti, Resnick, & Kilpatrick, 1991) nightmare frequency (r = .64) and disturbance (r = .45). The item assessing nights with nightmares was selected as it is thought to be a more clinical significant measure of the impact of nightmares than the total number of nightmares experienced.

31. Snoring, Tired, Observed, Blood Pressure (STOP) Sleep Apnea Screen (Chung et al., 2008). To better understand sleep disturbance associated with PTSD and PTSD treatment, the STOP screen will be administered to screen for sleep apnea. The STOP is a four-item questionnaire developed and validated in 211 pre-operative surgical patients. Using the answering of 2 or more questions "yes," the sensitivity of the STOP ranged from 66% to 80% as compared with the apnea-hypopnea index (AHI) of polysomnography depending upon the AHI cut-off used. Individuals answering "yes" to 2 or more of the questions will be advised that they may be at risk for having sleep apnea and advised that they may want to speak with their primary care provider to consider referral for an overnight sleep evaluation at the CRDAMC Sleep Clinic.

32. Epworth Sleepiness Scale (ESS; Johns, 1994). The ESS, 8-items rating likelihood of dozing off in various situations, will be used to assess daytime function. The ESS has good internal

consistency (α = .73 - .88) and adequate test-retest reliability and correlates with objective measures of daytime sleepiness (Chervin, Aldrich, Pickett & Guilleminault, 1997).

33. Insomnia Severity Index (ISS; Morin, 1993). The ISI is a 7-item self-report measure that assesses perceived severity of insomnia. Each item uses a 4-point Likert type scale from 0 (not at all satisfied) to 4 (very much satisfied). The items sum to produce a total score (range 0 – 28). The ISI has an internal consistency alpha coefficient of 0.74, and has shown convergent validity with other measures such as the Pittsburgh Sleep Quality Index (r = 0.67), the Dysfunctional Beliefs and Attitudes about Sleep (r = 0.55), and sleep diaries (range from 0.32-0.91) (Bastien, Vallieres & Morin, 2001).

34. Beliefs in a Just World (BJW) Scale. The BJW is a 16-item self-report measure that assesses the belief in a just world for self and others. Just world beliefs are the idea that everything happens for a reason and people get what they deserve in life. This may be protective for some people because it gives them the illusion that they have control over the world and what they experience. However, for trauma survivors, it can lead to feelings of self blame. For example, if people get what they deserve in life, then what did I do to deserve to be raped. This can lead to both behavioral and characterological self blame. Belief in a just world is related to psychological well-being. The BJW Scale has strong psychometric properties (Lipkus, et al., 1996). Factor analysis using promax rotation revealed 2 intercorrelator factors with eigenvalues greater than one. Items had moderate to high loadings on each factor. The BJW scale for self demonstrated good internal consistency (α=.84) in 2 studies. The BJW scale for others also demonstrated good internal consistency (α=.84 in one study and α=.83 in another). Homogeneity of the BJW scales was assessed using principal component analysis with oblique rotation. The scale for self had a single factor which accounted for 62% of the variance and the scale for others also had single factor which accounted for 64% of the variance. Additionally, the BJW Scale significantly correlated with existing measures of just world beliefs. Service Members with PTSD have been noted to endorse just world beliefs during therapy such as “It's not fair that this trauma happened,” or “People with young children are not supposed to die.” Potentially treatment for PTSD modifies these beliefs.

35. Patient Reported Outcomes Measurement Information System (PROMIS) Sexual Functioning Inventory: The PROMIS questionnaires are a system of reliable measures of patient–reported health status for physical, mental, and social well–being developed with funding under the National Institutes of Health (NIH) Roadmap for Medical Research Initiative to re-engineer the clinical research enterprise (http://www.nihroadmap.nih.gov). PROMIS measures can be across a wide variety of chronic diseases and conditions and in the general population (Cella et al, 2010). One of the PROMIS instruments is a Sexual Functioning Inventory (Jeffery et al, 2009). The PROMIS Sexual Function Inventory provides scores on seven different sub-domains of sexual function: interest in sexual activity, vaginal discomfort (women only), lubrication (women only), erectile function (men only), orgasm, and global satisfaction with sex life. Each question asks respondents to report on their experiences over the past 30 days. With the exception of the orgasm sub-domain, all sub-domain scores are expressed as T scores (mean = 50, standard deviation = 10). While the Inventory is intended for broad use, almost all of the development work was with patients with cancer. Research is ongoing to expand development beyond cancer. In testing with 819 individuals (388 males, 430 females, 1 person did not specify sex), correlations between the PROMIS Sexual Functioning Inventory and corresponding sub-domains of two well-established measures, the Female Sexual Function Index (FSFI) and the International Index of Erectile Function (IIEF), ranged between .48 and .92. The sub-

domains of the Inventory discriminate between people who had and had not asked a provider about sexual problems. Test-retest correlations over one month are >.65 for all sub-domains (Sexual Function and Satisfaction Measures User Manual, 2012).

4.9 Inclusion/exclusion criteria:

Inclusion Criteria:

- Adult male and female active duty, activated Reservist, or activated National Guard OIF/OEF/OND military personnel or OIF/OEF/OND veterans ages 18-65 seeking treatment for PTSD
- Diagnosis of PTSD as determined by a clinician-administered Posttraumatic Stress Scale – Interview (PSS-I) and clinical interview. Person has experienced a Criterion A event that is a specific combat-related event or high magnitude operational experience that occurred during a military deployment in support of OIF/OEF/OND. The diagnosis of PTSD may be indexed to that event or to another Criterion A event.
- Documentation of command support to attend treatment
- Able to speak and read English

Exclusion Criteria:

- Current bipolar disorder or other psychotic disorder
- Current alcohol dependence (as determined by the AUDIT)
- Evidence of a moderate or severe traumatic brain injury (as determined by the inability to comprehend the baseline screening questionnaires)
- Current suicidal ideation severe enough to warrant immediate attention (as determined by the Scale for Suicidal Ideation)
- Other psychiatric disorders severe enough to warrant designation as the primary disorder

4.10 Number of Subjects: We will recruit 560 subjects to randomize 380 (110 in Prolonged Exposure – Massed, 110 in Prolonged Exposure – Spaced, 110 in Present Centered Therapy, and 50 in the 4-week Minimal Contact Control)

5.0 Human Subject Protection

5.1 Recruitment, Screening and Consent:

Service Members who screen out from other BAMC IRB-approved STRONG STAR protocols including C.2009.020 / IRBNet 363399 (Cognitive Processing Therapy for Combat-Related PTSD), C.2011.120 / IRBNet 364801 (Comparing Internet and In-Person Brief Cognitive Behavioral Therapy of Insomnia), C.2011.004d / IRBNet 363539 (Genetic and Environmental Predictors of Combat-Related PTSD), and C.2011.120 / IRBNet 368445 (The Role of Exercise in the Treatment of PTSD Symptoms) will be offered the opportunity to be screened for participation in this study at the conclusion of their study visit for the previously-referenced protocol. If interested, a member of the research team will review eligibility with these potential participants (e.g., pre-screen) and either obtain informed consent at that time, if authorized, or schedule another visit at a later date.

Additionally, potential participants may be identified through referrals from various health care providers at CRDAMC clinics. Providers may forward contact information of interested individuals directly to STRONG STAR. Or, potential participants may self-refer in response to recruitment flyers and pamphlets previously approved by the IRB (Appendix F). Recruitment

materials will be distributed to various health care providers and will be posted in locations in CRDAMC and on Fort Hood frequented by Service Members. Primary locations on base will include the R&R Center, fitness centers, chapels, barracks, and the PX. Potential participants may also self refer in response to recruitment information on the STRONG STAR website (Appendix F). Interested persons may call or walk in to the STRONG STAR offices. Research staff will field incoming phone calls and walk-ins. Research staff will discuss the study treatment and eligibility requirements with the interested person. If the person believes they may qualify for the study, an appointment will be made for consent and screening. During this appointment, potential participants will have the study explained to them in a safe and private location. The potential participant will be given a copy of the informed consent document (ICD) to read. After the subject has read the ICD they will be given the opportunity to take the consent home to discuss the research with family and friends. The Research Team will be available to answer any questions about the research. Once the potential participant has reached a decision, the advising staff member will go over the risks and benefits of the study and ensure the subject understands the research. The advising staff member will have the Service Member sign the consent form. A copy of the signed ICD will be given to the subject. The advising staff member will document the informed consent process in the medical record of the participant. Following the consent process, screening will be done. This will include the completion of the questionnaires and interviews outlined in the table in Section 4.7 above. As part of screening and with the participant's consent, the Service Member's Commander will be contacted by a member of the Research Team to solicit his or her support for their Soldier's participation in this study. Once it is determined that the participant meets the inclusion criteria for the study, he or she will be randomized into a treatment arm and the Commander notified in writing of the treatment schedule. For Service Members not meeting study inclusion criteria, the Study Staff will contact the Resilience and Restoration Center staff to coordinate appropriate follow-up outside of the study.

5.2 Benefits: Potential benefits of participation in this study may include a reduction in PTSD symptoms over the course of therapy. In addition, the knowledge gained from this study will serve to inform the most effective early interventions for the prevention and treatment of combat-related PTSD in active-duty military personnel.

5.3 Risks:

Potential risks or discomfort that may arise from participation in this study include becoming emotionally upset or experiencing an initial increase of PTSD symptoms due to the discussion of traumatic events, including increase risk for suicide.

Although many individuals suffering PTSD recover from their symptoms without formal intervention, for many individuals PTSD becomes a chronic condition that, without intervention, can last years and is associated with poor functioning and low satisfaction. Potential risks or discomfort that may arise from participation in this study include becoming emotionally upset or experiencing an initial increase of PTSD symptoms due to the discussion of traumatic events, including increased risk for suicide. Concerns have been expressed about the safety of PE, particularly the concern that some individuals may find the treatment overwhelming and cause an increase in symptoms or further deterioration in functioning, or that individuals receiving PE may simply not complete treatment and thereby remain symptomatic. These concerns are based primarily on unsystematic clinical impression and the research data do not support such concerns.

It is true that individuals undergoing PE may experience increase in distress during exposure

exercises. Also, a small minority experience an increase in symptoms of PTSD after the initiation of imaginal exposure exercises. However, the distress and increased symptoms are temporary, are not predictive of poor outcome, and are not associated with increased likelihood of dropout (Foa et al., 2002). Indeed, with regard to the latter two points, there is evidence that greater anxiety experienced during imaginal exposure exercises can be associated with better outcome (Foa et al., 1995; Pitman et al., 1996), that dropout from PE is not greater than dropout from other forms of cognitive behavior therapy (Hembree et al., 2003), and that dropout rates from studies of PE are comparable or less than dropout rates from the studies of sertraline (brand name Zoloft) and paroxetine (brand name Paxil) in the treatment of PTSD, the only two medications with FDA indication for this condition. Recent unpublished analyses of data from four PE studies (Foa et al., 1999, 2005; Resick et al., 2002; Rothbaum et al., 2005) found that none of the patients who completed PE showed significant PTSD symptom worsening compared to 8% in waitlist conditions.

In summary, the primary foreseeable risk associated with PE is an increase in distress, and in some cases increased PTSD severity, that is temporary, not predictive of poor outcome, and not associated with increased likelihood of dropping out. PCT, shown to be effective at reducing PTSD and other trauma-related pathology in the recently published multi-VA study CSP-494; Schnurr et al., 2007), will likely yield improvement in target symptoms. Some participants receiving PCT may experience a temporary increase in distress when discussing their symptoms and difficulties, especially in the early sessions of treatment. The primary foreseeable risk associated with MC is that few patients are expected to improve and some may experience a temporary increase in their symptoms of PTSD.

With the handling of medical and research records there is always the possibility of a breach of confidentiality.

5.4 Safeguards for Protecting Subjects:

Participants will also complete weekly self-report assessment measures that will assess PTSD symptoms (i. e., PCL-M) and depressive symptoms (i. e., the Beck Depression Inventory). This will allow therapists to closely monitor any increase in distress. If a patient remains upset after a therapy session or psychological interview, he or she will be encouraged to contact their therapist or the interviewer before the next session should the need arise. If a participant needs or desires immediate attention and their therapist is not available, arrangements will be made for an appointment with an experienced mental health professional at their facility.

Distress experienced by participants is expected to be temporary. Any indication that the participant is considering suicide will be handled using processes developed by military and civilian consultants for the STRONG STAR Consortium studies. See Appendix C.

Data will be coded using an assigned number. Data collected during treatment will be placed into a lock box which will be transported by car to University of Texas Health Sciences Center San Antonio (UTHSCSA) STRONG STAR offices by a STRONG STAR staff member who will place it into the locked cabinets at the STRONG STAR offices. Audio and videotapes will be mailed to the Center for the Treatment and Study of Anxiety (CTSA) at University of Pennsylvania and the National Center for PTSD in Boston, MA for review using an express service (e. g., UPS or FedEx) and tracked for receipt. Every member of the Research Team will be trained and monitored about how to handle and protect both medical and research records. Furthermore, the Research Team strictly controls access to study data. See Appendix D.

A *STRONG STAR Repository* has been approved by both the UTHSCSA (HSC20100475H) and BAMC (C.2011.054d; IRBNet #363444) IRBs to enable the STRONG STAR Consortium to store specimens and data for future use. The STRONG STAR Repository will create a large comprehensive database of information, biological specimens and neuroimages related to the identification, assessment, and treatment of PTSD in our active duty and retired veterans of Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND). All information entered into the STRONG STAR Repository will be extracted from primary datasets collected as part of IRB-approved studies, including this study, being conducted and /or supported by the projects of the STRONG STAR Consortium. These study databases will be established and maintained by the Biostatistics and Data Management Core of the STRONG STAR Consortium, led by Dr. Jim Mintz. A unique, sequential alpha-numeric STRONG STAR ID will be assigned to each participant at the time of recruitment into this study. However, all repository data will be identified with a different code number that can be cross linked to the original study code only through records maintained by the STRONG STAR Biostatistics and Data Management Core. Data, biological specimens and images will constitute the STRONG STAR PTSD Repository. Participation in the repository will be completely voluntary and entirely optional which means that a potential participant's willingness to participate in the repository has no influence upon their eligibility to participate in the primary STRONG STAR study they have either already enrolled in or are considering enrolling in. At the conclusion of this study, participants who signed the consent to have their specimens and data placed in the STRONG STAR Repository will be maintained under the IRB-approved Repository protocol. Biological specimens and information from study participants who declined participation in the STRONG STAR Repository will be permanently de-identified (i. e., all PHI will be deleted from the study data bases) and the de-identified blood and information placed in the STRONG STAR Repository for future use.

A Data Safety and Monitoring Plan (DSMP) has been developed in accordance with the National Institutes of Health (NIH) Office of Human Research Protection (OHRP) to assure the appropriate clinical safety monitoring of study subjects participating in this study. See Appendix E.

5.5 Risk:Benefit Assessment: Benefits to participants are direct (expected reduction in PTSD severity along with reduction of general anxiety, depression, anger, and guilt) and indirect (enhancing our knowledge about the comparative efficiency and efficacy of different ways of delivering PE). The possible risks (i. e., temporary increase in distress and severity for the active treatment conditions, and possible increase in PTSD symptoms for those in the waitlist condition) associated are reasonable in this context. Given the significant protections in place for participants as outlined above, the benefits clearly outweigh the risks.

5.6 Alternatives: Alternative mental health treatment is available at the Resilience and Restoration Center at Carl R. Darnell Army Medical Center including various forms of psychotherapy, and drug treatments. There are two medications, sertraline (brand name Zoloft) and paroxetine (brand name Paxil) that have FDA indication for PTSD, although the efficacy of these medications in exclusively military samples is questionable or not yet demonstrated.

6.0 Data Analysis:

General considerations. Prior to statistical analyses, the data will be inspected to determine the advisability of scale transformation to normalize distributions or reduce variance heterogeneity (e.g., log) and to identify missing data, outliers, or other unusual features that may be influential. The primary analysis method for comparison of means on continuous outcome measures is the

general linear mixed effects regression model (SAS MIXED), including baseline as a covariate when available and repeated measures when appropriate. The mixed effects procedure permits modeling of variance heterogeneity while providing powerful options for specific contrasts to test hypotheses of both between and within group differences. Preliminary analyses are performed to compare treatment groups on descriptive and clinical characteristics at baseline to ensure that randomization has succeeded, and ancillary variables that are not the focus of hypotheses but relate to outcomes are candidates for inclusion as additional covariates in supplementary analyses. When covariates differentiate treatment groups, it is necessary to include them to remove effects of confounding. To address concerns about excessive Type I error rates, the principal analyses are restricted to stated primary hypotheses and outcome variables. More exploratory analyses will be clearly identified as such. All tests will be two-tailed at alpha=.05.

Dropout: If dropout is non-trivial, preliminary analyses will compare baseline characteristics of subjects available for analysis at each data point with those who are missing to evaluate possible sampling biases. Rates of attrition in the treatment groups will be depicted using Kaplan-Meier curves and simple comparisons performed using the log-rank test. We will compare subjects included in the analyses at any point with those who have dropped out on baseline variables and, when available, clinical status or trajectory of change. There is no perfect statistical solution to missing data, but if there is evidence that attrition might introduce bias into the analyses, we will consider supplementing the main analyses with propensity-weighting analyses. The propensity-weighting method is based on the assumption that subjects remaining in a study share to differing degrees characteristics with those who drop out, and these characteristics or predictor variables can be used to weight scores to assess possibly biasing effects of drop-out (Hirano, Imbens, & Ridder 2003). Lunceford and Davidian (2004) have recently done a rigorous statistical comparison of propensity weighting with the stratification method originally proposed by Rosenbaum and Rubin (1983, 1984) and unequivocally recommend the former.

Hypothesis Testing:

Research Question 1 is to evaluate the efficacy of PE-M relative to MC at Week 4 in the reduction of PTSD severity (primary measure = PSS-I severity score) and associated psychopathology (secondary measures = PTSD diagnosis and severity scores on measures of depression, general anxiety, anger, and PTSD-related cognitions). The primary analysis of severity will be done using a general linear mixed effects analysis of covariance model comparing the PE-M and MC groups on the PSS-I severity score at post treatment (Week 4) with repeated measures two weeks after the end of treatment, controlling for baseline severity with planned contrasts to evaluate within-group change in both conditions. Between-group hypotheses will be tested with t-tests at each assessment, and supplemental analyses will incorporate weighting or covariates as determined by preliminary analyses. Analysis of within-group changes will be determined using appropriate within-subject t-tests. Supplementary analyses will evaluate possible biases associated with dropout and incorporate any such covariates as appropriate. Analyses of secondary variables will be performed using the same analysis models for outcomes measured on continuous scales. Analysis of dichotomous outcomes, such as PTSD diagnosis at Week 4, will be done using the chi-square test. Analyses of dichotomous outcomes that include covariates or consider outcomes as repeated measures over time will be done using generalized linear mixed effects regression models (SAS GLIMMIX), specifying binomial error and a logit link function. This analysis model parallels the analysis design for continuous measures). Analyses of secondary outcomes will use the same methods.

Research Question 2 is to evaluate the non-inferiority of PE-M compared to PE-S two weeks and 12 weeks after completion of treatment, utilizing the same outcome measures described for research question 1. This analysis will be a mixed effects general linear model, with repeated measures two weeks after the end of each treatment and at follow-up, with baseline severity again included as a covariate. Between-group hypotheses will be tested with t-tests at each assessment, and supplemental analyses will incorporate weighting or covariates as determined by preliminary analyses. Analysis of within-group changes will be determined using appropriate within-subject t-tests. Supplementary analyses will evaluate possible biases associated with dropout and incorporate any such covariates as appropriate. Analyses of secondary variables will be performed using the same analysis models for outcomes measured on continuous scales. Analysis of dichotomous outcomes, such as PTSD diagnosis at Week 4, will be done using the chi-square test. Analyses of dichotomous outcomes that include covariates or consider outcomes as repeated measures over time will be done using generalized linear mixed effects regression models (SAS GLIMMIX), specifying binomial error and a logit link function. This analysis model parallels the analysis design for continuous measures). Analyses of secondary outcomes will use the same methods.

Research Question 3 is to evaluate the efficacy of PE-S relative to PCT in the reduction of PTSD severity (primary measure = PSS-I severity score) and associated psychopathology (secondary measures = PTSD diagnosis and severity scores on measures of depression, general anxiety, anger, and PTSD-related cognitions). The primary analysis of severity will be done using a general linear mixed effects analysis of covariance model comparing the PE-S and PCT groups on the PSS-I severity score at post treatment (Week 8) with repeated measures two weeks after the end of treatment and at follow-up points, controlling for baseline severity with planned contrasts to evaluate within-group change in both conditions. Between-group hypotheses will be tested with t-tests at each assessment, and supplemental analyses will incorporate weighting or covariates as determined by preliminary analyses. Analysis of within-group changes will be determined using appropriate within-subject t-tests. Supplementary analyses will evaluate possible biases associated with dropout and incorporate any such covariates as appropriate. Analyses of secondary variables will be performed using the same analysis models for outcomes measured on continuous scales. Analysis of dichotomous outcomes, such as PTSD diagnosis at Week 4, will be done using the chi-square test. Analyses of dichotomous outcomes that include covariates or consider outcomes as repeated measures over time will be done using generalized linear mixed effects regression models (SAS GLIMMIX), specifying binomial error and a logit link function. This analysis model parallels the analysis design for continuous measures). Analyses of secondary outcomes will use the same methods

Data analysis will be performed by the data analysis core staff of the STRONG STAR consortium.

7.0 Sample Size Estimation / Power Analysis. Power analyses were conducted using NCSS-PASS 2005 software (Hintze, J. 2004. NCSS and PASS. Number Cruncher Statistical Systems. Kaysville, UT, www.ncss.com). For a Non-Inferiority Test, N = 110 per arm yields power = 0.9 if the equivalence margin (i.e., the smallest standardized mean difference that still results in a conclusion of non-inferiority) is d = -0.4. For a two-sided Equivalence Test, power with d = 0.4 is 0.81. Ns of 110 in the active treatment arms and 30 in a minimal-contact group yield power = 0.88 to detect a standardized mean difference of 0.65 between active treatment and a minimal-contact control treatment. Planned comparisons will be conducted for (1) Spaced PE vs. Massed PE, (2) Spaced PE vs. PCT, and (3) Massed PE vs. minimal-contact control condition. The primary hypothesis tests are essentially discrete ANCOVA models at particular assessment

points rather than profile analyses over time. On the PSS-I, the primary outcome measure for this study, the standard deviation pooled across treatment and waitlist conditions before and after treatment or wait list is approximately 9 points. Thus, a difference of .50 SD is 4.5 points on the instrument. Given typical post-treatment scores for PE, a mean difference of less than 5 points between active treatments is considered clinically non-significant.

8.0 Duration of Study: estimated to be 7 years

9.0 Funding: The funding for this project is through a grant from the U. S. Army Medical Research and Materiel Command Congressionally Directed Medical Research Program (CDMRP) Psychological Health (PH) & Traumatic Brain Injury (TBI) Program with a grant to the University of Texas Health Sciences at San Antonio (UTHSCSA). Funding for this research will be accomplished through a Cooperative Research and Development Agreement (CRADA) between UTHSCSA and the U. S. Army represented by the Clinical Investigation Regulatory Office (CIRO).

10.0 Staff Monitor (for resident and fellow projects): not applicable.

11.0 Bibliography:

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4,* 561-571.

Cahill, S. P., Rothbaum, B. O., Resick, P.A., & Folette, V. M. (in press). Cognitive behavior therapy in adults with chronic PTSD. In *Effective treatments for PTSD: Practice guidelines from the International Society for Traumatic Stress Studies (2nd Ed.).* New York: Guilford Press.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. B. (1995). *Structured Clinical Interview for DSM-IV Axis I Disorders- Patient Edition (SCID-I/P, Version 2).* New York: Biometrics Research Department, New York State Psychiatric Institute.

Foa, E. B., Dancu, C. V., Hembree, E. A., Jaycox, L. H., Meadows, E. A., & Street, G. P. (1999a). A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. *Journal of Consulting and Clinical Psychology, 67,* 194-200.

Foa, E. B., Ehlers, A., Clark, D. M., Tolin, D. F., & Orsillo, S. M. (1999b). The posttraumatic cognitions inventory (PTCI): Development and validation. *Psychological Assessment, 11*, 303-314.

Foa, E. B., Hembree, E. A., & Rothbaum, B. O. (2007). *Prolonged Exposure Therapy for PTSD: Emotional Processing of Traumatic Experiences – Therapist Guide.* Oxford University Press.

Foa, E. B., Riggs, D. S., Massie, E. D., Yarczower, M. (1995). The impact of fear activation and anger on the efficacy of exposure treatment for PTSD. Behavior Therapy, 26, 487-499.

Foa, E. B., Riggs, D. S., Dancu, C. V., & Rothbaum, B. O. (1993). Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. *Journal of Traumatic Stress, 6,* 459-473.

Foa E.B., Rothbaum B.O., Riggs D., & Murdock T. (1991). Treatment of post-traumatic stress disorder in rape victims: A comparison between cognitive-behavioral procedures and counseling. *Journal of Consulting and Clinical Psychology, 59,* 715-723.

Guy, W. (1976). *ECDEU Assessment Manual for Psychopharmacology*. Washington, DC: Department of Health, Education and Welfare. Publication # ADM 76-338:217-222.

Hamilton, M. (1960). A rating scale for depression. *Journal of Neurological and Neurosurgical Psychiatry, 23,* 56-62.

Hembree, E.A., Foa, E.B., Dorfan, N.M., & Street, G.P. (2003) Do Patients Drop Out Prematurely from Exposure Therapy for PTSD? Journal of Traumatic Stress, 16(6):555-562

Hintze J. NCSS and PASS. (2004) Number Cruncher Statistical Systems. Kaysville, UT. www.ncss.com.

Hirano K, Imbens GW, Ridder G Efficient estimation of average treatment effects using the estimated propensity score ECONOMETRICA 71 (4): 1161-1189 JUL 2003

Hoge, C. W., Castro, C. A., Messer, S. C., McGurk, D., Cotting, D. L., & Koffman, R. L. (2004). Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *The New England Journal of Medicine, 351,* 13-220.

Institute of Medicine (2007). *Treatment of Posttraumatic Stress Disorder: An Assessment of the Evidence. Committee on Treatment of Posttraumatic Stress Disorder.* Institute of Medicine of the National Academies. Washington, DC: The National Academies Press.

Lunceford JK, Davidian M Stratification and weighting via the propensity score in estimation of causal treatment effects: a comparative study, STATISTICS IN MEDICINE 23 (19): 2937-2960 OCT 15 2004.

Resick, P. A., Nishith, P., Weaver, T. L., Astin, M. C., & Feurer, C. A. (2002). A comparison of cognitive-processing therapy with prolonged exposure and a waiting condition for the treatment of chronic posttraumatic stress disorder in female rape victims. *Journal of Consulting and Clinical Psychology, 70,* 867-879.

Rosenbaum, P.R. and D.B. Rubin, The central role of the propensity score in observational studies for causal effects. Biometrika, 1983. 70: p. 41-55.

Rosenbaum, P.R. and D.B. Rubin, Reducing bias in observational studies using sub-classification on the propensity score. Journal of the American Statistical Association, 1984. 79: p. 516-524.

Rothbaum, B. O., Cahill, S. P., Foa, E. B., Davidson, J. R. T., Compton, J., Connor, K., Astin, M., & Hahn, C. (2006). Augmentation of sertraline with prolonged exposure in the treatment of PTSD. *Journal of Traumatic Stress, 19,* 625-638.

Rothbaum, B. O., Atsin, Millie, & Marsteller, F. (2005). Prolonged exposure versus eye movement desensitization and reprocessing (EMDR) for PTSD rape victims. *Journal of Traumatic Stress, 18,* 607-616.

Schnurr, P. P., Friedman, M. J., Engel, C. C., Foa, E. B., Shea, M. T., Chow, B. K., Resick, P. A., Thurston, V., Orsillo, S. M., Haug, R., Turner, C., & Bernardy, N. (2007). Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. *JAMA, 297,* 820-830.

Spielberger, C.D. (1988). Anger expression scale. In M. Hersen & A.S. Bellack (Eds.), *Dictionary of Behavioral Assessment Techniques* (pp. 446-448). New York: Pergamon Press.

Spielberger, C. D., Gorsuch, R. L., & Lushene, R. E. (1970). *Manual for the State-Trait Anxiety Inventory (Self-Evaluation Questionnaire).* Palo Alto, CA: Consulting Psychologists Press.

Weathers, F. W., Litz, B. T., Herman, D. S., Huska, J. A., & Keane, T. M. (1993, October). *The PTSD Checklist: Reliability, validity, and diagnostic utility*. Paper presented at the Annual Meeting of the International Society for Traumatic Stress Studies, San Antonio, TX.

11.1 Measurement Bibliography:

Adler, A. B., Litz, B. T., Castro, C. A., Suvak, M., Thomas, J. L. Burrell, L., McGurk, D., Wright, K.W., & Bliese, P.B. (2008). A group randomized trial of critical incident stress debriefing provided to U.S. peacekeepers. *Journal of Traumatic Stress, 21*, 253-263.

Bastien, C. H., Vallieres, A., Morin, C.M., (2001) Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine, 2*(4), 297-307.

Bliese, P.B. (2008). A group randomized trial of critical incident stress debriefing provided to U.S. peacekeepers. *Journal of Traumatic Stress, 21*, 253-263.

Babor, T. F., Higgins-Biddle, J. C., Saunders, J. B. & Monteiro, M. G. (2001). *The Alcohol Use Disorders Identification Test: Guidelines for Use in Primary Care*, 2nd Edition. Geneva, Switzerland: World Health Organization.

Beck, A. T., Brown, G. K. & Steer, R. A. (1997). Psychometric characteristics of the scale for suicide ideation with psychiatric outpatients. *Behaviour Research and Therapy, 35*, 1039-1046.

Beck, A. T., Epstein, N., Brown, G. & Steer, R. A. (1988). An inventory for measuring clinical anxiety: Psychometric properties. *Journal of Consulting and Clinical Psychology, 56*, 893-897.

Beck, A. T., Kovacs, M. & Weissman, A. (1979). Assessment of suicidal intention: The scale for suicide ideation. *Journal of Consulting and Clinical Psychology, 47*, 343-352.

Beck, A. T., Ward, C. H., Mendelson, M., Mock, J. & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry, 4*, 564-571.

Bernat, J. A., Ronfeldt, H. M., Calhoun, K. S., & Arias, I. (1998). Prevalence of traumatic events and peritraumatic predictors of posttraumatic stress symptoms in a nonclinical sample of college students. Journal of Traumatic Stress, 11(4), 645-664.

Blanchard, E. B., Jones-Alexander, J., Buckley, T. C. & Forneris, C. A. (1996). Psychometric properties of the PTSD Checklist (PCL). *Behaviour Research and Therapy, 34*(8)*,* 669-673.

Borkovec, T. D & Nau, S. D. (1972). Credibility of analogue therapy rationales. *Journal of Behaviour Therapy and Experimental Psychiatry, 3*, 257-260l

Brewin, C. R., Andrews, B., & Valentine, J. D. (2000). Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. Journal of Consulting and Clinical Psychology, 68, 748–766.

Buysse, D. J., Reynolds III, C. F., Monk, T. H., Berman, S. R., & Kupfer, D.J. (1989). The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatric Research, 28*(2), 193-213.

Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, Amtmann D, Bode R, Buysse D, Choi S, Cook K, DeVeillis R, DeWalt D, Fries JF, Gershon R, Hahn EA, Lai JS, Pilkonis P, Revicki D, Rose M,

Weinfurt K, Hays R. (2010). The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. J Clin Epidemiol. 63(11), 1179-84.

Cernich, A. N., Brennana, D. M., Barker, L. M., & Bleiberg, J. (2007). Sources of error in computerized neuropsychological assessment. Archives of Clinical Neuropsychology, 22S, S39-S48.

Chervin, R.D., Aldrich, M.S., Pickett, R., & Guilleminault, C. (1997). Comparison of the results of the Epworth Sleepiness Scale and the Multiple Sleep Latency Test. *Journal of Psychosomatic Research, 42*(2),145-155.

Cohen, S. & Hoberman, H. (1983). Positive events and social supports as buffers of life change stress. *Journal of Applied Social Psychology, 58,* 304–309.

Cohen, S., Mermelstein, R., Kamarck, T., & Hoberman, H. M. (1985). Measuring the functional components of social support. In I. G. Sarason, & B. R. Sarason (Eds.), *Social Support: Theory, Research, and Applications*, (pp. 73-94). New York: Springer-Verlag.

Chung, F., Yegneswaran, B., Liao, P., Chung, S. A., Vairavanathan, S., Islam, S., Khajehdehi, A., & Shapiro, C. M. (2008). STOP questionnaire: A tool to screen patients for obstructive sleep apnea. *Anesthesiology, 108*, 812-921.

Davis, J. L., Wright, D., & Borntrager, C. (2001). *The Trauma-Related Nightmare Survey.* Tulsa, OK: University of Tulsa.

Davis, J. L., & Wright, D. C. (2007). Randomized clinical trial for treatment of chronic nightmares in trauma-exposed adults. *Journal of Traumatic Stress, 20*, 123-133.

Devilly, G. J., & Borkovec, T. D. (2000). Psychometric properties of the credibility/expectancy questionnaire. *Journal of Behavior Therapy and Experimental Psychiatry, 31*, 73-86.

Dobie, D. J., Kivlahan, D. R., Maynard, C., Bush, K. R., Davis, T. M., & Bradley, K. A. (2004). Posttraumatic stress disorder in female veterans: Association with self-reported health problems and functional impairment. *Archives of Internal Medicine, 164*, 394-400.

Dohrenwend, B. S., Askenasy, A. R., Krasnoff, L. & Dohrenwend, B. P. (1978). Exemplification of a method for scaling life events: The PERI Life Events Scale. *Journal of Health and Social Behavior, 19*, 205-229.

Foa, E. B., Cashman, L. J. & Perry, K. (1997). The validation of a self-report measure of posttraumatic stress disorder: The Posttraumatic Diagnostic Scale. *Psychological Assessment, 9*, 445-451.

Foa, E. B., Elhers, A., Clark, D. M., Tolin, D. F. & Orsillo, S. M. (1999). The Posttraumatic Cognitions Inventory (PCTI). *Psychological Assessments, 11*, 303-314.

Foa, E. B., Riggs, D. S., Dancu, C. V. & Rothbaum, B. O. (1993). Reliability and validity of a brief instrument for assessing post-traumatic stress disorder. Journal of Traumatic Stress, 6, 459-473.

Foa, E. B. & Tolin, D. F. (2000). Comparison of the PTSD Symptom Scale-Interview version and the Clinician-Administered PTSD Scale. Journal of Traumatic Stress, 13, 181-191.

Friedl, K. E., Grate, S. J., Proctor, S. P., Ness, J. W., Lukey, B. J., & Kane, R. L. (2007). Army research needs for automated neuropsychological tests: Monitoring soldier health and performance status. *Archives of Clinical Neuropsychology, 22S*, S7-S14.

Garnefski, N. & Kraaij, V. (2006). Cognitive emotion regulation questionnaire – development of a short

18-item version (CERQ-short). *Personality and Individual Differences, 41*, 1045-1053.

Garnefski, N., Kraaij, V. & Spinhoven, P. (2001). Negative life events, cognitive emotion regulation and emotional problems. *Personality and Individual Differences, 30*, 1311-1327.

Gray, M. J., Litz, B. T., Hsu, J. L., Lombardo, T. W. (2004). Psychometric properties of the Life Events Checklist. *Assessment, 11*, 330-341.

Grieger, T. A., Cozza, S. J., Ursano, R. J., Hoge, C., Martinez, P. E., Engel, C. C. & Wain, H. J. (2006). Posttraumatic stress disorder and depression in battle-injured Soldiers, *American Journal of Psychiatry, 163*(10), 1777-1783.

Hoge, C. W., Castro, C. A., Messer, S. C., McGurk, D., Cotting, D. I., & Koffman, R. L. (2004). Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *New England Journal of Medicine, 351*(1), 13-22.

Hoge, C. W., McGurk, D., Thomas, J. L., Cox, A. L., Engel, C. CC. & Castro, C. A. (2008). Mild traumatic brain injury in U. S. Soldiers returning from Iraq. *New England Journal of Medicine, 358*(5), 453-463.

Jeffery, D. D., Tzeng, J. P., Keefe, F.J., Porter, L. S., Hahn, E. A., Flynn, K. E., Reeve, B. B., & Weinfurt, K. P. (2009). Initial report of the cancer Patient-Reported Outcomes Measurement Information System (PROMIS) sexual function committee: Review of sexual function measures and domains used in oncology. Cancer, 115(6), 1142-53.

Johns, M.W. (1994). Sleepiness in different situations measured by the Epworth Sleepiness Scale. *Sleep.17*(8),703-710.

Johnson, D. C., Polusny, M. A., Erbes, C. R., King, D., King, L., Litz, B. T., Schnurr, P. P., Friedman, M., Pietrzak, R. H. & Southwick, S. M. (2008). Resilience and response to stress: Development and initial validation of the Response to Stressful Experiences Scale (RSES). Unpublished manuscript, Naval Health Research Center, San Diego, CA.

Kane, R. L., Roebuck-Spencer, T., Short, P., Kabat, M., & Wilken, J. (2007). Identifying and monitoring cognitive deficits in clinical populations using Automated Neuropsychological Assessment Metrics (ANAM) tests. *Archives of Clinical Neuropsychology, 22S*, S115-S126.

Kazis LE, Lee A, Spiro III. A, Rogers W, Ren XS, Miller DR, Selim A, Hamed A, and Haffer SC. (2004b). Measurement comparisons of the Medical Outcomes Study and the Veterans SF-36® Health Survey. *Health Care Financing Review, 25*(4), 43-58.

Kazis LE, Miller DR, Clark JA, Skinner KM, Lee A, Ren XS, Spiro III. A, Rogers WH, Ware Jr. JE. (2004a). Improving the response choices on the veterans SF-36 health survey role functioning scales: Results from the Veterans Health Study. *Journal of Ambulatory Care Manage, 27*(3), 263-280.

Kazis LE, Miller DR, Skinner KM, Lee A, Ren XS, Clark JA, Rogers WH, Spiro III A, Selim A, Linzer M, Payne SM, Mansell D, Fincke BG. (2006b). Applications of methodologies of the Veterans Health Study in the VA Health Care System: Conclusions and summary. *J Ambulatory Care Management, 29*(2), 182-188.

Kazis LE, Nethercot VA, Ren XS, Lee A, Selim A Miller DR. (2006c). Medication effectiveness studies in the United States Veterans Administration Health Care System: A model for large integrated delivery systems. *Drug Development Research, 67*, 217-226.

Kazis LE, Selim A, Rogers W, Ren XS, Lee A and Miller DR. (2006a). Dissemination of methods and results from the Veterans Health Study: Final comments and implications for future monitoring

strategies within and outside the Veterans Health Care System. *Journal of Ambulatory Care Management, 29(*4), 310-319.

Keen, S. M., Kutter, C. J., Niles, B. L. & Krinsley, K. E. (2008). Psychometric properties of PTSD CheckList in sample of male Veterans. *Journal of Rehabilitation Research & Development, 45*(3), 465-474.

Keen, S. M., Kutter, C. J., Niles, B. L. & Krinsley, K. E. (2008). Psychometric properties of PTSD CheckList in sample of male Veterans. *Journal of Rehabilitation Research & Development, 45*(3), 465-474.

Kilpatrick, D. G., Resnick, H. S., Freedy, J. R., Pelcovitz, D., Resick, P. A., Roth, S., & van der Kolk, B. (1998). The posttraumatic stress disorder field trial: Evaluation of the PTSD construct: Criteria A through E. In T.A. Widiger, A. J. Frances, H.A. Pincus, M.B. First, R. Ross, & W. Davis (Eds.) *DSM-IV Sourcebook* (vol. IV). Washington, DC: American Psychiatric Press.

King, D. W., King, L. A. Foy, D. W. Keane, T. M. & Fairbank, J. A. (1999). Posttraumatic stress disorder in a national sample of female and male Vietnam veterans: Risk factors, war-zone stressors, and resilience-recovery variables. *Journal of Abnormal Psychology, 108*, 164-170.

King, D. W., King, L. A., Foy, D. W., & Gudanowski, D. M. (1996). Prewar factors in combat-related posttraumatic stress disorder: Structural equation modeling with a national sample of female and male Vietnam veterans. *Jouranl of Consulting and Clinical Psychology, 64,* 520-531.

King, L. A., King, D. W., Fairbank, J. A., Keane, T. M., & Adams, G. (1998). Resilience-recovery factors in posttraumatic stress disorder among female and male Vietnam veterans: Hardiness, postwar social support, and additional life events. *Journal of Personality and Social Psychology, 74,* 420-434.

King, L. A., King, D. W., Vogt, D. S., Knight, J. & Samper, R. E. (2006). Deployment risk and resilience inventory: A collection of measures for studying deployment-related experiences of military personnel and veterans. *Military Psychology, 18*, 89-120.

Kroenke, K., Spitzer, R. L., & Williams, J. B. (2002). The PHQ-15: Validity of a new measure for evaluating the severity of somatic symptoms. *Psychosomatic medicine*, 64, 258-266.

Kubany, E. S., Haynes, S. N., Abueg, F. R., Manke, F. P., Brennan, J.M., Stahura, C. (1996). Development and validation of the Trauma-Related Guilt Inventory (TRGI). *Psychological Assessments, 8*, 423-444.

Lipkus, I. M., Dalbert, C., & Siegler, I. C. (1996). The importance of distinguishing the belief in a just world for self and others: Implications for psychological well being. *Personality and Social Psychology, 22*(7), 666-677.

Litz, B. T. & Gray, M. J. (2004). *Early intervention for trauma in adults: A framework for first aid and secondary prevention*. In B. Litz (Ed.), Early Intervention for Trauma and Traumatic Loss (pp. 87-111). New York: Guilford Press.

Litz, B. T. (2007). Research on the impact of military trauma: Current status and future directions, *Military Psychology, 19*, 217-238

Litz, B. T., Gray, M. J., Bryant, R., & Adler, A. B. (2002). Early intervention for trauma: Current status and future directions. *Clinical Psychology: Science and Practice, 9*, 112-134.

Litz, B. T., Miller, M., Ruef, A., and McTeague, L. (2002). Psychological assessment of adults exposed to trauma. In M. Antony, & D. Barlow (Eds.). *Handbook of assessment and treatment planning for*

psychological disorders (pp. 215-258). New York: Guilford Publications.

McCarroll, J. E., Ursano, R. J., Liu, X., Thayer, L. E., Newby, J. H., Norwood, A. E. & Fullerton, C.S. (2000). Deployment and the probability of spousal aggression by U.S. Army soldiers. *Military Medicine, 165*, 41-44.

Milliken, C. S., Auchterlonie, J. L. & Hoge, C. W. (2007). Longitudinal assessment of mental health problems among active reserve component soldiers returning from the Iraq War. *Journal of the American Medical Association, 298*, 2141-2148.

Morin, C.M. (1993). Insomnia: Psychological Assessment and Management. New York, NY: The Guilford Press.

Nash, W. (2007). Combat/operational stress adaptations and injuries. In C. Figley & W. Nash (Eds.), *Combat Stress Injury: Theory, Research, and Management* (pp. 33-63). New York: Routledge.

Ozer, E. J., Best, S. R., Lipsey, T. L., Weiss, D. S. (2003). Predictors of posttraumatic stress disorder and symptoms in adults: A meta-analysis. *Psychological Bulletin, 129(1)*, 52-73.

Podsakoff, P. M. & MacKenzie, S. B. (1994). An examination of the psychometric properties and nomological validity of some revised and reduced substitutes for leadership scales. Journal of *Applied Psychology, 79*, 702-713.

Reeves, D. L., Winter, K. P., Bleiberg, J., & Kane, R. L. (2007). ANAM® genogram: Historical perspectives, description, and current endeavors. *Archives of Clinical Neuropsychology, 22S*, S15-S37.

Resick, P.A., Falsetti, S.A., Resnick, H.S., & Kilpatrick, D.G. (1991). *The Modified PTSD Symptom Scale – Self-Report*. St. Louis, MO: University of Missouri & Charleston, SC: National Crime Victims Research and Treatment Center, Medical University of South Carolina.

Resick, P. A. Jordan, C. G., Girelli, S. A., & Hutter, C. K. (1988). A comparative outcome study of behavioral group therapy for sexual assault victims. *Behavior Therapy, 19*, 385-401.

Resick, P. A., Iverson, K. M., & Artz, C. E. (2009). Participant reactions to a pretreatment research assessment during a treatment outcome study for PTSD, Journal of Traumatic Stress, 22(4), 316-319.

Rizvi, S. L., Kaysen, D., Gutner, C. A., Griffen, M. G., Resick, P. A. (2008). Beyond fear: The role of peritraumatic responses in posttraumatic stress and depressive symptoms among female crime victims. *Journal of Interpersonal Violence, 23*, 853-868.

Roebuck-Spencer, T., Sun, W., Cernich, A. N., Farmer, K., & Bleiberg, J. (2007). Assessing change with the Automated Neuropsychological Assessment Metrics (ANAM): Issues and challenges. *Archives of Clinical Neuropsychology, 22S*, S79-S87.

Saunders, J. B., Aasland, O. G., Babor, T. F., De La Fuente, J. R. & Grant, M. (1993). Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction, 88*, 791-804.

Schwab, K. A., Baker, G., Ivins, B., Sluss-Tiller, M., Lux, W., & Warden, D. (2006). The Brief Traumatic Brain Injury Screen (BTBIS): Investigating the validity of a self-report instrument for detecting traumatic brain injury (TBI) in troops returning from deployment in Afghanistan and Iraq. [Abstract]. Neurology, 66(5)(Supp. 2), A235.

Schwab, K. A., Ivins, B., Cramer, G., Johnson, W., Sluss-Tiller, M., Kiley, K., Lux, W. & Warden, D.

(2006). Screening for traumatic brain injury in troops returning from deployment in Afghanistan and Iraq: Initial investigation of the usefulness of a short screening tool for traumatic brain injury. *Journal of Head Trauma Rehabilitation, 22*(6), 377-389.

Seel, R. T., Wright, G., Wallace, T., Newman, S. & Dennis, L. (2007). The utility of the FIM+FAM for assessing traumatic brain injury day program outcomes. *Journal of Head Trauma Rehabilitation, 22*, 267-277.

Sexual Function and Satisfaction Measures User Manual. Assessment Center website, www.assessmentcenter.net/documents/Sexual%20Function%20Manual.pdf. Accessed March 8, 2013.

Sheehan, D.V., Lecrubier, Y., Harnett-Sheehan, K., Amorim, P., Janavs, J.,Weiller, E., Hergueta, T., Baker, R., Dunbar, G., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IVand ICD-10. J. Clin. Psychiatry, 59 (suppl 20), 22–33.

Spielberger, C. D. (1988). *State-Trait Anger Expression Inventory: Research Edition, Professional Manual*. Odessa, FL: Psychological Assessment Resources, Inc.

Spitzer, R. L., Kroenke, K., & Williams, J. B. W. (1999). Validation and utility of a self-report version of the PRIME-MD: The PHQ primary care study. *Journal of the American Medical Association, 282*, 1737-1744.

Straus, M. A. (1979). Measuring intrafamility conflict and violence: The Conflict Tactics (CT) Scales. *Journal of Marriage and the Family, 41*, 75-88.

Straus, M. A. & Douglas, E. M. (2004). A short form of the revised conflict tactics scales, an dtypologies for severity and mutuality. *Violence and Victims, 19*(5), 507-520.

Straus, M. A., Hamby, S. L., Boney-McCoy, Sugarman, D. B. (1996). The Revised Conflict Tactics Scales (CTS2): Development and preliminary psychometric data. Journal of Family Issues, 17(3), 283-316.

Taft, C.T., Street, A.E., Marshall, A.D., Dowdall, D.J., & Riggs, D.S. (2007). Posttraumatic stress disorder, anger, and partner abuse among Vietnam combat veterans. *Journal of Family Psychology, 21,* 270-277.

Vaitkus, M. A. (1994). *Unit Manning System: Human dimensions filed evaluation of the COHORT company replacement model* (Walter Reed Army Institute of Research Tech. Rep. No. 94-0017). Fort Detrick, MD: U.S. Army Medical Research and Material Command. (DTIC No. AD-A285 p42).

Vanderploeg, R. D., Collins, R. C., Sigford, B., Date, E., Schwab, K., Warden, D. & the Defense and Veterans Brain Injury Center, Veterans Health Administration study planning group (2006). Practical and theoretical considerations in designing rehabilitation trials: The DVBIC cognitive-didactic versus functional-experiential treatment study experience. *Journal of Head Trauma Rehabilitation, 21*, 179-193.

Veterans Affairs Office of Performance and Quality & U. S. Army Medical Command Quality Management Directorate. (2004, January). Veterans Affairs / Department of Defense clinical practice guideline for the management of post-traumatic stress. Retrieved May 22, 2009, from the Veterans Affairs Office of Quality Improvement Web site: www.ncptsd.va.gov/ncmain/ncdocs/nc_prod/VAPracticeGuidelines1_2004.pdf.

Vogt, D., Proctor, S. P., King, D. W., King, L. A., & Vasterling, J. J. (2008). Validation of scales from the

Deployment Risk and Resilience Inventory (DRRI) in a sample of Iraq War veterans. *Assessment, 15*(4), 391-403.

Wilken, J. A., Sullivan, C. L., Lewandowski, A., & Kane, R. L. (2007). The use of ANAM to assess the side-effect profiles and efficacy of medication. Archives of Clinical Neuropsychology, 22S, S127-S133.

Weathers, F. W., Litz, B. T., Herman, D. S., Huska, J. A. & Keane, T. M. (1993, October). The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility. Paper presented at the annual meeting of the International Society for Traumatic Stress Studies, San Antonio, TX.

Wolfe, F,, Clauw, D. J., Fitzcharles, M. A., Goldenberg, D. L, Katz, R. S., Mease, P., Russell, A. S., Russell, I. J., Winfield, J. B., & Yunas, M. B. (2010). The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. Arthritis Care and Research, 62(5), 600-610.

Wolfe, F., Clauw, D. J., Fitzcharles, M. A., Goldenberg, D. L., Hauser, W., Katz, R. S., Mease, P., Russell, A. S., Russell, I. J., & Winfield, J. B. (2011). Fibromyalgia criteria and severity scales for clinical and epidemiological studies: A modification of the ACR preliminary diagnostic criteria for fibromyalgia. Journal of Rheumatology, 38(6), 1113-1122.

12.0 Support Services Required (Impact Statement/Letter of Support): none

13.0 Use of Investigation Drugs: not applicable

14.0 Use of Investigational Devices: not applicable

15.0 Appendices:

A – Manuals
- Prolonged Exposure – Spaced (PE-S)
- Prolonged Exposure – Massed (PE-M)
- Present Centered Therapy (PCT)

B – Summary of the Assessments and Timing of Administration
C – STRONG STAR SOP for Suicide Risk Assessment & Management (dated 12-12-13)
D – STRONG STAR Database Policies & Procedures
E – Data Safety Monitoring Plan (DSMP)
F – Recruitment Flyer & Pamphlet & www.STRONGSTAR.org Screen Shots for Recruitment