Study Cover Page

Official Study Title: Treatment of Prolonged Grief Disorder in Combat Veterans
NCT02283333
Protocol date: August 4, 2014

Data Analytic Plan

Baseline data were compared across groups using t-tests for continuous variables and chi-square tests for proportion variables to examine differences in demographic factors, pre-treatment symptom intensity (i.e., grief, depression, and PTSD), and co-variates that are particularly relevant to research with veterans (i.e., social support, time since death, and overall number of sessions completed). No differences in scores or proportionate representation were noted in terms of any demographic, baseline symptoms, or potential covariates. Next, repeated measures analysis of variance were conducted to determine the relative effectiveness of BATE-G vs. CT-G in terms of grief (i.e., ICG-R), depression (i.e., BDI-II) and PTSD (i.e., PCL-5) symptom outcomes. Although no covariation control (i.e., ANCOVA) was employed because covariates did not differ between groups. Baseline scores on primary dependent measures were included in the ANOVA model to test overall effects of time. The intent to treat (ITT) sample served as the primary analytic sample, and missing data were conservatively replaced through total sample mean substitution, which shares variance of missing data across groups and lessens likelihood of finding spuriously significant results. All analyses were repeated with the 'per protocol' sample, here defined as those who completed at least 5 of the 7 sessions specified in each treatment protocol. No differences in statistical significance were noted for any variable between ITT and per protocol samples, and thus the ITT sample data alone are reported.

Protocol

SIGNIFICANCE

Prevalence of Prolonged Grief Disorder (PGD) (also referred to as complicated grief or complicated bereavement) in returning OEF/OIF/OND Veterans appears to equal that of Post-Traumatic Stress Disorder (PTSD). This is not altogether surprising, given that loss is widespread in most combat theatres. For example, Toblin et al. (2012) recently studied a sample of over 1,500 OIF/OEF Veterans and found that 77% "knew someone who was killed." Similarly, Thomas et al. (2010) found that 80% "knew someone who had been seriously injured or killed" and Hoge et al. (2004) reported that 75% lost someone in their immediate unit and 68% personally saw dead or seriously injured Americans. These numbers are also very reflective of the Vietnam Veterans' experience (Currier & Holland, 2012).

Perhaps even more important is the finding that fully 21.3% of the Toblin OIF/OEF sample reported significant difficulty coping with grief over combat death. These authors also noted that this difficulty predicted negative emotional and health outcomes. Specifically, those reporting difficulty coping with grief were 2.4 times as likely to report health problems, and significantly more likely to report both missing work and increased medical care use. Even more striking was the finding that effects of grief were independent of either PTSD or Major Depression (MDD), in that, after controlling for both PTSD and MDD, risk of reporting poor health was doubled among those reporting high grief (Toblin et al., 2012).

These findings are not unique to Veterans of the current conflict. Indeed, Pivar and Field (2004) also found that grief was distinct from depression symptoms in a sample of Vietnam Veterans (Pivar & Field, 2004). This is consistent with a large body of work by Prigerson, Boelen and others in civilian samples (Boelen et al., 2010; Bonanno et al., 2007; Prigerson et al., 2009; Prigerson et al., 2008) demonstrating that PGD is distinct from depression and PTSD, both in terms of its symptoms and treatment response (Boelen et al., 2010; Currier & Holland, 2012; Papa, Neria, & Litz, 2008), and if untreated, represents a significant risk of functional impairment in physical and mental health areas, as well as suicidality.

There may be even greater cause for concern about PGD and its effects in military populations, particularly those experiencing combat, than in civilian populations. This is because the context of loss facing military personnel is significantly different from bereavement typically experienced by civilians who, for example, face losing one's spouse to a prolonged illness. That is, combat Veterans experience not only loss of a person close to them, but experience this loss in the context of severe personal danger and trauma. Thus, combat Veterans experience a 'Dual Burden' (Iverson et al., 2005; Papa, Neria, & Litz, 2008) of (a) loss and (b) trauma exposure, in which the potentially added negative impact of repeated significant life threat combines with loss of close attachment and support. Moreover, loss in the context of combat is often extremely violent, and the especially violent nature of the person's death may further complicate the bereavement process.

Prolonged Grief in Combat Veterans: Relevant Treatment Targets for this Population. Several recent reports outline features of PGD in combat Veterans that are relevant targets for intervention, and may be somewhat unique to this patient

population. Most obvious is the aforementioned 'dual burden' of loss in the context of trauma exposure (Papa, Neria, & Litz, 2008), involving both the impact of significant life threat events and loss of close attachment and support. Given that social support is protective against PTSD (Acierno et al., 2010; Iversen et al., 2005) and that, by definition, PGD is in response to an event that diminishes one's social support network, treatment strategies that enhance social interaction and diminish withdrawal will be key for Veterans with prolonged grief disorder.. Thus, activity-focused behavioral interventions, particularly activities of a social nature, will be key in treatment strategies with this group.

With respect to distinction between PTSD treatment targets and PGD treatment targets in Veterans, Pivar et al. (2004) found the following thematic areas loaded high on measures of PGD and low on measures of PTSD, indicating treatment targets for the former: difficulty accepting the death of a friend, images and thoughts of the death, and distress associated with this, along with feelings of overwhelming loss and separation. Boelen et al. (2007) were successful in targeting these areas through exposure based strategies in which subtle avoidance strategies were identified and countered. For example, withdrawal from activities involving other Veterans, or withdrawal from social activities with mutual friends of lost service personnel are forms of avoidance that might be employed in order to escape from reminders of loss. Exposure to these cues in a repeated and structured format was successful in reducing the impact of these triggers on functioning. Thus, in addition to active, behaviorally based activities that counter social withdrawal, therapeutic exposure strategies will play a key role in treatment of PGD in military personnel.

Existing Treatment Options. Few controlled trials of interventions for PGD and grief related problems exist, and none exist with Veterans, for whom the context of loss (e.g., combat violence) may present additional problems. The VA's National Center for PTSD, in collaboration with the DoD, developed the Iraq War Clinician Guide, 2nd ed. and included a chapter dedicated to traumatic grief and its treatment. Despite these guidelines, in practice, most VA-based treatment for PGD is offered in the form of supportive counseling, or, if evidence based treatments are available, for related comorbid conditions (i.e., MDD). As mentioned, very little research on treatment of PGD in Veterans exists independent of treatments for MDD or PTSD. Unfortunately, as is the case for PTSD and MDD, non-directive supportive therapies appear largely ineffective in the context of severe bereavement reactions (Allumbaugh & Hoyt, 1999), and there is some evidence that these treatments might worsen symptoms (Farberow et al., 1992; Wittouck et al., 2011). Moreover, evidence based treatments for PTSD and MDD, when offered individually, do not seem to effectively diminish PGD symptoms (Bonanno et al., 2007; Neria et al., 2007). By contrast, pilot data by Acierno et al. (2012) suggest that focused integration of key components of these evidence-based treatments might be useful (See Pilot Studies, below).

Given the need for evidenced-based treatments for PGD, Shear and colleagues developed an intervention based upon Interpersonal Psychotherapy for depression (Shear & Frank, 2006; Weissman, Markowitz, & Klerman, 2000) and modified it to incorporate imaginal exposure such as used in Prolonged Exposure for PTSD (Foa, Keane, & Friedman, 2000). This treatment used a dual processing model of coping with loss as proposed by Stroebe and Schut (2007), and was delivered over 16 sessions

targeting personal goals, psychoeducation, resolution of prolonged grief symptoms, imaginal exposure, and future planning (Shear & Frank, 2006; Shear & Mulhare, 2008). Data supported the efficacy of this approach (Shear et al., 2005). However, this intervention also has significant limitations in that it may not be readily accessible to the majority of adults with PGD due to the relatively high costs associated with delivering a 16-session, 4-month protocol. A second intervention consistent with the dual process model of coping was evaluated in a controlled trial by Wagner et al. (2006). This study used the internet to deliver a combination treatment in which exposure based components (e.g., to avoided bereavement cues) were offered along with cognitive reappraisal training and memory integration. Unfortunately, more than half the participants never returned questionnaires, and the constitution of the final sample was in question, leading to some concern regarding the generalizability of the results. Another study by Boelen et al. (2007) similarly described a 12 session cognitive behavioral treatment (6 cognitively oriented sessions plus 6 exposure based sessions) vs. supportive counseling vs. a third group in which the order of cognitive and exposure session was reversed. This controlled trial showed that treatment was mildly effective in reducing symptoms of bereavement, and exposure based therapy components appeared particularly effective with this group of patients. However, Veterans were not included in the study sample, and the length of treatment was again perhaps longer than that which is optimal for dissemination and completion by Veterans. Thus, while some effective intervention components (e.g., exposure) have proven effective with PGD, none of these controlled studies included Veterans with combat related bereavement foci.

Behavioral Activation and Therapeutic Exposure for Prolonged Grief Disorder (BATE-G). Behavioral Activation and Exposure therapies are in widespread use with Veterans, and it makes sense to use these strategies as applied to PGD. In order to assure greater access to effective PGD treatment, Acierno and colleagues (Acierno et al., 2012) designed a componential intervention focusing on the 'active ingredients' of evidence based treatments for disorders with characteristics and symptoms similar to PGD (i.e., PTSD and Depression). This packaged intervention leveraged technology by creating a video component of the treatment and by delivering sessions 2-6 via televideo in order to: (1) maintain intervention standardization through video summary of key treatment components for joint viewing by patients and counselors so that the treatment could be delivered by minimally trained peer counselors, as well as in order to: (2) increase contextual relevance of treatment components while reducing stigma, and logistical and cost barriers associated with obtaining standard office based treatments by using televideo to deliver 5 of the 7 sessions into patients' homes. This treatment was designed to address effects of withdrawal and isolation, and incorporated core components of both Behavioral Activation (BA) and Therapeutic Exposure (TE). Note that BA is hypothesized to reduce depression via formal attempts to increase the frequency of positively reinforcing and/or less enjoyable albeit functional (negatively reinforcing) activities, particularly those of a social nature. This has the effect of decreasing social isolation and inactivity, two commonly noted problematic behaviors in combat Veterans experiencing grief. This shift in balance of activities (and subsequent

reinforcement density) has long been posited to facilitate increased positive mood and cognitions (see Lejuez,et al., 2011 and Lewinsohn, 1973). In combination, exposure is considered therapeutic when extinction/habituation of negative stress responses to environmental cues, memories, and emotions results following repeated presentation of these cues. Exposure also seems to provide a cognitive forum for integration of memories of the lost comrade that may allow for adaptive responses related to guilt and longing. **The goal of BATE-G is to concurrently address avoidance/withdrawal behaviors commonly observed in Veterans of combat, while promoting active and social coping behaviors to reduce symptoms associated with PGD.**

BATE-G is structured as a very behaviorally based, active treatment designed to be delivered via both in person and televideo forums. These aspects may both be appealing to active-duty personnel and Veterans, who frequently forgo traditional mental health treatment. Therefore, BATE-G follows a format that: (1) is highly exportable and affordable to those agencies providing grief services, such as informal Veterans support agencies and non-profits; Veterans Administration sponsored “Vet Centers” staffed by paraprofessionals and peers, (2) maintains standardization and treatment quality through use of video modules available via dvd or internet and developed for simultaneous viewing by counselors and patients, and (3) is implemented in only 7 sessions using a multi-context delivery format (in person sessions and home based televideo sessions) to limit costs and maximize usability of the treatment for both patients and providers. Results of the non-randomized clinical trial were encouraging, with improvements noted on virtually all measures of both mental health and general health self-report ratings. Whereas this treatment demonstrated high feasibility and produced promising effects with respect to symptom outcomes in the open trial pilot, no formalized, randomized controlled trial (RCT) has been conducted to date to evaluate the efficacy of BATE-G among Veterans suffering with PGD.

PRELIMINARY STUDIES

We have recently published BATE-G pilot data from our National Institutes of Health funded R21 project (**R21AG023495**) that supports the proposed treatment (Acierno et al., 2012). This treatment includes a video component as well as an accompanying brochure to reinforce the intervention content. The present proposal will involve specific adaptations of the video portion of the intervention for Veterans, followed by a randomized controlled trial (RCT) to evaluate its effectiveness in reducing PGD. Pilot study participants were 22 women and 4 men (M age = 65.6 years; SD = 10.5) referred by agencies that served bereaved individuals, university hospital nurse supervisors, or self-referred in response to posted brochures. Mean number of days since death upon study enrollment was 180 (SD = 196.1; range = 24-884), indicating the intervention is applicable both to recent and delayed loss reactions. One week following completion of an initial assessment battery by the study interviewer, participants met with a BATE-G study therapist in person for about 75 minutes for the initial session. To demonstrate the exportability of this treatment to counselors of various degrees of training, therapists ranged from BA level community agency counselors to PhD intern candidates. At pre-treatment, 34.6% met full criteria for complicated bereavement / PGD (not considering the 6 month post-death requirement). By post-treatment, only 7.7% met criteria. Figures 1-4 (below) provide graphical illustration of the most relevant outcome data in the form

of pre-post treatment overlaid scatter plots for each continuous dependent measure, illustrated in terms of the number of days post-death, which served as the covariate in all analyses. Note that each participant's pre- and post-treatment scores are joined by a vertical line illustrating change after treatment; note also that virtually every participant improved.

Figure 1: Scatter plot of Complicated Grief Assessment Int. scores

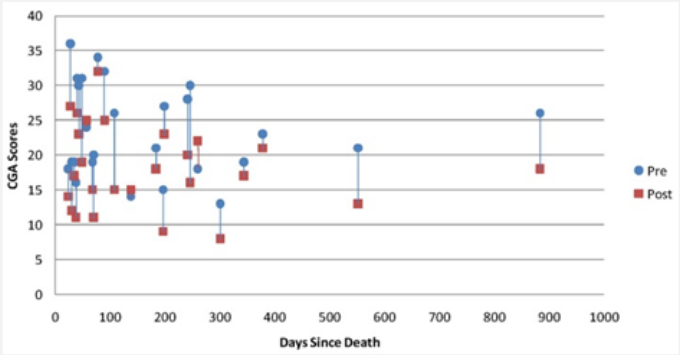


Figure 2 Scatter Plot of Pre-post PTSD symptom count

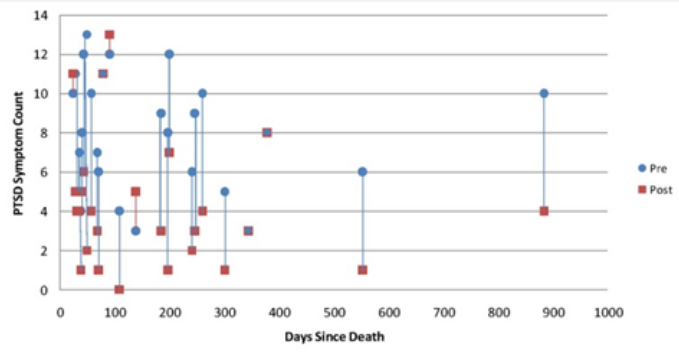


Figure 3: Scatter plot of pre-post MDD symptom count scores

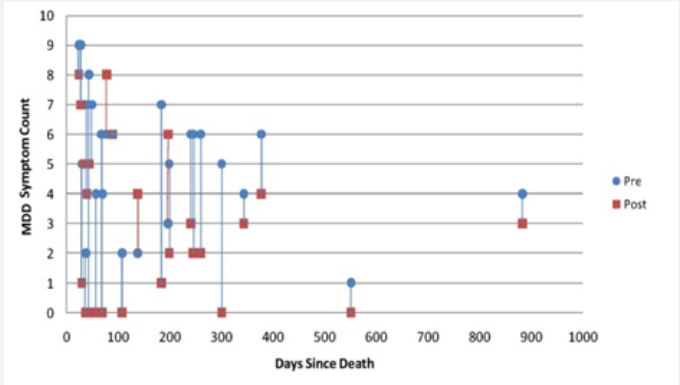
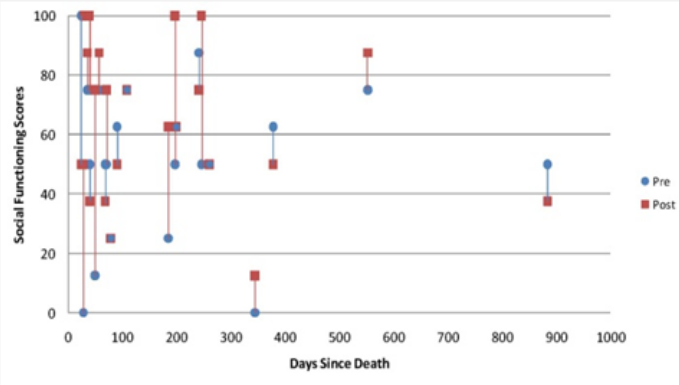


Figure 4: Scatter plot of SF-36 Social Functioning (higher is better)



ANCOVAs revealed that neither the covariate (days since death) nor its interaction with the independent variable was significant. Therefore, focus was turned to the main effect of time (pre-post treatment change). **Complicated Grief (CGA-I)** scores were reduced from a mean of 23.4 (SE = 1.3) to a mean of 18.2 (SE = 1.2) $p < .001$, effect size partial $\eta^2 = .46$; **PTSD** symptom count scores were reduced from 8.0 (SE = 0.6) to 4.3 (SE = 0.7) $p < .001$, $\eta^2 = .41$; **MDD** symptom count scores were reduced from 5.2 (SE = 0.4) to 2.8 (SE = 0.5), $p < .01$, $\eta^2 = .38$. **BDI** scores were reduced from 19.9 (SE = 2.4) to 12.7 (SE = 2.0) $p < .01$, $\eta^2 = .27$; the **SF-36 Social Functioning** scale was significantly improved from 52.7 (SE = 5.6) to 64.7 (SE = 5.4) $p \leq .05$, $\eta^2 = .17$

These data support the feasibility and initial efficacy of BATE-G, a highly portable intervention for PGD designed around the principles of behavioral activation and therapeutic exposure, as well as logistic aspects of the treatment such as patient safety protections for home based treatment and patient use of technology.

RESEARCH DESIGN AND METHODS

We will use a 2 x 4 (treatment by time) randomized controlled trial design to compare the BATE-G treatment for PGD to the VA/DoD recommended treatment for PGD: Cognitive Restructuring and Supportive Grief Counseling (from the *Iraqi War Clinician Guide, 2nd ed.*) *currently the best practices treatment advocated by VA/DoD for Veterans at Veterans Affairs Medical Center (VAMC) facilities with bereavement*. Dependent measures will include assessment of both psychological and health-related functioning at pre- treatment, post-treatment (approx 8 weeks later), and at 3 & 6 months post treatment follow up to demonstrate effectiveness of the treatment. Participants will be *140* active duty Veterans of OIF/OEF/OND or discharged Veterans of OEF/OIF/OND service who meet PGD cutoff criteria, but not criteria for PTSD, and who present for services at the VA Medical Center, Charleston. The componential BATE-G treatment (15-minute video and therapy), offered in a combined in person / televideo package, will be compared to individual Cognitive Restructuring and Supportive Grief Counseling delivered in the same number of sessions & format (a combination of in person and televideo). Participants who complete treatment and follow-up assessments will be *140* OEF/OIF/OND Veterans who meet PGD cutoff criteria outlined below. Assignment to treatment condition will be evenly distributed and randomly determined using a method identical to that of our two ongoing treatment outcome studies for PTSD in Veterans and described below.

Participants and Inclusion/Exclusion Criteria. Participants will be 140 Active Duty Service Personnel / Veterans of OIF, OEF, or OND: Participants will be male or female, age 21 and above, with PGD. Actively psychotic or demented persons, individuals with both suicidal ideation **and** clear intent, or individuals with significant homicidal ideation and or intent, and individuals meeting criteria for substance dependence will be excluded from participation; however, in order to maximize generalization of results, presence of other forms of psychopathology will not be a basis for exclusion. All structured interviews will be audiotaped to calculate inter-rater reliability on a randomly selected 20%. A 4-week medication stabilization will be required.

Recruitment and Retention Procedures. The RHJ VAMC is home to a large number of mental health treatment outcome studies, including several studies on suicide, depression, and anxiety. As such, all RHJ VAMC Mental Health Clinic staff are cross trained in research referral to study staff for all potential participants, and research staff are housed alongside clinic staff. Specifically, treatment outcome studies conducted at the RHJ VAMC typically use the following recruitment plan, which involves multiple potential entry paths to the project. We will post IRB-approved recruitment flyers in prominent locations in VA hospitals and clinics within the Charleston VAMC catchment area, as well as using various wide-range advertising techniques and popular social media websites (i.e., facebook, twitter, craigslist, radio and tv ads, billboards, etc.). Each of the advertisements will provide information about the study and a telephone number that interested subjects can call to receive detailed information about the study. Furthermore, Veterans for whom PGD is suspected by primary care and mental health clinicians may be referred to the study by these clinicians. In the latter scenario, the Veteran will be informed that researchers at the VA are evaluating a treatment for PGD and the Veteran will be asked for permission to release contact information only to study

personnel.

Recruitment Estimates**:** As mentioned, several initial local sites under the PI's authority are proposed for recruitment. The PI of this proposal is the Associate Dean of Research in the College of Nursing at the Medical University of South Carolina, and the coordinating liaison for 3 local satellite VA mental health clinics, and the local Vet Center mental health clinic. Moreover, the VA PTSD Clinic, to which the PI is a staff clinician and senior researcher, also treats active duty service personnel from Joint Base Charleston, and the Charleston Naval Weapons Station. OIF/OEF/OND patient referrals from these clinics in aggregate is between 8 and 15 per week for PTSD and 15-20 per week for MDD. We expect that about 20-25% of these referrals (about 5-6 per week, 20-24 per month) are actually misdiagnosed cases of PGD, as indicated by a 3 month retrospective review of these clinic referral data and intake reports. Therefore, access to Veterans experiencing PGD will be relatively constant and referrals are made directly to the PTSD Clinical Team. Based on past clinical research recruitment data from this study site and the PI's 2 ongoing treatment outcome studies, and adopting a conservative perspective, we predict that approximately 20% of those eligible for participation will do so (20% of the 24 per month), yielding 4-5 participants per month during recruitment phases.

Minority and Female Recruitment: The inclusion of minorities in PTSD research with Veterans is recognized as being of critical importance (Freuh, Brady, & de Arellano, 1998). Based on our previous VA data (Acierno, 2012; Magruder et al., 2005), we will have satisfactory minority representation: 35-50% African American, 8-10% Hispanic, and 4-6% Asian American. We also will include female participants; however, the percentage of female Veterans appearing for services in our catchment area is low relative to males (< 15%).

Randomization Procedures. A random size block randomization schedule will be generated. In Aggregate, participants will be randomly assigned (1:1) to one of the two study conditions. After determining eligibility, enrolled patients will be assigned to treatment groups by the Project Coordinator and research assistant using a web-based computer generated randomization scheme. Specifically, numbered, sealed envelopes containing a sheet of paper with the randomly generated condition assignment by the study statistical coordinator (Knapp) will be created. After consent and assessment, the envelope for each participant will be opened to randomly assign the participant to his/her condition. The randomization results then will be recorded on the master tracking table by the research assistant (independent evaluators are blind), overseen by the Project Coordinator. Randomization will occur at the patient level. Once a patient is randomized and attends the first session, he or she will be entered into the study and included in the intent-to-treat analysis plan. The only members of the research team who will be aware of randomization assignment will be the project therapists, the Research Assistant, and the statistical analyst in charge of randomization.

Participant Payment. All participants will receive $30 for the baseline assessment, $30 for the post-treatment assessment, $35 for the 3-month follow-up assessment, and $45 for the 6-month follow-up assessment for a combined possible total of $140. In some cases where financial difficulty associated with study completion can be mitigated by small increases in study payment, we request to do so, up to $60.

Treatments

Decision Point - Selection of the Comparison Condition: Two comparison treatment conditions were considered for this study: Shear et al.'s 15-20 session protocol for complicated grief vs. the treatment suggested by the VA / DoD in the Iraqi War Clinician Guide, 2nd ed. for VA populations. The former treatment has not been tested with Veterans, is not currently used in VA settings, and, if offered per protocol, represents a significant confound with respect to overall number of treatment sessions compared to the proposed 7 session experimental treatment. The latter treatment has not been empirically evaluated, but is specifically directed toward treatment of Veterans, is actually outlined on the VA's National Center for PTSD website is distributed to VA and DoD clinicians in the Iraq War Clinicians Guide, 2nd ed. and represents what should be, if VA recommendations were followed nationwide, the most commonly offered treatment. Thus, our decision balanced the advantages of (a) comparing our new treatment to a one that may well be effective but will rarely be offered, and if offered, rarely completed in VA settings, due to its complexity and length, vs. (b) comparing our treatment to one that is actually suggested and advised to be offered across VA settings. Setting aside the obvious problem of confound regarding number of sessions, we concluded that comparing our intervention to one that is not offered now, and is unlikely to be offered in the future would provide less direction to VA clinicians than comparing our treatment to what is actually being suggested, and more likely to be implemented in VA clinics the future, unless some equally rapid, easily disseminated alternative were demonstrated to be more effective. However, our decision was finalized by consistent findings that the modal number of mental health treatment sessions received by Veterans with mental health diagnoses was **one** (Cully et al., 2008; see also Gibbons et al., 2011). Thus, this treatment, albeit brief, is 7 times longer than the modal number of treatments typically received by Veterans. As such, we chose Cognitive Restructuring and Supportive Grief Counseling intervention, as suggested and outlined by the VA/DoD Iraq War Clinician Guide, 2nd edition, is far more representative of the type of treatment that might ever be used in the VA and by Veterans.

Decision Point - Use of Televideo delivery of treatment sessions: We understand that, while preserving the 'typical' treatment content we are adding an innovation to the grief counseling approach suggested by the VA/DoD Clinician Guide insofar as the Cognitive Restructuring and Supportive Grief Counseling is here being delivered via televideo for sessions 2, 3, 4, 5, and 6. We felt it necessary to experimentally balance the delivery of services insofar as this technology is concerned because the PI's data from ongoing clinical trials indicates lower attrition and missed appointments in persons receiving home based televideo delivered treatment (e.g., in our current RCT of BATE-G for PTSD in Veterans, individuals in the televideo condition evinced 45.8% fewer missed appointments (Acierno, 2012)). As differential attrition was considered a greater threat to experimental validity than novelty of treatment delivery modality, and as the content of the control treatment is exactly that of typically offered bereavement supportive counseling, we feel that this decision is well justified.

Home-Based Televideo Procedures for Both Conditions: We will follow the VA

approved home based telemedicine procedures for delivering evidence based psychotherapy. We will also follow VA policy for home-televideo patient protection, in part validated by Dr. Acierno's VA HSRD study (See Gros et al., 2011) and approved nationally (see http://vaww.visn20.portal.va.gov/sites/clinical/BH/HBTMH/default.aspx note, must access from within VA firewall). One procedural, not skill, modification centers on reviewing homework (daily planners, thought lists, etc.). VA offers two current solutions: encrypted file transfer or simply holding the completed worksheet up to the camera for a screen shot. In past 3 telemedicine trials, the latter solution was overwhelmingly adapted. However, there may be instances where signal degradation causes such screenshots to be difficult to read. In these instances, participants simply read responses to therapists. Therapists using this approach report that they feel they are validating their patients' efforts more significantly, and patients report similar experiences. Thus, all participants are initially given this option, as well as the aforementioned two options. With respect to technical procedures: for participants who do not have a tablet or computer with internet connection, Dr. Acierno's telemental health research lab has 175 tablets available for study use and software (VA approved JABBER) is preloaded. All one must do is turn on the tablet, touch the icon for JABBER, and touch the therapist name to initiate session. For those who prefer to use their own equipment, a download link for JABBER or AKSummit (a FIPS encryption level, VA approved televideo software package for non-Mac computers) is given. Downloads require a grand total of 2 clicks of the mouse and selection of a username and password, and are initiated much like a skype session.

Experimental Condition - Behavioral Activation and Therapeutic Exposure for Prolonged Grief Disorder (BATE-G) (Acierno et al., 2012; Lejuez et al., 2011). The BATE-G treatment of PGD includes two components that will assure its relevance to military mental health experts and the services personnel they serve while maintaining its standardization and cost effectiveness. First, a video-based outline and rationale of BATE-G is given to maintain integrity and standardization of the intervention. This video will be complemented by the 7 session BATE-G intervention designed to treat the symptoms that comprise PGD. Second, BATE-G will be delivered via both televideo and in person modalities to optimize military and Veteran participation and satisfaction. Thus, standard office based sessions 1 and 7 will be complemented by televideo home-based sessions (sessions 2, 3, 4, 5, & 6) to increase contextual relevance of treatment components and reduce travel and time burden on participants, resulting in increased likelihood of session attendance. By delivering treatment into the environmental context in which treatment strategies will be used, we hope to enhance generalizability of techniques for both conditions. Our extensive research on home based televideo-delivered treatment for PTSD with Veterans and Active Duty personnel indicates that they prefer this modality for its time and cost savings, convenience, and confidentiality (Acierno, 2012).

The recorded video and accompanying brochure components of the BATE-G treatment for PGD outline the core treatment strategies and their rationales, and thus serve the dual purpose of (1) educating participants regarding effective interventions, as well as (2) 'centering' mental health providers on treatment components (i.e., preventing therapist drift) such that a significant focus of their therapeutic work remains consistent

with the intervention as specified. This video and accompanying brochure are complemented by an active therapy component, based on principles of Behavioral Activation for depression, and Therapeutic Exposure for stress and anxiety. This treatment incorporates daily planners and worksheets used to generate, rate and monitor positively and negatively reinforcing behaviors, as well as lists of stimuli avoided since the death of one's fellow service member (e.g., going to military related memorial events, looking at pictures of the deceased). For the present study, a list of activities and resources for military and Veteran personnel will also be generated for each Veteran (see below), and specific video scenes reshot with characters and locations more relevant to Veteran actors. Note that no changes to the therapeutic content or key points of the existing video script will be made. The current video compliment to the intervention was purposefully created with a core Behavioral Activation and Therapeutic Exposure component that is uniformly applicable across populations, combined with specific opportunities for nuances in scene construction and actor representation to enhance relevance for specific populations. Thus, a nearly identical overall script and an identical therapeutic component script is used, and can subsequently be complimented by population-specific actors and scenes to enhance personal relevance. We have created such "context modifiable" video interventions before, most notably in our cognitive-behavioral treatment to reduce PTSD and Substance Abuse symptoms in rape victims presenting to the emergency room in which we adapted the initial video by altering scenes and narrators to be tailored for a Native American audience. Therefore, the major modifications to the existing treatment will be to the video, using Veteran and Active duty scenes and actors, and the brochure. Scenes will be revised to reflect typical Veteran avoidance patterns in PGD such as avoiding crowds). The video serves to review core treatment components in a standardized fashion, requiring therapists to cover each point, and offering consistent explanation of treatment component rationale.

After the video presentation, the behavioral activation intervention begins with a review 5 of life areas and identification of values they hold as important in each area: Personal Relationships, Education/Career, Recreation/Interests, Mind/Body/Spirit, and Daily Responsibilities. From each value, participants derive specific behaviors in which they can engage to support that value (e.g., if the patient states "Time with Family" as a value, the specific behavior might be "throw the football with my son for 30 minutes"). Each participant subsequently uses the values form as a prompt to generate 10 to 20 highly defined activities that are either positively reinforcing or functional (i.e., negatively reinforcing in that an aversive but necessary task was completed, leading to a sense of relief or accomplishment). Each activity will be rated in terms of desirability and difficulty, with relatively easier and more desirable activities entered on daily planners before equally desirable, but more difficult activities.

In addition to valued activities, a second list of behaviors will also be generated that focuses on the often subtle avoidance responses of most individuals with PGD. This list will be highly personalized for each Veteran, but often includes things such as looking at pictures of the deceased, avoiding reminders of the deceased, etc. Thus, as with every correctly implemented BA treatment, tailoring to the individual, be he or she Veteran or construction worker or police officer, is necessary and central. Therefore, major modifications to the treatment are not done per class of individuals, but rather, for each and every individual. It is for this reason that generic 'activity lists' are no longer used,

and are in fact, antithetical to the interventions core learning theory basis (Learning theory holds that the organism determines the reinforcer).

Next, these two lists will be used to generate activities for the following two days (to be repeated each night, so that the participant is always planning two days in advance). A pocket sized daily planner (or smart phone, if patient prefers and already uses) is used to guide behaviors, and is kept by patients throughout the day so that planned activities are known in advance, and any changes to activities recorded. In this way, activities that are ineffective in altering mood, or that are routinely not accomplished despite being scheduled are removed or modified. Treatment is delivered in 7, once weekly, 75-minute sessions over 7 weeks, consistent with the following general outline:

Session 1: (OFFICE-BASED) In the first session, the rationales for Behavioral Activation and Therapeutic Exposure are given in the video and again in the accompanying brochure. The core points made are that (1) what one does often plays a role in how one feels and (2) if one develops patterns of avoidance, specifically as it relates to the memories of lost comrades and the military, the pain of loss may endure longer and more intensely than it has to. After playing the video, this rationale is restated by the counselor, and any questions answered. Participants are asked to describe the rationale in their own words. Therapists then proceed to outline the first step in the intervention, which is daily monitoring of all behaviors in order to get a 'snapshot' of their day on a calendar form. The importance of knowing exactly what they do each day, all day is outlined, and the rationale that this foundation will be used to define and modify the behavioral structure of each day in the future in order to maximize reinforcing and exposure based activities, and minimize withdrawal is reviewed. The session ends with a review of the televideo equipment. If patients have their own computer and internet connection, they are given the HIPAA compliant encryption software offered by MUSC/RHJ VA clinical services. If they do not have equipment or connection, they are given a "tablet" (these are already in the PI's possession) with HIPAA compliant software to use for the duration of the treatment.

Session 2: (TELEVIDEO) Session 2 is conducted via televideo directly into the participant's home and begins with a review of homework and verbal reinforcement of completed daily assessment monitoring forms, restatement of the rationale, and problem solving. Next, the five values areas are discussed (relationships, vocation, recreation, physical/spiritual, and responsibilities) and specific values under these categories generated and listed. These are then used to derive highly specific behaviors that illustrate these values, and these specific, values-consistent behaviors are placed on the Values and Activities form. Behaviors are classified as either positively reinforcing (i.e., enjoyable behaviors), negatively reinforcing (e.g., behaviors such as chores that, when completed, result in reduction of stress or aversiveness), or exposure-based, such as behaviors that are incompatible with bereavement-related avoidance (e.g., looking at photos of the deceased, going to a military-focused event). Each reinforcing behavior is rated from 0 - 10 in terms of its reinforcing potential as well as its difficulty to complete. Whenever possible, behaviors are framed in a social context. It is at this point that the daily monitoring form the patient used in the first session is translated into a daily planning form. Thus, participants are instructed to

select activities that they have just generated from the Values and Activities form, and use them to plan events for the remainder of the current day, and the next two days, with the objective of at least 3 hours of reinforcing activities and 30 minutes of exposure behaviors planned each day. Participants are instructed to plan ahead to the next day, and keep ahead one day.

A discussion of the bereaved and how they are currently playing a part in the patient's life is also initiated. The concept of exposure to these memories and thoughts as a way of honoring those who did not make it home, not simply as a way to become desensitized to these memories, is reviewed. We frame the grief processing in this way because we have noted that many bereaved individuals state that they do not want to 'heal' and that they equate lessening of negative affect related to the loss of their comrade with 'forgetting' him or her. We are very careful to validate feelings of loss and assure patients that 'getting better' is not the same as 'forgetting', with focus placed on what their friend would have wanted for them, which is probably good memories, rather than painful memories. Thus, as an exposure exercise the therapist and patient review in extensive detail the thoughts and feelings experienced with respect to the bereaved. This also helps to identify any actual behavioral avoidance (e.g., military events) that may be taking place and these are also addressed.

Session 3: (TELEVIDEO) These sessions begin with a review of homework, followed by asking the participant to state, in their own words, their interpretation of the rationale for Behavioral Activation and Therapeutic Exposure. Obstacles to completing scheduled behaviors are discussed and additional exposure based and reinforcing behaviors are generated, consistent with participant values, and placed on the Values and Activities form. The need to constantly update this form is stressed, and therapists illustrate that this form should be used in conjunction with the daily planner so that planning is easier, and values-consistent. If a participant failed to use the planner, therapists address the difference between planning for a good day and 'hoping' for a good day, comparing this to planning for effective combat based on training and hard work vs. "hoping" for successful combat outcomes based on only hope. Behaviors that were consistently planned on the daily planner but not completed are removed and alternative behaviors suggested. A discussion of avoidance behaviors related to bereavement is held, and exposure activities derived from this are added to the list. The next day's activities are planned. Following the behaviorally focused work, the discussion / processing of bereavement related memories and feelings is reviewed, with a focus on the events up to and including the death of the friend, and the ensuing days and months. Again, the major emphasis is on exposure to, rather than avoidance of these cognitions and feelings. The next 2 days of activities are planned.

Sessions 4, 5, and 6: (TELEVIDEO) Homework is reviewed with an emphasis on reinforcing the participant for following the daily planner. Values and Activities lists are expanded, as is the list of avoided behaviors. Each behavior that was planned but not completed is addressed, and those that are consistently planned but not completed are removed from the planner. Each session is focused on problem solving and implementing both planning, and execution of planned, exposure-oriented activities. The last half of each session is again devoted to an in depth discussion of the bereaved and

processing the thoughts and feelings associated with this discussion. At the end of each session, the next 2 days of activities are planned as per above.

Session 7: (OFFICE-BASED) The final session includes discussion of the rationale and treatment gains obtained thus far. Discussion is also centered on the need to continue planning activities and using a daily planner for at least 6 months. Relapse prevention strategies are reviewed.

Comparison Condition: Cognitive Restructuring and Supportive Grief Counseling as Outlined by the VA/DoD Iraq War Clinician Guide (Chapter 11): The primary purpose of this condition is to serve as a 'current standard of care' comparison control condition, matched to the experimental condition in both duration and modality of treatment delivery. Therefore, specific components of the Experimental treatment, such as focused and specific activity scheduling will not be present. The same counselors will deliver this treatment according to the same schedule of in person and televideo sessions as the experimental intervention (1 in person, followed by 5 televideo, followed by a final in person).

As with BATE-G, sessions will be conducted once per week for 75 minutes. The VA's National Center for PTSD Iraq War Clinician Guide, 2nd ed. offers the following summary (Pivar, 2007) of treatment for traumatic grief, which overlays highly with standard supportive grief counseling. The Guide Summarizes:

"There have been no outcome studies of treatments of veterans for prolonged and complicated grief symptoms at this time. Clinical experience supports the importance of education about normal and complicated grief processes, education about the cognitive processes of guilt, restructuring of cognitive distortions of events that might lead to excessive guilt, looking at the function of anger in bereavement, restoring positive memories of the deceased, restoration and acknowledgment of caring feelings towards the deceased, affirming resilience and positive coping, retelling the story of the death, and learning to tolerate painful feelings as part of the grieving process. Regardless of the techniques that are used, what is central to treating veterans for prolonged and complicated grief is recognition of the significance of their losses, provision of an opportunity to talk about the deceased, restructuring distorted thoughts of guilt, and validation of the pain and intensity of their feelings."

Session 1: (OFFICE-BASED) The first session will involve review of the Veteran's loss, and recognition that the loss was significant, enduring and painful. In addition, education about normal vs. problematic grief reactions will be discussed. The parameters of the loss, its meaning and its current impact will be explored. A discussion of positive memories of the deceased will be initiated and the Veteran will determine the course of this discussion.

Session 2: (TELEVIDEO) The second session will focus on a review of points raised in the first session, followed by further discussion of cognitive processes of guilt often associated with bereavement. Positive memories of the lost comrade will be explored, and the meaning of guilt in the context of these positive images outlined and discussed.

Sessions 3-6: (TELEVIDEO) The third through sixth sessions will review points raised in the prior session, and then address the function of anger in bereavement. This is often a sensitive, guilt-facilitating issue, and sufficient time will afforded to process these conflicting feelings of guilt, loss, longing and anger. Again, the concept of restoring positive memories about the deceased, a common thread across these sessions, will be raised. Discussion of the story of the

death will take place, with attention directed to specific cognitive distortions in the context of the aforementioned conflicting emotions addressed.

Session 7: (OFFICE-BASED) will focus on restoring positive memories of the deceased, focusing on the concept of tolerating painful or mixed feelings in the context of these memories. In addition, integration of 'lessons learned' from prior sessions regarding guilt, anger, sadness, and also positive emotions attached to the memory of the lost comrade will be reviewed.

Treatment Integrity and Training. Counselors will receive the video and brief treatment manual and will be asked to review these prior to a 4-hour training with the study PI. At this training, the study PI will go over key points of the intervention outlined above. A key treatment tool, the video, has been specifically designed as a treatment training mechanism in itself. In addition, all treatment sessions will be audio taped and 20% of case tapes will be reviewed for treatment integrity by two trained independent raters according to session checklists. In this way, we will assure that directive treatment procedures found in the BATE-G condition are not delivered in Cognitive Restructuring and Supportive Grief Counseling.

Treatment Providers. Treatment providers will be master's level counselors with at least 2 years of experience providing bereavement counseling to adults. All providers will perform both treatments.

HIPAA Compliance for Home-Based Televideo Equipment. In order to assure patient Confidentiality and HIPAA compliance, we will use the MUSC/Charleston VAMC contracted version of HIPAA compliant software for televideo patient care. If participants do not have a computer, we will supply them with a tablet for use during the study, as we have done with our two ongoing telemedicine treatment studies with Veterans.

Dependent Measures & Interviewers. All measures will be administered by master's level research assistants who are blind to experimental condition and who achieve interrater reliability on 5 practice assessments of 90%. All participants in both conditions will complete most measures at pre-treatment/baseline (at least 6 months post-death), post-treatment, and 3 & 6 months post-treatment. The timing of assessments with study procedures is described in the diagram below. In pilot testing of the assessment battery, 42 minutes was the average time of completion for self report, with another 30-40 minutes necessary for the selected modules of the Structured Clinical Interview for DSM 5.

DOMAIN	MEASURE	DESCRIPTION	TIMING
Demographics	Race Gender etc.	Descriptive self-report	Baseline
Prolonged Grief Disorder	Inventory of Complicated Grief, Revised (Prigerson, et al, 2001)	34item self-report; total intensity score; high reliability, concurrent validity with BDI & satisfactory criterion validity (Prigerson et al., 1995; 1997; Silverman et al., 2000; 2001)	Base, Post-Tx, 3 & 6 month
Selected Axis I Mental Diagnoses	Structured Clinical Interview for DSM-5 (To Be released)	Clinician administered, gold standard; Dx: Major Depression, Panic Disorder, Generalized Anxiety Disorder, PTSD, Sub. Use Disorder. (Last version TBA)	Base, Post-Tx, 3 & 6 month

Depression	Beck Dep Inventory-II (Beck et al, 1996)	21 item self-report; high reliability and concurrent validity (Beck, Steer, & Brown, 1996)	Base, Post-Tx, 3 & 6 month
PTSD	PTSD Symptom Scale (Foa et al., 1993)	17 item self-report; 3 subscales. High reliability and concurrent validity (Foa et al., 1993)	Baseline, Post-Tx 3 & 6 month

Power Analysis. The primary longitudinal efficacy outcome variables are: intensity of PGD symptoms (ICG), and depression symptom severity (BDI) and PTSD (PCL) variables. In several studies of behavioral activation for mood disorders by Lejuez and colleges (Hopko, Lejuez, & Hopko, 2004; Hopko et al., 2003; Lejuez et al., 2011, Lejuez, Hopko, & Hopko, 2001; MacPherson et al., 2010), effect sizes of .7 to 1.5 were obtained. In addition to behavioral activation, the present intervention also includes a video-based treatment for PTSD-like symptoms of complicated bereavement based on our existing treatment for PTSD in combat Veterans. In the pilot study, this treatment achieved an effect size of 0.7 on psychological outcomes, and .25-.3 on health outcomes. For comparing the longitudinal profile of continuous outcomes for the BATE-G versus Comparator groups across the study period [assuming 4 measurement time points, level of significance alpha=0.05, two-tailed comparison, correlation between pairs of measurements within subjects (interclass correlation) no larger than p=0.5], we estimate that with 44 subjects per group (88 total), we will have approximately 90% power to detect a standardized effect size of at least 0.35 (difference in comparison group means in units of standard deviation (sd)). For outcome variables having standard deviations (sd) in the range 5-15, for example, the raw effect sizes that can be detected range from approximately 2.3 to 6.9 raw units. To account for attrition during treatment (28%), and loss to followup (10-15%), we inflate the sample size accordingly to achieve a final sample size of approximately 140 subjects: 140 x 28% attrition = 101; 101 x 12% loss = 89 total participants completing all measures (note, ITT sample size will be 28% larger than power estimate requires, as treatment dropouts are included in ITT analyses).

Data Management. Charleston is the site of a VA HSRD COIN, of which Dr. Acierno is an Executive Committee Member. The COIN provides all Charleston VA researchers, including Dr. Acierno, with VA server space, data cleaning and management services, and when requested, statistical consultation. Data entry will be by the project assistants using SPSS with range violation parameters and will follow double entry protocols (the same value must be entered twice for acceptance at two different times by two different data entry personnel for each entry). Data will be compiled using codes in lieu of personal identifiers. Access to study data will be limited to research personnel. Development of and security oversight for the electronic database for this study will be performed by study personnel trained for this purpose using a secure VA approved software to support data capture. Only de-identified case report forms will be entered into the electronic database. Thus, no protected health information (PHI) will be entered into the database. The data entry management system will be accessed and housed at the VAMC. Although no PHI will be entered into the database, data system security will be ensured by implementing multiple layered firewalls and a network intrusion prevention system for identifying and blocking malicious network activity in real time. A hard copy study log linking patient names with study ID numbers will be kept in a locked cabinet in a secure room at the VAMC, and access to this log will be limited to only key study personnel

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