

**An adjunctive family intervention for individual PTSD treatment**

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## (1) Rationale

(a) Statement of the Problem. Post-traumatic stress disorder (PTSD) is a significant public health problem, with lifetime prevalence rates of 8% (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995). The national burden of the disorder, and particularly its impact on the VA system, has increased in magnitude as military personnel return from the recent conflicts in Iraq and Afghanistan; rates of PTSD among these veterans are estimated at 13-20% (Kok, Herrell, Thomas, & Hoge, 2012). Although trauma-focused cognitive-behavioral treatments have been shown to be effective in the treatment of PTSD (Foa, Keane, Friedman, & Cohen, 2009), up to two-thirds of Veterans from Iraq and Afghanistan receive less than minimally adequate levels of care for PTSD (Lu, Duckart, O'Malley, & Dobscha, 2011; Spooner, Murdoch, Hodges, & Nugent, 2010). This is in part due to very high levels of treatment dropout, which can reach 36% (Imel, Laska, Jakupcak, & Simpson, 2013). These high dropout rates are consistent across clinical trials and civilian studies of PTSD treatment (Edlund et al., 2002; Imel, Laska, Jakupcak, & Simpson, 2013; Swift, Greenberg, Whipple, & Kominiak, 2012; Wang et al., 2005). Premature treatment termination is clearly a critical predictor of PTSD treatment failure, and thus bolstering engagement/retention is central to improving the effectiveness of evidence-based treatments.

Family members represent one potentially powerful resource that could be harnessed to enhance treatment engagement and outcomes. Lack of social support is one of the strongest predictors of the development and maintenance of PTSD (Brewin, Andrews, & Valentine, 2000; Ozer, Best, Lipsey, & Weiss, 2008), and poor family functioning negatively affects treatment outcomes (Evans, Cowlishaw, Forbes, Parslow, & Lewis, 2010; Evans, Cowlishaw, & Hopwood, 2009; Tarrier, Sommerfield, & Pilgrim, 1999). In the case of Veterans, family involvement in mental health services is now a national priority (Department of Veterans Affairs, 2006; New Freedom Commission on Mental Health, 2003), and all mental health providers are encouraged to involve families in Veterans' care (Veterans Health Administration, 2008). However, analysis of data from the VA's national records system showed that only 4.2% of Veterans receiving mental health care in the VA had any type of family session; this included sessions with or without the Veteran present, multi-family groups, or family psychoeducation (Laws & Hoff, 2015). In 2013 family sessions accounted for <1% of all VA mental health visits (Laws & Hoff, 2015), despite social support being associated with 15-20% of the variance in PTSD symptoms (Brewin et al., 2000; Wright, Kelsall, Sim, Clarke, & Creamer, 2013).

### (b) Hypotheses or Key Question.

**Hypothesis 1:** Levels of feasibility and acceptability of the family-inclusive treatment among Veterans, family members, and VA clinicians will be high.

**Hypothesis 2a:** Patients whose family members receive family-inclusive treatment will show lower levels of PTSD symptoms at post-treatment and greater engagement throughout treatment compared to control patients.

**Hypothesis 2b:** Family members who receive family-inclusive treatment will show more active support for treatment and less accommodation than control family members.

(c) Specific Objectives. Immediate objectives are to test the feasibility and effectiveness of a family-inclusive intervention for Veterans with PTSD. Longer-term objectives are to examine the mechanisms of family-inclusive treatment and the factors associated with its successful use in VA clinics.

## (2) Background and Significance

(a) Background.

Family-involved PTSD treatment can enhance Veterans' sense of support and connection to their family members; positive, active encouragement of treatment by family members such as verbal support, practical help getting to appointments, and reminders to practice homework assignments is likely to reduce Veterans' levels of perceived criticism. Perceived criticism is associated with worse PTSD treatment outcomes (Tarrier et al., 1999), whereas positive family encouragement may be a powerful source of motivation for patients and a way for families to interact in a positive manner. The sense of the family being on the same "team" against the disorder, along with the practical assistance in attending sessions and remembering homework assignments, will likely enhance Veterans' treatment participation.

On the other hand, families may also be inadvertently engaging in behavior that undermines the Veterans' PTSD treatment. One such problematic behavior is symptom accommodation, or changes that family members make to their own behavior in order to reduce or prevent disorder-related distress in patients. Although often driven by compassion or by simple practical concerns (Boeding et al., 2013; Calvocoressi et al., 1995, 1999; Thompson-Hollands, Kerns, Pincus, & Comer, 2014), accommodation allows patients to avoid their emotional experience, and therefore reinforces the disorder pathology. Accommodation has been most well-studied in OCD, where it has been found to have strong associations with increased symptoms and functional impairment (Amir, Freshman, & Foa, 2000; Calvocoressi et al., 1999; Stewart et al., 2008), and both cross-sectional and longitudinal studies have shown that higher levels of family accommodation are associated with poorer treatment outcomes (Amir et al., 2000; Merlo, Lehmkuhl, Geffken, & Storch, 2009). Although the research literature is most robust in patients with OCD, accommodation is a transdiagnostic phenomenon that is found across a range of disorders (Lebowitz et al., 2013; Lebowitz, Scharfstein, & Jones, 2014; Thompson-Hollands et al., 2014). In PTSD, accommodation may involve family behaviors such as a partner avoiding topics of conversation related to the military or combat, or the partner doing all of the family's shopping because the Veteran can't tolerate crowded stores (Fredman, Vorstenbosch, Wagner, Macdonald, & Monson, 2014). Accommodation of PTSD symptoms is associated with patients' PTSD symptoms and relationship distress (Fredman et al., 2014). Furthermore, accommodation also conflicts with a fundamental goal of current gold-standard treatments for PTSD: patients allowing themselves to experience and accept their emotions surrounding the trauma, and the elimination of trauma-related avoidance in their daily lives (Foa, Hembree, & Rothbaum, 2007; Resick & Schnicke, 1992). A recent study by Campbell and colleagues (Campbell, Renshaw, Kashdan, Curby, & Carter, in press) found evidence of a bi-directional relationship between PTSD symptoms and accommodation: PTSD symptoms among military service members predicted later accommodation by romantic partners, and partners' earlier accommodation behaviors contributed specifically to service members' later avoidance symptoms. Taken together, these results indicate that accommodation is an especially important interpersonal variable to target as Veterans begin a course of trauma-focused treatment.

**Existing Family Treatments:** Several family-based interventions for PTSD have been developed, but these are quite extensive in terms of both their clinical targets and their number of sessions. For example, Cognitive-Behavioral Conjoint Therapy (Monson, Stevens, & Schnurr, 2005) (CBCT) is a 15-session treatment designed to treat the symptoms of PTSD while also improving overall relationship functioning. A family-based intervention for PTSD that was specifically developed for use in the VA, REACH (Reaching out to Educate and Assist Caring, Healthy families; formerly the S.A.F.E. program) involves attending sessions for up to 9-months (Fischer, Sherman, Han, & Owen, 2013; Glynn et al., 1999; Sherman, 2006). These treatments are generally effective in reducing PTSD symptoms and improving relationship satisfaction (e.g.,

Monson et al., 2011, 2012). However, they are costly to the healthcare system, demanding many hours of time from highly trained staff. In addition, the lengthy commitments are difficult for families, who may need to arrange child/elder care or take time off from work to attend. The protocols are also burdensome to clinicians; in addition to the time cost, many clinicians do not have expertise in family or couples treatment, which may make them reluctant to take on this work. Furthermore, the large number of intervention targets in each of these treatments (psychoeducation, problem-solving, communication skills, etc.) makes isolating specific mechanisms of change much more complex. There is no currently existing short-term family intervention that focuses solely on increasing treatment engagement and reducing avoidance.

**The Brief Family Intervention (BFI):** The PI has previously developed and tested a brief family intervention (BFI) for reducing family accommodation in the context of treatment for OCD (Thompson-Hollands, Abramovitch, Tompson, & Barlow, 2015). The intervention is not a stand-alone treatment, but is rather designed to complement the patient's course of evidence-based treatment. The protocol is delivered to an adult family member individually, without the patient present, in two 50-minute sessions scheduled at the beginning of the patient's individual treatment. The goals of the BFI are to increase family members' active support for treatment and to reduce family accommodation of the Veteran's PTSD symptoms. The approach is highly behavioral, focusing on identifying relevant examples and practicing how to complete them. The clinician and the family member each play an active role during the sessions, and there is an approximately equal amount of time devoted to didactic information and discussions/role-plays.

The BFI's strengths in comparison to existing family-based treatments in PTSD include: shorter duration, reducing burden to families, clinicians, and the system; individual rather than couples' sessions, negating the need for clinicians to be comfortable with couples or family work; and a limited, highly behavioral focus, relying on concepts and strategies which will be familiar to any clinician with CBT experience.

(b) Significance. The proposed study may identify a new, feasible, and effective family-inclusive treatment to enhance existing PTSD treatments. A substantial number of Veterans with PTSD who complete trauma-focused treatment are not completely symptom-free at treatment termination, or they drop out of treatment prematurely. The proposed intervention may reduce these numbers by enhancing the effect of treatment and encouraging Veterans not to drop out.

(c) Relevance to Veterans Health. There are large numbers of Veterans who suffer from PTSD, and PTSD in turn affects Veterans' relationships with significant others. Family-inclusive treatment has the potential to enhance existing treatments in terms of their effects on PTSD symptoms, while also improving relationship functioning. An increase in treatment effectiveness and Veteran quality of life would be a substantial benefit. Furthermore, the BFI has the potential to provide these benefits in an extremely cost-effective and efficient manner compared to existing family-focused interventions. Should the BFI prove to be effective in this population and setting, it would provide a more parsimonious way for clinicians and administrators to fulfill the directive to involve families in Veterans' care.

### (3) Work Accomplished

As noted above in section 2a, Dr. Thompson-Hollands (PI) has already developed and tested the BFI, which was originally piloted among a sample of family members of patients with obsessive-compulsive disorder (OCD). In that study, a randomized clinical trial with 36

participants (18 patient-family member dyads), the BFI was rated by family members as being highly satisfactory (mean satisfaction = 6.88 out of 7, SD = .35) and useful (mean = 6.29/7, SD = .76) (Thompson-Hollands et al., 2015). Family members who received the BFI demonstrated significantly greater decreases in accommodation compared to controls; at the end of the study, average accommodation scores in the control group remained at 78% of their baseline levels, while scores in the BFI group had dropped to 37% of baseline. Moreover, patients whose family member had participated in the BFI had significantly lower levels of OCD symptoms following their individual treatment ( $d = 1.27$ ), and changes in family accommodation significantly predicted patients' later symptom levels. These promising initial efficacy outcomes support the use of the BFI in the present effectiveness trial.

Although the BFI has only been previously tested in the context of OCD, the protocol's applicability is not limited to OCD. Accommodation is not a disorder-specific phenomenon; any disorder that involves avoidance (essentially all of the so-called "emotional disorders" (Moses & Barlow, 2006)) is likely to produce family accommodation in addition to the patient's own attempts to avoid. Indeed, previous work by the PI and others has shown that accommodation occurs across a wide range of disorders (Lebowitz et al., 2013; Thompson-Hollands et al., 2014), including PTSD (Fredman et al., 2014).

#### (4) Work Proposed

We expect to begin enrollment in the winter of 2016/2017. A total of 48 Veteran-family member participants will be enrolled (24 dyads). We will enroll approximately 2 participants (i.e., a dyad of one Veteran and their adult family member) per month, for a recruitment rate of 12 dyads over the course of a year. Veterans and their family members will participate in the study for 16 weeks total.

The proposed study will use an effectiveness design to evaluate a brief intervention targeting reductions in family accommodation and increases in active family support for treatment (the BFI). Veterans with PTSD who are beginning a course of trauma-focused treatment and their adult family members (one family member per Veteran) will be recruited at VA Boston.

All Veterans enrolled in the study will be beginning a course of either Prolonged Exposure (PE) or Cognitive Processing Therapy (CPT), which will be delivered as usual by PTSD clinical staff. As the BFI is an adjunctive intervention, Veterans' trauma-focused treatment is considered separate from the present study. The Veterans will be seen by regular clinical staff and no artificial limits will be imposed upon their treatment, although treatment engagement will be tracked (see Assessment section, below). Veterans and their family members will be recruited for the present study at the beginning of a course of treatment at the clinic. Phase I will be an open pilot trial of 4 dyads. All family members in Phase I will receive the BFI, which will be delivered as 2 weekly 50-minute sessions of the BFI, consistent with the application with the BFI in previous work (Thompson-Hollands et al., 2015). Phase II will include 20 dyads (N=40) using identical recruitment, inclusion/exclusion criteria, and assessment structure; however, in this second phase family members will be randomly assigned to receive or not receive the BFI, and VABHS clinicians will deliver the BFI sessions (rather than the PI as in *Phase I*).

#### **Veterans:**

*Inclusion criteria.*

(1) has a current diagnosis of PTSD

- (2) is 18 years of age or older
- (3) has an eligible family member (defined as a spouse/significant other, parent, adult child, sibling, etc., 18 years of age or older who currently has substantial daily or weekly contact with the Veteran)
- (4) is beginning a course of either CPT or PE at VA Boston.

*Exclusion criteria.*

- (1) has current diagnoses of unstable bipolar disorder, past or present psychosis, or organic mental disorder
- (2) has clear and current suicidal risk (assessed via the MINI-Suicide Module (Sheehan et al., 1998), see Assessment section below)
- (3) has current moderate or severe substance use disorder
- (4) is currently participating in family-based therapy/couples-counseling

**Family members:**

*Inclusion criteria.*

- (1) is 18 years of age or older
- (2) is the family member (defined as a spouse/significant other, parent, adult child, sibling, etc.) of the Veteran
- (3) currently has substantial daily or weekly contact with the Veteran

*Exclusion criteria.*

- (1) has a current diagnosis of PTSD
- (2) has current diagnoses of unstable bipolar disorder, past or present psychosis, or organic mental disorder
- (2) has clear and current suicidal risk (assessed via the MINI-Suicide Module (Sheehan et al., 1998), see Assessment section below)
- (3) has current moderate or severe substance use disorder
- (4) is currently participating in family-based therapy/couples-counseling

Recruitment of Veterans and family members will occur through the VABHS outpatient mental health clinics (e.g., the PTSD Clinic, the Women's Clinic, General Mental Health, Center for Returning Veterans, etc.). All interested participants will be contacted by the PI for a phone screen, where the study and its procedures will be described and a short screen for eligibility will be administered. If the initial screening requirements are met, participants will be invited to an in-person assessment. During the first appointment, the Veteran and family member will be provided with a thorough description of the project and the informed consent form will be reviewed and signed. Baseline assessment measures will then be administered (see Assessment section).

Veterans will proceed with PE or CPT as usual through the clinic, with no restrictions or limitations. Should a Veteran choose to discontinue PE or CPT, he or she will continue to be enrolled in the proposed study for follow-up assessments, as treatment drop-out is a variable of interest. All family members who are to receive the BFI (i.e., all family members in *Phase I* and half of family members in *Phase II*) will participate in the two BFI sessions, and then move into the follow-up portion of the study.

**BFI:** The BFI is a 2-session individual intervention delivered by a clinician to the adult family member of a Veteran with PTSD who is beginning a course of CPT or PE treatment. The BFI sessions are guided by a manual, which has previously been developed by the PI but will

be revised for the purposes of the current study as described earlier to enhance its relevance to the families of Veterans with PTSD. The BFI may be completed either in person or remotely via telephone.

The protocol begins with a brief assessment of the family member's current accommodation behaviors, as captured by the SORTS interview (Fredman et al., 2014). The clinician explores the circumstances in which the family member engages in accommodation and helps to determine the primary motivations for that accommodation (e.g., fears that upsetting the Veteran will cause emotional damage, or a desire to communicate support to the Veteran by "taking care of him" or "not stressing him out"). This discussion helps the clinician to begin conceptualizing how best to approach reducing accommodation, as well as providing an important view of how PTSD has affected this individual family or relationship.

The family member is next provided with psychoeducation regarding a cognitive-behavioral conceptualization of PTSD, with particular attention paid to how avoidance of distress results in temporary relief but ultimately reinforces the psychopathology and increases further avoidance in the long term. The model of exposure is then explained as a powerful mechanism for testing fears and learning to tolerate discomfort. The clinician explicitly addresses issues regarding the safety of exposure-based treatment, including whether exposure makes patients "go crazy" and why a modest, temporary increase in intrusive thoughts about the trauma early in treatment is a positive sign. The clinician also briefly describes the research support for trauma-focused treatment, to assure family members that these interventions have been rigorously studied and found to be safe and effective.

The clinician then works with family members to brainstorm ideas of how they can support the Veteran's efforts in treatment. Relatives are encouraged to come up with as many possibilities as they can, from large (e.g., committing to driving the Veteran to each treatment session) to small (e.g., making a note in the calendar to ask the Veteran if he or she needs to complete any homework before the next session). In addition to these practical forms of support, the family member is also strongly encouraged to provide verbal support to the Veteran. This can include praising the Veteran's efforts in treatment (e.g., consistency in attending sessions, challenging him or herself to change unhelpful behaviors) as well as reminders that seeking treatment benefits and is appreciated by the family. Family members are coached to explicitly note any positive changes they observe in the Veteran as treatment progresses; such comments may increase the Veteran's motivation to continue with treatment, and also convey pride, gratitude, and hope on the part of the family member.

Following the overview of the treatment and treatment support, the clinician returns to the topic of accommodation. Accommodation is described as an understandable and common response from family members, but one which is also a form of avoidance. Personalized examples from the SORTS are used to illustrate how accommodation results in short-term relief for the patient but ultimately prevents him or her from testing out maladaptive beliefs and learning to tolerate discomfort. Family members are encouraged to capitalize on the Veteran's starting treatment by shifting their own behavior to be more consistent with the treatment approach. By highlighting the benefits of making these family changes now, while the Veteran is making other positive changes to address his or her PTSD, we reduce shame regarding the family member's past accommodation behavior and focus on their potential to work in coordination with this new phase of treatment.

All BFI sessions across both Phases will be audiotaped and quality assurance will be assessed by an independent study staff member familiar with the BFI. Family members will be

provided with \$10 in travel compensation for each BFI session that they attend in person (total of \$20); sessions conducted remotely will not be eligible for travel compensation.

During the pilot *Phase I* the PI will serve as the BFI clinician. The PI has considerable clinical experience in the treatment of Veterans with PTSD. Additionally, as described above, the PI designed the BFI and has successfully tested its efficacy in a study of patients with OCD and their family members. Beginning in *Phase II* the PI will no longer deliver the intervention; instead, a minimum of 3 clinicians from the VABHS PTSD clinic will be recruited and trained to deliver the BFI.

**Comparison condition:** Family members in the control or comparison condition of *Phase II* will not receive the BFI or any other study-specific family sessions (aside from the assessments described below). In keeping with the effectiveness aims of the present study, family members in the comparison condition (and the BFI condition) will not be prohibited from receiving any family-inclusive services or sessions that would normally be offered to them in the context of usual VA care.

**Independent variables:** Receiving or not receiving the BFI (for Veterans/family members); receiving or not receiving training in the BFI (for clinicians).

**Dependent variables:** Treatment engagement and PTSD symptoms (for patients); accommodation and active treatment support (for family members); qualitative feedback and rates of participation (for Veterans, family members, and clinicians).

**Assessment:**

Measures and assessment points are shown in Table 1. Qualitative interviews with stakeholders (Veterans, family members, and clinicians) will continue throughout both Phases of the study, as described below. Clinician-rated assessments of Veterans and family members will be completed (in person or via telephone/mail, or a combination of in person and remotely) at baseline and weeks 6, 12, and 16; Veterans and family members will be compensated \$50 for each of these 4 assessment visits that they complete (total of \$200 for the major assessments). Finally, PE and CPT therapists will complete ratings of Veterans' treatment engagement at each session, and will monitor dropout.



**Table 1. Assessment Measures and Timepoints**

	<i>Time of Administration</i>					
	<i>Baseline</i>	<i>Weeks 0-6</i>	<i>Every PE/CPT session</i>	<i>Week 6</i>	<i>Week 12</i>	<i>Week 16</i>
CAPS-5	X <sup>v</sup>			X <sup>v</sup>	X <sup>v</sup>	X <sup>v</sup>
SCID-5	X <sup>v, f</sup>					
Demographics form (Vet/FM)	X <sup>v, f</sup>					
Demographics form (Clin)	X <sup>tx</sup>					
Relationship information form (Vet)	X <sup>v</sup>					
Relationship information form (FM)	X <sup>f</sup>					
LEC-5	X <sup>v, f</sup>					
WTAR	X <sup>v, f</sup>					
MOCA	X <sup>v, f</sup>					
AUDIT	X <sup>v, f</sup>					
MINI-Suicide module*	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
PCS	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
MSPSS	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
RDAS	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
DERS	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
ODSIS	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
OASIS	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
IPF-80	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
PCL-5	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
CTS-2SF	X <sup>v, f</sup>			X <sup>v, f</sup>	X <sup>v, f</sup>	X <sup>v, f</sup>
PABQ	X <sup>v</sup>			X <sup>v</sup>	X <sup>v</sup>	X <sup>v</sup>
PTCI	X <sup>v</sup>			X <sup>v</sup>	X <sup>v</sup>	X <sup>v</sup>
Homework Compliance Scale			X <sup>tx</sup>			
Treatment attendance/dropout			X <sup>tx</sup>			
SORTS	X <sup>f</sup>			X <sup>f</sup>	X <sup>f</sup>	X <sup>f</sup>
Caregiving appraisal scale	X <sup>f</sup>			X <sup>f</sup>	X <sup>f</sup>	X <sup>f</sup>
ITC				X <sup>f</sup>	X <sup>f</sup>	X <sup>f</sup>
TEQ		<i>Administered to family members after BFI sessions 1 and 2, respectively</i>				
CSQ						
WAI						

*Note:* X<sup>v</sup> = measure completed with/by Veteran; X<sup>tx</sup> = measure completed by Veteran's individual therapist; X<sup>f</sup> = measure completed with/by family member; \*MINI-Suicide module is only administered to family members at follow-up if they scored ≥ 1 at baseline

**Veteran-specific assessments:**

Clinician Administered PTSD Scale for DSM-5 (CAPS-5) (Weathers et al., 2013).

Structured Clinical Interview for DSM-5 – Research Version (SCID-5) (First, Williams, Karg, & Spitzer, 2015).

Demographics form. This form collects basic demographic information (age, marital status, etc), as well as a very brief overview of medical, social, and psychiatric status/history.

Relationship information form

Life Events Checklist for DSM-5 (National Center for PTSD)

Wechsler Test of Adult Reading (WTAR; Wechsler, 2001)

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005)

Alcohol Use Disorders Inventory (AUDIT)

MINI-Suicide module (Sheehan et al., 1998) Individuals will be excluded from enrolling in this study if they score 17 or higher (high risk) on the MINI suicide module at the initial assessment.

The Revised Dyadic Adjustment Scale (RDAS; Busby, Christensen, Crane, & Larson, 1995) is a 14-item scale measuring relationship satisfaction in couples. The scale consists of 3 subscales: dyadic consensus, stability, and engagement.

Perceived Criticism Scale (Hooley & Teasdale, 1989)

Multidimensional Scale of Perceived Social Support (Zimet, Powell, Farley, Werkman, & Berkoff, 1990)

Difficulties in Emotion Regulation Scale (Gratz & Roemer, 2004)

The Beck Depression Inventory-II (BDI-II; Beck et al., 1996)

The Beck Anxiety Inventory (BAI; Beck et al., 1988)

The Inventory of Psychosocial Functioning (IPF-80; Bovin et al., 2018) will be used to index objective role functioning/impairment in the following domains: romantic relationship, family, parenting, work, friendships and socializing, education, and self-care

PTSD Checklist-5 (PCL-5) (Weathers, Litz, Huska, & Keane, 1994)

Revised Conflict Tactics Scale (CTS-2; Straus, Hamby, Boney-McCoy, & Sugarman, 1996)

Posttraumatic Avoidance Behavior Questionnaire (PABQ; van Minnen & Hagenaars, 2010)

Posttraumatic Cognitions Inventory (PTCI; Foa, Ehlers, Clark, Tolin, & Orsillo, 1999)

At each PE or CPT session, the Veteran's therapist will complete (1) a record of session attendance (or dropout, if applicable), along with (2) the Homework Compliance Scale (Leung & Heimberg, 1996) (HCS).

**Family member-specific assessments:**

Family members will complete/be assessed using the following previously described measures, as outlined in Table 1:

SCID-IV

Demographics form

Relationship information form

AUDIT

LEC-5

WTAR

MOCA

MINI-Suicide module (only administered at follow-up if score was  $\geq 1$  at baseline, see DSMB section)

RDAS

PCS

MSPSS

DERS

BDI-II

BAI

IPF-80

CTS-2-SF

PCL-5 (family members will rate the PCL-5 based on their perception of the Veteran's current symptoms)

Family members will also complete the following (timing outlined in Table 1):

Significant Others' Responses to Trauma Scale (Fredman et al., 2014) (SORTS)

Caregiving Appraisal Scale (Lawton, Moss, Hoffman, & Perkinson, 2000)

Involvement in Therapy Checklist (ITC). This measure consists of a checklist of involvement in the Veteran's treatment since the last assessment (assisting with therapy homework, driving patient to appointments, attending therapy sessions with the Veteran, etc.).

Treatment Expectancy Questionnaire (TEQ; Borkovec & Nau, 1972). The TEQ will be administered immediately after the first BFI session. Wording was modified slightly to better describe the family program.

The therapeutic alliance following the BFI will be assessed using the 12-item therapist and client versions of the Working Alliance Inventory (WAI; Horvath & Greenberg, 1989; Tracey & Kokotovic, 1989). Wording was modified slightly to better describe the family program.

The Client Satisfaction questionnaire (CSQ) will assess family members' satisfaction with the overall program.

**Clinician-specific assessments:**

Demographics form

**Assessment Quality Assurance.** The CAPS-5 and SCID-5 will be administered by assessors who have at least MA-level education background. IEs will be trained to reliability by Dr. Sloan as part of the ongoing training process in her lab. After achieving gold-standard reliability, assessors will continue to have ongoing supervision by Dr. Sloan throughout the course of the study. *Reducing assessor drift.* All assessments will be audio recorded and 15% of randomly selected interviews will be re-rated at regular intervals to establish interrater reliability. If reliability falls below criteria, IEs will be retrained.

**Data Management.** All study data will be entered into SPSS database, which will be housed on a secure network server accessible only by project staff. SPSS software is provided by the NC-PTSD and the license fees are paid by the NC-PTSD. The PI will check all data on the same day as entry to ensure completeness. Any incomplete data will be brought to the attention of the assessor and/or therapist and every effort will be made to complete ratings. Field parameters will be specified such that suspect or missing values are either disallowed or flagged for the immediate attention. Prior to data analysis, all data will be cleaned and rechecked for accuracy before conducting data analysis. Three times per year, blinded data will be compiled and reviewed by the PI and Co-I's to ascertain overall completeness and issues requiring clarification, as well as for purposes of providing information to the data safety and monitoring board. Files will be destroyed according to the VA Record Control Schedule.

#### **Power analysis:**

Given the aims and scope outlined here, the present study is considered preliminary. It will provide pilot data to assess the feasibility and preliminary effectiveness of the BFI. The use of repeated measures increases our ability to detect significant relationships. Our results will inform next steps in the investigation of the effectiveness and implementation of the BFI, including a fully powered study examining the BFI in comparison to an established family-based treatment in a routine VA clinic.

#### **k. Human Studies Section**

##### **1. Risks to the Subjects**

###### **a. Human subjects involvement, characteristics, and design**

Over the two phases of the study, the participant population is to be composed of 48 Veterans and family members. Veterans will be recruited on the basis of the presence of a current diagnosis of PTSD; family members will be adult relatives of the Veterans. These individuals will be recruited on a volunteer basis. As indicated in the Method section, inclusion criteria for Veterans are: (1) Currently enrolled in the VA Healthcare System; (2) meets current criteria for DSM-5 PTSD; (3) 18 years of age or older; (4) has an eligible family member who is willing to participate; and (5) beginning a course of Cognitive Processing Therapy (CPT) or Prolonged Exposure (PE) at VA Boston. Inclusion criteria for family members are: (1) Spouse/significant other, adult child, parent, sibling, or other relative of the Veteran; (2) currently has substantial daily or weekly contact with the patient; (3) 18 years of age or older.

Exclusion criteria for Veterans and family members are: (1) Presence of current unstable bipolar disorder, past or present psychosis, organic mental disorder, or significant cognitive impairment (standard cut-off score of <14 on the Mini Mental Status Examination-Brief Form (Folstein, Folstein, & Fanjiang, 2001)); (2) clear and current suicidal risk (assessed via the MINI-Suicide Module (Sheehan et al., 1998)); (3) current moderate or severe substance use disorder, and (4) current participation in family-based therapy/couples-counseling.

Only individuals who provide written informed consent will participate. A participant may withdraw his or her consent at any time and without prejudice. A clear and detailed explanation will precede all procedures. At the beginning of the first session participants will be fully informed about their condition assignment (BFI during Phase I; random assignment to BFI or no BFI during Phase II). Participants will also be informed that they are free to withdraw from the study at any time without any consequences. It will be clearly explained to all

participants that a decision by either the Veteran or the family to withdraw from this study will not affect the Veteran's individual CPT or PE treatment in any way.

At the conclusion of the study, an in-depth debriefing will explain all procedures and hypotheses, and answer any remaining questions. The debriefing will be conducted at the final follow-up assessment session. Participants will be told the exact nature of the study cannot be revealed to them until completion of the follow-up visits to reduce any bias in the results. Any participant withdrawing early from the experiment will be provided with a debriefing at the time of withdrawal.

This application also involves clinician participants currently working in a VA Boston mental health clinic and regularly providing CPT and/or PE ( $n \leq 20$ ). This part of the proposed study involves: (1) Conducting qualitative interviews with providers regarding family-inclusive PTSD treatment; (2) providing training to providers in the delivery of the BFI; (3) collecting recordings of BFI sessions for the purposes of training and measuring fidelity; and (4) notes and recordings from supervision. Clinicians administering the BFI in Phase II will be asked to complete qualitative interviews at posttreatment and turn in audio recordings of sessions. Data in the form of ratings of digital audio recordings of BFI sessions will be collected from the clinicians to monitor their in-session use of the BFI and assess modifications/adaptations to the protocol. These digital audio recordings will either be hand-delivered to the PI (on the recording device) for her to upload onto a secure research drive, or the recordings will be uploaded to a subfolder on the research drive by the clinicians themselves. Each clinician will have access to a dedicated subfolder on the PI's research drive in which to deposit session recordings; these personal subfolders will also include any training materials or other relevant study information from the PI to the clinician. Clinicians will be therapists who are providers in the VA Boston Healthcare System. Thus they will be over 18, as they will need to have completed their training to become therapists.

#### **b. Sources of research materials**

All information pertaining to this project (e.g., screening forms, questionnaire data, recordings of assessment sessions and BFI sessions for all participants) will be held in the strictest confidence and will be kept in locked files located within the PI's locked office at the National Center for PTSD (NCPTSD) (or, during construction on the 13<sup>th</sup> floor of Building 1 in JP, in a secure basement storage area appropriate for materials containing PII). Data will be available only to individuals directly involved with the project. Under no circumstances will individually identifiable data be released to anyone without written consent of the participant. Results will be published as group findings only. Experimental results will be discussed with the participant at their request.

Additionally, clinician-related data collection will include surveys and digital audio recordings of BFI sessions and interviews. Notes will be taken at meetings with clinicians during training and used for research. Audio recordings of BFI sessions will be obtained and will be rated using a standardized rating instrument by an adherence rater. Interviews will be reviewed and coded. Veteran symptom inventories and feedback forms will be collected for the purposes of the study. All data obtained in the study will be used exclusively for the purposes of the proposed research.

#### **c. Potential Risks**

**Intervention:** Some risks are associated with the administration of psychosocial interventions. The primary risk is the evocation of uncomfortable levels of anxiety or other emotions during the sessions. Some participants may find sessions or assignments stressful and react to them with anxiety. We have no reason to anticipate that these potential negative reactions will be of any greater magnitude than would be experienced in standard family-inclusive interventions.

**Recording:** Some participants may feel uncomfortable about the assessment, intervention, and interview sessions being recorded. However, this will be a required procedure. The purpose of the recording will be explained, confidentiality will be respected, and both informed consent and authorization for recording will be obtained as per requirements put forth by the Healthcare Information Portability and Accountability Act

(HIPAA). Recordings will be marked only by subject identification codes and stored on a password-protected research drive.

**Self-Report Measures and Assessor Ratings:** No risks are seen associated with these assessment procedures other than discomfort associated with the recording. These will be handled as described above for recording of assessment and BFI sessions.

**Clinician Data:** The major types of risk stemming from study participation include the discomfort of revealing personal information and opinions during surveys or interviews, and an unforeseen breach of confidentiality, which could affect employment. Every effort will be made to minimize this risk. Providers who participate will experience risks associated with the evaluations and monitoring of the effects of training on their ability to use the BFI. The major types of risk stemming from study participation include: the discomfort of revealing personal information on the surveys or interviews and discomfort at having their in-session behaviors evaluated and monitored to assess their ability to adhere to the protocol.

## **2. Adequacy of Protection Against Risks**

### **a. Recruitment and consent procedures**

Following the recruitment procedures used in recent clinical trials within BSD, we plan to recruit participants from various specialty clinics at VABHS. Patients will be recruited in these clinics by providing clinic staff and directors information about the study and placing study advertisements around VABHS. A recent PTSD trial using this technique was able to randomize 3 participants per month. Given that the criteria are not very stringent for the proposed study, we expect a good flow of recruitment. The study announcements will state that the free family intervention is part of a research study that is available to qualified individuals. Interested individuals will be instructed to call for further information.

In accordance with HIPAA regulations, written informed consent will be obtained from each participant after a thorough explanation of procedures by a project staff person and the opportunity for the participant to ask and receive answers to questions. Participants will be informed of the nature of the investigation, the types of assessments and treatments involved, alternative treatments, and the potential risks involved in participation and will be asked to sign an informed consent statement prior to participating in the proposed study. In addition, the participant will receive an explanation of how information related to their case will be handled including all parties involved, data management, and plans to publish data in group format without identifying information. Participants will also be informed that if suicidal intentions are disclosed confidentiality may be broken in order for protective measures to be taken. See Section 5 (Data Safety and Monitoring Plan) for specific information on assessment of suicidal information from participants and at what point action(s) would be taken.

To prevent clinic staff from feeling pressure to participate, the following measures will be taken: Several clinics that commonly treat PTSD (e.g., the PTSD Clinical Team, Women's Stress Disorders Treatment Team, General Mental Health, Center for Returning Veterans) and employ multiple clinicians (more than 5) will be contacted at the time of recruitment and informed of the option to participate. It will be made clear that surveys and interviews assessing information that is gathered during the study will not be shared with the administration (other than in the prepared research report, which will not disclose participant name or identifying characteristics). Providers who participate will receive a thorough description of study-related procedures, will have the opportunity to ask questions, and will provide informed consent. Providers who participate by providing the intervention, and/or completing surveys and interviews all will be asked to provide informed consent. Interview, survey responses, and competence and adherence data collected will not be made available to employers or become a part of their employment records and will remain confidential.

### **b. Protection against risk**

1. We will carefully screen to identify individuals whose risk for potential adverse outcomes is elevated were they to participate in the proposed research. Such individuals will be excluded from the study. As an

example, an actively suicidal person would be excluded from study participation and appropriate clinical treatment or referrals provided.

2. Clinical staff will be trained to cope with any anxiety/distress experienced by participants during the assessments and intervention. Staff will also monitor assessment items that ask about risk of suicide or current domestic violence at each timepoint. These items will be reviewed immediately upon completion, and participants who endorse elevated risk of suicide or current domestic violence will meet with the PI for further assessment. See Section 5b ("Safety monitoring plan") below for details of the standard procedure for suicidal risk. For current domestic violence, the PI (in consultation with a licensed clinical supervisor on site) will assess risk and provide the participant with clinical and community referrals as needed.

3. Careful monitoring of participants during study participation will be conducted by the project staff. Participants will be monitored for any increase in symptoms as the study progresses. Each participant will see the same clinician for each of their treatment or intervention visits (in the case of Veterans, their same usual care clinician. In the case of family members, the same BFI clinician), and the same assessor for each assessment occasion when appropriate. Following the clinical trial policy of the VA Boston Healthcare System, all participants will be given an emergency number to call in case of an emergency. This number will be the psychiatry on call system of the VA Boston Healthcare System.

4. Participants will be instructed to contact study personnel at any time (including during the follow-up period) in the event of worsening symptoms. Participants whose clinical condition has deteriorated will be removed from the study and given appropriate clinical care. See DSMP for details.

5. Veterans will be under treatment with clinicians at the VA Boston Healthcare System, and thus will be monitored by their clinicians and will be provided with appropriate referrals as necessary at the end of their PTSD treatment. Family members failing to benefit from the study intervention will be provided with appropriate clinical care and referrals. The exact nature of these referrals will be determined by the judgment of clinicians and supervisor familiar with the specific participant and may include services delivered by the Social Work Service of VA Boston or other community resources.

6. As in any type of treatment or clinical research program, participants' (those receiving interventions and all clinician participants) confidentiality must be carefully guarded and respected. All data with identifying information will be stored in locked files or password-protected computer servers. Data being analyzed will be identified by subject codes, and identifying information will be removed. The identity of participants will not be revealed in the presentation or publication of any results from the project. All personnel working on the project will be educated about the importance of strictly respecting participants' rights to confidentiality and will have completed several training courses including proper practice in accordance with HIPAA regulations, protection of human subjects, and computer security.

### **3. Potential Benefits of the Proposed Research to the Subjects and Others**

There is no direct benefit to participants who enter this study, although some may experience relief from PTSD symptoms, decreased avoidance, decreased conflict, and increased quality of life.

The clinician participants may receive benefit from the training in a new brief family intervention, from access to expert consultation on the intervention, and/or by providing feedback about the potential barriers that require addressing within the mental health clinics. Providers who participate in the treatment portion of the study will receive free training in a new psychotherapy intervention, and this training will also be made available to clinicians who would like the training but do not wish to provide the intervention in the context of the study. Over the longer term, they may also benefit professionally (e.g., future job opportunities at agencies that value family-inclusive approaches to treatment) from the training. Consequently, the potential risks of participation in the study are outweighed by the potential benefit to the participants.

### **4. Importance of the Knowledge to be Gained**

PTSD is a significant public health problem, with national lifetime prevalence rates of 8%(Kessler et al., 1995) and estimated rates in Veterans of the current conflicts in Iraq and Afghanistan of 13-20%(Kok et al., 2012). Family members may serve as a unique resource that can be harnessed to improve outcomes for PTSD treatment; social support is one of the most important predictors of the development and maintenance of

PTSD(Ozer et al., 2008), and family members may provide substantial practical and emotional support for treatment. However, relatives may also inadvertently behave in ways that contribute to the maintenance of the disorder(Erbes et al., 2008). The proposed study will examine a brief family intervention (BFI) delivered in conjunction with individually-delivered trauma-focused treatment.

## **5. Data Safety and Monitoring Plan (DSMP)**

**a. Data Monitoring Plan.** Data will be collected using standardized forms and will only be identified using the participants' ID number (no names or identifying information will be on the forms). A username and password is required to gain access to the network server, permission is needed to access the data drive, and a separate password is needed to gain access to the database. Data will be stored on a VABHS server (VHABOSCLURES1) and is backed up nightly; no data will be stored on a hard drive.

The codes that link the names of participants and their ID numbers will be kept confidential by the PI in a secured cabinet located within the PI's office (JP campus, room 13B-60) (or, during construction on the 13<sup>th</sup> floor of Building 1 in JP, in a secure basement storage area appropriate for materials containing PII). Collected data forms will be in a locked file cabinet located in the PI's office (or, during construction on the 13<sup>th</sup> floor of Building 1 in JP, in a secure basement storage area appropriate for materials containing PII). These data are accessible to the PI and personnel working on the project. Data will be entered electronically by trained staff, and data entry discrepancies will be corrected by the data entry supervisor based on source documents. The quality of the data will be monitored quarterly. Data will be securely transmitted using VA approved methods.

Audio recordings will be captured using Philips recorders with FIPS 140-2 validated encryption. Recordings may be obtained while study staff are teleworking; in these cases the recorders will be stored in the home in a locked cabinet/drawer that is only accessible to the study staff member. Recorders will be hand-carried to the VA as soon as it is feasible and safe to do so, at which point the recordings will be uploaded to the PI's personal research drive behind the VA firewall and deleted from the recording device.

The primary outcomes measures will be CAPS-5 total scores and ratings of homework completion (from the Homework Completion Scale), and number of sessions attended/dropout. Data quality will be monitored by inspection of the completed forms by the research assistant and any problems detected will be discussed with the PI. All assessors will be fully trained on the assessment measures, per the usual training procedures within BSD. Adherence to the intervention will be monitored using recordings of sessions and weekly supervision, as described previously. If diagnostic and/or intervention drift is observed, staff will be retrained until acceptable reliability is reached.

**b. Safety Monitoring Plan.** In the proposed study we will use the FDA definition of adverse events (AE) and serious adverse events (SAE). Any SAE, whether or not related to the study intervention, will be reported immediately to the IRB. In the event that a participant either withdraws from the study or the PI decides to discontinue a participant due to an SAE, the participant will be monitored by the PI via ongoing status assessment until (a) a resolution is reached (e.g., the problem has resolved or stabilized with no further change expected), (b) the SAE is determined to be clearly unrelated to the study intervention, or (c) the SAE results in death. Outcomes of SAEs will be regularly reported to the IRB. A summary of the SAEs that occurred during the previous year will be included in the annual IRB renewal. Suicidal ideation and AEs will be formally assessed at baseline and at all other assessment visits (see below for detailed information regarding assessment of suicidal ideation).

Participants will be informed that the interim results of the study will not necessarily be revealed to them, even if there is a suggestive trend in favor of the treatment, so as to maintain the scientific integrity of the study(Slutsky & Lavery, 2004). During the first in person screening, potential participants will undergo a comprehensive screening to determine their eligibility for, and safety for, participation in the study. Attention will



be paid to current suicidal ideation. Individuals who report imminent risk will be excluded from participation in the study and will be provided with appropriate clinical referrals.

**b.1. Assessment of suicidal ideation:** During the course of the study the clinician-administered MINI suicide module will be used to thoroughly assess participant suicidal risk and distress beyond what would be expected in treatment for trauma. The MINI suicide module consists of 9 questions related to suicidal ideation and behaviors, with possible scores ranging from 0 to 53. Low suicide risk is defined as 0-8 points, moderate suicide risk is defined as 9-16 points, and high suicide risk is defined as scoring 17 or greater. The MINI suicide module includes clear guidelines for determining suicide risk, and requires approximately 10 minutes to administer. Individuals will be excluded from enrolling in our proposed trial if they score 17 or higher on the MINI suicide module at the initial assessment. Individuals who are excluded will be provided with appropriate clinical referrals. The PI will follow up with each of these individuals within one week to make sure they have connected with appropriate clinical care.

Additionally, if at any point during the study (either baseline or follow-up) a participant describes a clear intent or inability/unwillingness to develop and follow a Suicide Prevention Safety Plan, which is a VA standard of care, then they will be terminated from the study and the crisis will be managed. Specifically, staff will immediately locate Dr. Sloan, who is a licensed psychologist, or another licensed psychologist, who will follow standard VA suicide prevention and risk management procedures. A licensed clinical psychologist will always be on-site when assessments are conducted. The psychologist will intervene by (a) following up with direct questions about suicidal behaviors, (b) assessing mental status by asking about psychotic symptoms, mood symptoms, and drug and alcohol use, (c) scheduling extra contacts if necessary, emphasizing problem solving, (d) helping the participant to generate short-term objectives, and (e) collaboratively developing or refining a Safety Plan using the VA's comprehensive Safety Planning template and manual. The plan will address what actions need to be taken in the succeeding days to solve the problems that precipitated suicidal behavior. The plan will also address the use of voluntary and involuntary hospitalization, if necessary. In addition to these formal assessments, all participants will be given the number of the on-call psychiatry service at VA Boston Healthcare System and informed that they should call this number after normal business hours in the event that they are feeling suicidal and/or distressed, as well as the National Suicide Prevention hotline number, which is a 24-hour service with a specific line dedicated to Veterans. During business hours the participants will be instructed to contact the PI. Should a participant call to indicate suicidal risk, then the previously described intervention plan will be followed. All Veterans in the study will also be under non-study care through the VABHS, and will be monitored as appropriate by their individual clinicians.

Veteran participants will be administered the MINI-Suicide module at baseline and at each follow-up assessment. Family members will be administered the MINI-Suicide module at the baseline assessment; those family members who score a 0 at baseline on the MINI-Suicide module will not be reassessed at future follow-up points. However, any family members that score  $\geq 1$  baseline will continue to have the MINI administered at follow-up assessments to monitor risk. If at any point during these follow-up assessments a family member indicates that they are experiencing high levels of suicidal thoughts, study staff will proceed with the steps outlined above (e.g., further assessment by a licensed psychologist of the intensity of thoughts, assessment of any related behaviors, collaborative completion of a Safety Plan, scheduling of additional contacts in the near term, and/or potentially a voluntary or involuntary hospitalization, as determined by the licensed psychologist).

In the event that a participant experiences high distress (i.e. exacerbated symptoms) but without any suicidal ideation or threat, then the PI will intervene by asking direct questions about the nature and causes of the distress, conduct a symptom assessment, and schedule extra contacts (assessments) and/or work closely with the patient's other VA providers if deemed necessary. Veterans' PTSD care will not be constrained or limited in any way by their participation in the study; therefore, their individual clinicians will be free to make any appropriate treatment decisions in response to increased distress, including seeking hospitalization or another higher level of care, discontinuing PE/CPT and instead conducting supportive or crisis-oriented therapy, etc. Any such changes in treatment focus will be monitored and reported to the IRB as appropriate.

## **DATA ANALYSIS.**

*Data management:* All clinician-administered and self-report questionnaire data will be entered into the database by the Research Assistant (RA) on the same day of administration to ensure completeness. All data will be cleaned and rechecked for accuracy before being exported into the appropriate program (e.g., SPSS, MPlus, and NVivo) for analysis. Data collected via mEMA will be continuously available via the secure cloud-based storage system and accessible via a unique access site available only to study staff.

*Overview of data analysis:* Quantitative data analysis will be performed using MPlus and SPSS, and NVivo management software will be used for qualitative data. Prior to full data analysis, the balance of randomization will be checked and unbalanced factors between groups will be controlled for in subsequent analyses. Similarly, all major variables will be assessed for skewness and outliers, and in cases where parametric analytic assumptions are violated we will use transformations. Preliminary analyses will consist of descriptive statistics by assessment period. All quantitative outcomes will be tested at a two-sided  $\alpha=.05$  level.

*Data checking:* Standard data checking procedures will include checking forms for missing data, double entry with discrepancy resolution, daily back-up copies of computer files, and examination of key variables for skewness, variability, missing data, and outliers. Data will be transformed to achieve normality if needed. If any outcome variable is too zero-inflated to allow for transformation, it will be analyzed with logistic regression or generalized estimating equation techniques (appropriate for this small pilot study).

*Missing data:* We will make every effort to retain participants, but as treatment engagement is a key outcome of the present study we will also carefully tabulate and report dropout rates and patterns in the present study, including exact timing of dropout. Multilevel regression models will be used to evaluate treatment outcomes; this approach is robust to missing data and is considered "state of the art" for use with unbalanced data sets due to treatment dropout (Schafer & Graham, 2002). There are also several methods for correcting biases due to missing data when using a multilevel regression approach (e.g., pattern-mixture modeling).

*Power analyses:* Determining sample sizes for multilevel models is a complex issue and "rules of thumb" are disputed (Maas & Hox, 2005; Mok, 1995). Furthermore, "effective" sample sizes in MLMs (as opposed to nominal sample sizes) will vary according to the model's predictors (Bickel, 2007). Given the aims and scope of this funding mechanism, the present study is considered preliminary. It will provide pilot data to assess the effectiveness of the BFI as well as exploring the proposed mechanisms of action. The use of repeated measures increases our ability to detect significant relationships. Our results will inform next steps in the investigation of the effectiveness and implementation of the BFI, including a fully powered R01 application to examine the BFI in comparison to an established family-based treatment in a routine VA clinic.

### **Defining key concepts for analyses:**

*Treatment dropout:* Consistent with past trials of CPT and PE, treatment dropout will be defined by ending treatment prior to the allocated treatment period. In the case of CPT full treatment duration is 12 sessions, while in the case of PE full treatment duration is at least 8 sessions and the concomitant agreement of the therapist that an appropriate ending place has been reached. Any Veteran who ends treatment prior to these milestones will be considered a dropout.

*Feasibility/Acceptability:* In the current study, feasibility and acceptability will refer to the evaluation and analysis of recruitment, randomization, retention, treatment adherence and fidelity, and use of the BFI with the families of Veterans beginning PTSD treatment. These variables help to determine the acceptability of the treatment and procedures for future studies.

**Aim 1:** Collect qualitative and quantitative data on feasibility and acceptability of the BFI in a routine care setting.

**Hypothesis 1:** Levels of feasibility and acceptability of the BFI among Veterans, family members, and clinicians will be high and comparable to levels found in the previous efficacy trial in OCD.

**Hypothesis 1 analytic strategy:** We will examine the feasibility and acceptability of the BFI by examining rates of BFI recruitment and refusal, as well as level of drop-out from the BFI sessions. These data will be benchmarked to previous BFI efficacy data. We will also assess the success of the clinician training program by reviewing rates of clinician recruitment and attitudes reported on the EBPAS-50. Furthermore, we will conduct detailed in-person, semi-structured exit interviews with Veterans, family members, and clinicians in order to collect qualitative data. These data will allow us to contextualize our findings related to the protocol's fit in this novel setting and its acceptability to Veterans, families, and providers. The qualitative interviews will provide more nuanced feedback regarding the perceived fit of the BFI, and further identify necessary modifications to the protocol (see below for qualitative analytic strategy).

**Aim 2:** Assess the BFI's effects on symptoms as well as potential mechanisms of change using multilevel modeling.

**Hypothesis 2a:** Veterans whose family members receive the BFI will show lower levels of PTSD symptoms at post-treatment and greater engagement throughout treatment compared to control Veterans.

**Hypothesis 2b:** Family members who receive the BFI will show more active support for treatment and less accommodation than control family members.

**Hypothesis 2c:** Family members' active support for treatment will be positively related to Veterans' treatment engagement, and Veterans' levels of perceived criticism will be negatively related to their treatment engagement

**Hypothesis 2a-2c analytic strategy:** Multilevel regression (i.e., hierarchical linear modeling (HLM), growth curve analysis, etc.) will be used to evaluate change in continuous outcome variables (Singer & Willett, 2003). Multilevel regression is a robust method for analyzing change over time, with excellent options for handling missing data, powerful estimation abilities, and flexibility of modeling. This approach will allow for the analysis of an intent-to-treat sample in line with CONSORT guidelines (Altman et al., 2001). For our analysis of change in the variables of interest we will use a multilevel framework in the Mplus program to model time as a Level 1 predictor of the outcome variables (baseline and weeks 6, 12, and 16). We will first specify an unconditional model to ascertain the shape of the change trajectories (e.g., linear versus quadratic change over Time), and will subsequently specify conditional multilevel models to examine treatment effects and the impact of other variables as predictors of individual differences in change. We will also calculate the Cohen's *d* effect size and 95% confidence intervals in order to provide a benchmark for future trials.

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