Official Title: A Novel Posttraumatic Stress Disorder Treatment for Veterans with Moral Injury

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Study Protocol

Background: The prevalence of PTSD is estimated to be 12-15% in returning combat veterans,[1-3] and PTSD is now the most common mental health diagnosis among the youngest generation of veterans who use Veterans Health Administration care (55%),[4] Furthermore, veterans that have experienced trauma related to killing in war have high rates of suicide and more severe PTSD symptoms than those reporting other types of trauma(s).[5-7] As a result of killing in war, individuals may experience moral injury, which is defined as, "perpetrating, failing to prevent, bearing witness to, or learning about acts that transgress deeply held moral beliefs and expectations."[8] A recent study found that PTSD and moral injury were distinct constructs with unique signs and symptoms,[7] and preliminary evidence indicates that the feelings of guilt and anger that characterize moral injury associated with killing may contribute to worsening symptoms over the course of existing treatments for PTSD.[9] For these reasons, the development of targeted moral injury interventions is critical.

We have developed a treatment for moral injury called Impact of Killing (IOK), that is based on focus groups, quantitative studies, a moral injury framework, interviews with clinicians, and consultation with PTSD experts.[10] In our randomized, controlled pilot trial of IOK in veterans with PTSD, we found that compared to the wait-list control group, the IOK group experienced a significant improvement in PTSD symptoms, general psychiatric symptoms, and quality of life functional measures. [10]

Objectives: The first aim of this project was to assess the efficacy of an individual treatment for PTSD stemming from moral injury called IOK. The primary outcome measure assessed self-reported psychosocial functioning (World Health Organization Quality of Life-BREF; WHOQOL-BREF).[11] The secondary outcome measures examined clinician-assessed PTSD severity (Clinician Administered PTSD Scale for DSM-5; CAPS-5)[12] and self-report measures of PTSD (PTSD Checklist for DSM-5; PCL-5)[13], guilt (Trauma-related Guilt Inventory; TRGI)[14], and other mental health symptoms (Brief Symptom Inventory; BSI).[15] Our second aim was to determine whether IOK gains made by veterans in treatment were durable, as measured by a six-month follow-up assessment of the self-report outcomes (i.e., WHOQOL-BREF, PCL-5, TRGI, and BSI).

Design: The study was a parallel design, randomized, controlled trial to test the efficacy of IOK, compared to a present-centered therapy (PCT) control condition. PCT has been used as a

comparison treatment in prior PTSD research trials.[16] To evaluate the durability of IOK gains, veterans also participated in a six-month follow-up visit to complete primary and secondary self-report outcome measures.

Methods: The study was managed by the principal investigator and research staff at the San Francisco VA Health Care System (SFVAHCS) and all recruitment, screening and data collection procedures were conducted by researchers at the James J. Peters VA Medical Center (JJPVAMC) in the Bronx, NY or the Durham VA Medical Center (DVAMC) in Durham, NC. Veterans between 18-82 years of age living in the continental U.S. were recruited through direct mailings, advertisements, and referrals from VA clinicians or other VA research studies. Interested veterans participated in an initial brief phone screen to ensure they met preliminary criteria. Those who passed the phone screen were invited to an in-person or video appointment to learn more about the study and complete consent procedures prior to additional screening. Participants completed demographic and medical history questionnaires, and a clinician-administered, mental health diagnostic interview (Structured Clinical Interview for DSM 5 [SCID-5][17] and CAPS-5). These diagnostic interviews were repeated at post-treatment. Veterans that passed the diagnostic interview were randomized to treatment. Study clinicians were clinical staff at one of the three study sites (SFVAMC, JJPVAMC, DVAMC).

A total of 100 veterans with moral injury were randomized 1:1 to either the IOK or PCT control arm within strata therapist treatment site (one of three locations) within randomly generated block sizes (4 and 6). IOK is a ten session individual psychotherapy, with 60- to 90-minute appointments conducted in-person or by video. PCT was matched for number and duration of treatment sessions. Primary and secondary self-report outcome measures were completed at baseline, mid-treatment, post-treatment and at six-month follow-up and the clinician diagnosed secondary outcome of PTSD severity (CAPS-5) was completed at baseline and post-treatment.

All participants randomized to treatment were included in the intent-to-treat analyses. Twelve of these individuals dropped out during treatment and 88 individuals completed study treatment. Of the treatment completers, one individual chose not to complete the self-report measures (i.e., WHOQOL-BREF, PCL-5, TRGI, and BSI) at the post-treatment time point and a different individual opted out of the post-treatment diagnostic interview (CAPS-5). As such, complete data for 87 responses through the post-treatment time point were included in the analyses.

Further, five of the 88 individuals that completed treatment were lost to follow-up and analyses of these data included complete data for 83 participants.

Statistical Analysis Plan: The primary and secondary outcome variables were analyzed with separate linear mixed models on the intent-to-treat sample, with participants as a random effect and fixed effects for treatment group (IOK, PCT), time point (baseline, mid-treatment, post-treatment, six-month follow-up), therapist treatment site (SFVAHCS, JJPVAMC, DVAMC), and the group-by-time interaction. Time point was treated as a categorical variable to avoid assumptions of linearity or any other functional form for outcome variables over time. Treatment effects were defined as the difference between treatment groups at the post-treatment time point, after adjusting for therapist site. IOK treatment durability was assessed using simple marginal contrasts comparing outcomes at the post-treatment to the follow-up time point.

Results: A total of 100 participants were randomized to study treatment and included in the intent-to-treat analysis (IOK=49; PCT=51). Participants ranged in age from 28 to 82 years (M=48.4 years); 98% were male (n=98) and 2% were female (n=2); 68% were Caucasian (n=68), 25% were Black/African American (n=25), 1% were Asian (n=1), 1% were American Indian or Alaska Native (n=1), 4% identified as multiracial or other (n=7), and 1% did not report their race (n=1). A total of 19% were Latino/Hispanic (n=19).

Participants randomized to IOK (n=49) reported statistically significant improvement on self-report measures of PTSD severity (p=.006) and guilt (p=.043) compared to veterans that were assigned to PCT (n=51). Furthermore, participants in the IOK arm continued to report greater improvement in self-reported PTSD (p=.008) and guilt (p=.028) at the six-month follow-up time point relative to the PCT arm. These results indicate that IOK treatment gains seen at post-treatment were maintained during the follow-up period. Further, veterans in the IOK group reported greater improvement in general mental health symptoms at six-month follow-up (p=.016) compared to the PCT group. There were no differences between groups on the primary (WHOQOL-BREF) or secondary (CAPS-5) outcomes, although both groups improved on these measures.

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