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## The impact of prolonged exposure on PTSD symptoms and associated psychopathology in people living with HIV: A randomized test of concept

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### Abstract

People living with HIV (PLWH) report elevated levels of posttraumatic stress disorder symptoms (PTSS) and associated comorbidities. The present study tested the efficacy of prolonged exposure (PE) at reducing PTSS, depression, negative posttraumatic cognitions, and substance use in PLWH. Participants were randomly assigned to receive PE ( $n = 40$ ) or to a weekly monitoring control group ( $n = 25$ ). Assessments occurred at baseline, post-intervention and 3-months post-treatment. Following the 3-month assessment, controls were offered the intervention. All PE recipients (whether originally from the PE or control group) completed a 6-month assessment. Intent-to-treat mixed model repeated measures ANOVAs were conducted through 3-months post-treatment; within group analyses were conducted through 6-months. PE recipients reported fewer PTSS and negative posttraumatic cognitions and were more likely to achieve good end-state functioning; gains were maintained at 6-months. No between-group differences emerged for substance use. Overall, results support the efficacy of PE in PLWH.

### Keywords

people living with HIV; prolonged exposure; posttraumatic stress disorder; depression; intervention

### Introduction

With the publication of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)[1], diagnosis with a life-threatening or terminal disease was first

recognized as a traumatic event that could lead to the development of posttraumatic stress disorder (PTSD). Since then, research has established that PLWH report some of the highest rates of PTSD observed for any medical trauma/diagnosis population (e.g., cancer patients, myocardial infarction, cardiac surgery, stroke, childbirth, miscarriage, abortion, *etc.*) [2]. Between 30–61% of PLWH develop HIV-related PTSD at some point in their lives from either a diagnosis of HIV, or from other issues related to the disease [3–6]. In addition, PLWH report disproportionately high levels of nonHIV-related traumatic experiences (i.e., childhood sexual and physical abuse, sexual assaults, parental neglect [7–9]), and rates of PTSD in general (from either HIV- or nonHIV-related events) ranging from 14–61% [3, 4, 10–13]. These percentages are significantly higher than reported rates of PTSD in the general population (7–10%) [14, 15].

To receive a diagnosis of PTSD, an individual must react with intense fear, helplessness, or horror after exposure to a traumatic event that involved actual or threatened death to oneself or others. Additionally, PTSD involves a host of symptoms generally categorized in the following three clusters: reexperiencing, avoidance and numbing, and hyperarousal [1]. Individuals who suffer from PTSD also display heightened risk of comorbid disorders (e.g., depression, anxiety) [14, 16, 17], suicidal ideation [17], impaired psychosocial functioning [18, 19], physical health complications [20, 21], and poor quality of life [21]. In addition, individuals with PTSD often have negative posttraumatic cognitions, such as negative thoughts about the self and the world, and self blame [22, 23].

PTSD may be particularly detrimental to PLWH; research has suggested that the course of HIV infection is susceptible to influence by psychosocial factors including PTSD [24]. It has been suggested that the presence of traumatic stress and depression may explain some of the variability in HIV disease course [24 – 29]. Both PTSD and depression have been associated with lower CD4/CD8 cell count ratios [12, 30], and HIV-related PTSD specifically has been associated with greater reporting of physical symptoms [31]).

PTSD may also indirectly impact disease course in PLWH through several mechanisms. PTSD symptoms of avoidance may lead PLWH to not adhere to medication regimens or to miss more doctors' appointments, as both of these events serve as reminders of their diagnosis [32, 33]. Avoidance symptoms may also prevent individuals from disclosing their HIV status to significant others (i.e., friends or sexual partners), which may have serious implications for the spread of the disease [33].

PTSD rarely occurs in a “pure” form and is often comorbid with depression; rates of PTSD/ depression comorbidity range from 35–50% [14, 29, 34–36]. Depression has been associated with faster HIV disease progression [14, 29, 37 – 39] and three times the risk of nonadherence to medical treatment regimens in a variety of medically ill populations [39]. Though it is difficult to isolate the unique effects of PTSD and depression on disease progression and adherence due to the high rates of comorbidity, results from a recent cross-sectional study revealed that depressive symptoms (as compared to PTSD symptoms and comorbid symptomology) had the strongest relationship to CD4 cell counts and medication adherence [41]. Similarly, Boarts and colleagues [37] found that both PTSD and depression

were associated with low medication adherence, but that depression, and not PTSD, predicted lower CD4 cell counts and higher viral load.

Substance use is also commonly comorbid with PTSD. PTSD rates range from 30–50% in substance abusers [42], and comorbidity rates of substance abuse/dependence in PTSD are high (up to 43%)[14, 43 46]. Further, HIV is associated with increased risk for substance use disorders, as alcohol and substance use disorders are between 2.5–7.5 times more prevalent in PLWH than in the general population [7]. Substance use alone is independently associated with faster disease progression, less than optimal medication adherence, failure of HAART medication regimens, and immune suppression [30, 47, 48], and comorbid PTSD/ substance use is associated with a greater decline in immune function and health status [11, 49, 50]. Taken together, PTSD, depression, and substance use independently and collectively confer a detrimental effect on HIV disease course, adherence to medication regimens, and negative health behaviors [30. 51].

Given the high incidence of post-traumatic distress and the negative consequences of PTSD and comorbid disorders, PLWH are in need of effective mental health interventions [9, 24, 52, 53]. Despite the demonstrated efficacy of psychotherapeutic interventions for depression [54 – 56], the majority of mental health needs, specifically regarding PTSD, are unmet in PLWH [9]. In a sample of female HIV patients seeking medical care, Martinez and colleagues [4] estimated that 78% of women with partial PTSD and 59% of women with full PTSD were not receiving treatment for their disorder. Additionally, Israelski and colleagues [57] reported that 43% of patients recruited from a primary care services system who met criteria for either depression, PTSD, or acute stress disorder were not being treated.

### **Prolonged Exposure therapy**

Prolonged exposure (PE) therapy, a form of cognitive-behavioral therapy, is considered the most appropriate first-line PTSD treatment [58 – 60]. To date, PE is the only empirically supported evidence-based treatment available for individuals with PTSD [61]. Research has demonstrated the efficacy of PE for the treatment of PTSD and comorbid symptoms across several controlled studies with varied trauma samples (for a review, see Powers and colleagues [62]). Recent research has suggested that the treatment of PTSS in substance-using individuals may consequently result in decreases in substance use, and PE may be beneficial for those who are substance dependent [63]. Further, in a recent state-of-the-science review, Nemeroff and colleagues [64] reported that the Substance Abuse and Mental Health Services Administration recommends PE for national dissemination, as it represents a model program for PTSD treatment. The superior efficacy of PE (as compared to cognitive restructuring and the combination of cognitive restructuring and PE) at producing improvements in good end-state functioning was also cited [64].

PE involves repeated imaginal exposure to the traumatic event (trauma reliving) and repeated in-vivo exposure to situations encountered in daily life that may be avoided due to the traumatic memory or PTSS [65]. Through habituation, the traumatic memory becomes incorporated into normal cognitive schemas which then prevent generalization of the traumatic memory to safe situations [66]. PE also involves systematic repeated confrontation with traumatic memories that serve to disconfirm negative posttraumatic cognitions [22]. PE

therapy has been found to be just as effective at reducing negative posttraumatic cognitions, depression, and general anxiety as PE combined with cognitive restructuring in a sample of adult female assault victims [22]. Despite the high rates of PTSD in PLWH, and the demonstrated efficacy of PE therapy in individuals with PTSD, no study to date has examined the efficacy of PE for PTSD in a sample of PLWH.

The present study aimed to test the efficacy of PE therapy at reducing PTSD symptoms in male and female PLWH in a small randomized controlled trial design. Further, given the lack of evidence concerning efficacious treatments for PTSD stemming from diagnosis/living with HIV, we assessed the efficacy of PE at decreasing PTSD symptoms both from HIV- and nonHIV-related traumas. We hypothesized that HIV- and nonHIV-related PTSS, depression symptoms, negative posttraumatic cognitions, and substance use would decrease over time for PE recipients. It was also hypothesized that participants receiving PE therapy would report significantly fewer PTSD symptoms regarding both HIV and nonHIV-related trauma compared to the control group. Further, we hypothesized that the PE group would report fewer depression symptoms, fewer negative posttraumatic cognitions, and lower levels of substance use than the control group. Additionally, we hypothesized that a higher percentage of PE versus control participants would meet criteria for good end-state functioning.

## Method

### Participants

PLWH were recruited between 2005 and 2008 from two social service agencies near Cleveland, OH. Eligible participants were fluent in English, met criteria for a likely diagnosis of PTSD as assessed through the self-report PTSD Diagnostic Scale (PDS [67]) and were currently taking antiretroviral medications for HIV. Exclusionary criteria included diagnosis of a psychotic disorder, current or previous diagnosis of schizophrenia, and current suicidal ideation. Of 99 PLWH screened for the study, 34 did not meet eligibility requirements (see Figure 1 for a flow diagram of participant progress). Thus, 65 (24 females and 41 males) eligible participants completed the baseline questionnaires. The sample at baseline consisted of 29 (44.6%) African Americans, 25 (38.5%) Caucasians, 4 (6.1%) Hispanics, and 7 (10.8%) individuals who identified with more than one race. The mean age was 46 years (Range: 31–61). Participants had been living with a diagnosis of HIV for approximately 13 years (Range: 13 months to 26 years) and were a low income sample, with 85% ( $n = 55$ ) of the participants earning below 20,000 dollars annually.

Thirty-four participants were randomly assigned to the PE treatment group, while 24 were assigned to the weekly monitoring control group. At the post-intervention assessment, 23 participants were retained in the PE group (32% drop-out rate) and 24 participants were retained in the control group (0% drop-out rate). At the 3-month follow-up 19 PE recipients were retained as were all the control participants.

After completion of the 3-month assessment, participants in the control group were given the opportunity to participate in the intervention; nineteen chose to receive the intervention. All participants receiving PE (whether they had originally been in the control group or not)

were assessed at 6-months post-intervention. Seventeen of the original PE participants were retained throughout 6-months (2 participants lost to follow-up between 3- and 6-months) and 13 (68.4% retention rate) of the original nineteen control participants who opted to receive the intervention were retained throughout the 6-month follow-up. Therefore, we were able to analyze data on 30 individuals (18 males and 12 females) through the 6-month follow-up.

At the post-intervention follow-up, a greater number of participants in the PE group dropped out of the study than participants in the control group ( $\chi^2(1, n = 65) = 11.38, P < .001$ ). Participants who dropped out of the study reported lower levels of PTSS in reference to the nonHIV-related trauma than participants who were retained at this time point ( $F(1,62) = 5.49, P = .02$ ). There were no significant differences in any other demographic or study variables between participants who dropped out and those who were retained at any time point. Further, drop-out rates did not differ between participants whose most distressing trauma was HIV-related compared to nonHIV-related.

### Study groups

**Prolonged Exposure**—Individual PE therapy sessions were conducted in the social service agency by one of two trained clinical psychology post-doctoral fellows. The treatment followed standard PE protocol [65] and consisted of 10 sessions (lasting between 90–120 minutes each) conducted twice per week for 5 weeks. The therapy was individually tailored to each participant (their most distressing trauma) and focused on HIV-related trauma for some, and nonHIV-related trauma for others.

**Weekly monitoring/wait list control group**—Participants assigned to the weekly monitoring/wait list control group continued with their standard visits to the social service agency, but were also contacted by their case manager once a week for the duration of the PE therapy to ensure that they were not experiencing any symptom exacerbation.

### Procedure

The study protocol was approved by the human subjects review boards of Kent State University and Summa Health System. Potential participants were initially approached about the study by their case manager at the social service agency. Interested participants completed the PDS [67] to determine eligibility for the study. Participants who likely met criteria for PTSD then met with a Ph.D.-level clinical psychology student who described the study in detail to them. Interested participants provided written informed consent. The Structured Clinical Interview with Psychotic Screen for the DSM-IV (SCID [68]) was then administered to ensure the presence of diagnostic levels of PTSD, including endorsing Criterion A, associated functional impairment, and the absence of any psychotic disorder or other exclusionary criteria.

The baseline assessment occurred within one week of this initial screening procedure. All eligible participants were administered the PTSD Symptom Scale-Interview (PSS-I) with regards to both HIV-related PTSD and the most severe nonHIV-related trauma. They then completed self-report baseline questionnaires including the Center for Epidemiological

Studies – Depression Scale (CES-D), the Posttraumatic Cognitions Inventory (PTCI), and a self-report scale assessing substance use over the past 30 days. Following this baseline assessment, participants were randomly assigned to the PE therapy or the weekly monitoring/wait list control group. The principal investigator (DLD) generated the allocation sequence using blocked randomization (4:3 ratio of experimental: control participants), and the graduate student conducting the assessments remained blind to group membership. Unequal numbers of participants were assigned to each group, as it was anticipated that the PE group would have a higher dropout rate. PE participants completed the self-report PSS at every other therapy session (i.e., 2, 4, 6, 8, and 10) to track symptom progression through therapy, and reported on substance use at the start of each therapy session.

All follow-up assessments were conducted at the social service agency by the same blind interviewer who conducted the baseline assessment. Participants completed the same questionnaire battery that was administered at baseline. Finally, all participants who received PE (the original PE group and the weekly monitoring/wait listed control group who elected to receive the intervention) also completed the same assessment 6-months post-intervention. Participants received \$25 for each assessment and \$10 for every intervention session they completed (up to \$100 total with an extra \$25 if they completed all of the intervention sessions).

## Measures

**Sociodemographics**—Standard demographic questions about age, gender, race/ethnicity, number of years living with HIV, sexual orientation (rated on a scale of 1–9 where 1 = exclusively homosexual/gay, 5 = bisexual, and 9 = exclusively heterosexual/straight), and income were administered at baseline.

**PTSD**—Participants completed the 17-item Posttraumatic Stress Diagnostic Scale [67, 69] at screening to determine whether they met likely criteria for a PTSD diagnosis. Participants were asked to rate the frequency (0 = not at all or only one time; 3 = five or more times a week/almost always) with which they experienced each of the 17 PTSD symptoms corresponding to the criteria in the DSM-IV within the past month. A likely diagnosis of PTSD was considered present if the participant endorsed at least one reexperiencing symptom, three avoidance symptoms, and two arousal symptoms. Diagnoses were verified at screening with the SCID with Psychotic Screen for the DSM-IV [68]. The SCID is a gold standard structured interview that allows interviewers to make psychiatric diagnoses based on DSM-IV criteria.

At each assessment participants completed the PTSD Symptom Scale-Interview (PSS-I [70]). The PSS-I is a 17-item semi-structured interview designed to measure the frequency and severity of PTSD symptoms. The total score is calculated based on the sum of the individual items. Internal consistency for the PSS-I was acceptable in our sample (HIV-related trauma baseline alpha = .81; Post-intervention = .89; 3-month = .86; 6-months = .84; NonHIV-related trauma baseline alpha = .81; Post-intervention = .93; 3-month = .86; 6-months = .78).

**Depression**—The Center for Epidemiological Studies – Depression Scale (CESD [71]) was administered to assess participants' level of self-reported depression symptoms within the week prior to assessment at all time points. The CES-D consists of 20 items summed to create a total score. The CES-D displayed acceptable internal consistency in our sample (baseline alpha = .71; Post-intervention = .76; 3-months = .77; 6-months = .84).

**End-state functioning**—End-state functioning represents a composite of psychological outcomes, and is typically computed from scores on measures of PTSD, depression, and anxiety [64, 72]; however, end-state functioning has also been computed from PTSD and depression scores alone [75]. Given relatively low rates of anxiety in PLWH, composite scores for good end state functioning were created based on reports of HIV-related PTSS, nonHIV-related PTSS, and depression. The criteria for good end-state functioning (yes or no) were calculated based on the following cut-off scores: 20 or less on the HIV-related PSS-I [59], 20 or less on the nonHIV-related PSS-I, and 16 or less on the CES-D [71].

**Substance Use**—A self-report substance use questionnaire was administered at each time point to assess the frequency (measured in # of days) of use of 11 different substances including alcohol, marijuana, cocaine, ecstasy, amphetamines, GHB, PCP, hallucinogens, rohypnol, ketamine, and heroin. At the baseline, 3- and 6-month follow-up assessments, frequency of substance use was assessed within the past 30 days. However, given that substance use was tracked during each PE therapy session to ensure no exacerbation of use, at the post-intervention time point (which occurred 1 week post-therapy), substance use was assessed over the past 7 days. Total frequency was obtained by summing the number of days during which substances were used.

**Posttraumatic Cognitions**—The self-report Posttraumatic Cognitions Inventory [23] was used to assess negative posttraumatic thoughts. Participants rated each of the 36 items based on how much they agreed or disagreed with the negative thought. This instrument yields a sum total score as well as three individual subscale scores: negative cognitions about the self, negative cognitions about the world, and self-blame. Higher scores on the PTCI indicate greater endorsement of negative posttraumatic cognitions. Internal consistency for the present sample was high (baseline alpha = .94; Post-intervention = .94; 3-month = .96; 6-month = .95).

## Data Analysis

**Preliminary Analyses**—Preliminary analyses were conducted with Statistics Package for the Social Sciences Version 16 (SPSS 2006). An alpha level of .05 (two-tailed) was used to determine significance in all analyses. In order to test for possible control variables, chi square analyses were applied between categorical variables (group, gender, race). One-way ANOVAs were conducted between categorical and continuous variables to examine group differences in age, time living with HIV, and sexual orientation. If significant differences emerged, these variables were used as covariates. Further, to test whether randomization was successful, one-way ANOVAs were conducted to determine whether the study groups differed on any demographic or study-related variables.

**Intent-to-Treat Analyses**—A series of mixed-model repeated measures ANOVAs were conducted to test whether PE was efficacious at reducing HIV- and nonHIV-related PTSS, depressive symptoms, negative posttraumatic cognitions, and substance use on the randomized sample from baseline to the 3-month follow-up. For these analyses, group (PE vs. control) was the between subjects factor and time of assessment was the within subjects factor. An intent-to-treat (ITT) method was used in order to remove potential bias due to participant attrition and non-compliance with the study protocol [76]. The conservative approach of last observation carried forward (LOCF) was applied, such that missing values at each assessment were replaced by the last known value reported by the participant. Therefore, between group analyses were conducted on the 65 participants ( $n = 40$  for the intervention group;  $n = 25$  for the control group) randomized to the original study conditions. In the presence of a significant group  $\times$  time interaction, post-hoc analyses were conducted in the form of one-way ANOVAs on the change scores between each time point.

To test whether the gains of PE therapy were maintained over the 6-month follow-up (non-randomized sample), within subjects repeated measures ANOVAs were conducted using data from the baseline, post-treatment, 3-month, and 6-month post-treatment assessments on outcomes of interest for all participants who received the PE therapy (including control group participants who later received PE). The sample size for this analysis consisted of 59 participants; the participants randomized to receive PE ( $n = 40$ ) and the original weekly monitoring/wait list control participants who opted to later receive PE ( $n = 19$ ). If a significant main effect of time emerged, pairwise comparisons within SPSS were conducted to determine which time points were significantly different from each other.

**Secondary Completer Analyses**—A series of mixed-model repeated measures ANOVAs were also conducted on participants who completed the entire study protocol. Between group analyses conducted on the randomized sample throughout 3-months consisted of 43 participants, and within group analyses throughout 6-months consisted of 30 participants. Finally, chi square analyses were conducted to determine whether groups differed in good end state functioning at the 3- and 6-month follow-up assessments.

**Missing data**—To include data from retained participants, missing values were imputed for less than 1% of missing data points.

## Results

### Preliminary Analyses

On average, participants reported experiencing 4.91 (standard deviation (SD) = 1.78) different types of prior trauma, and 34% of the participants reported that their most distressing trauma was related to their HIV diagnosis. Sixty-four of the participants reported experiencing both an HIV- and nonHIV-related trauma, and one participant only endorsed an HIV-related trauma. Baseline descriptive statistics for all study variables are presented in Table 1, and descriptive statistics for the outcomes at the follow-up assessments are displayed in Table 2. Results from chi square analyses revealed that the PE and control groups did not differ by gender or race. Results from one-way ANOVAs also revealed no significant differences between groups on age, time living with HIV, sexual orientation,



HIV-related PTSS, nonHIV-related PTSS, depression, posttraumatic cognitions, and substance use (see Table 1).

### Mixed Model Repeated Measures ANOVAs: ITT Analyses

After applying the LOCF method, mixed model (between and within group) repeated measures ANOVAs were conducted on HIV-related PTSS, nonHIV-related PTSS, depression, negative posttraumatic cognitions, and substance use. Inferential and descriptive statistics for all group x time interactions are displayed in Table 3. Results revealed a main effect of time for both HIV-related PTSS (Wilk's  $\lambda = .67$ ;  $F(2, 62) = 15.65$ ,  $P < .001$ ; partial  $\eta^2 = .34$ ) and nonHIV-related PTSS (Wilk's  $\lambda = .50$ ;  $F(2, 61) = 31.85$ ,  $P < .001$ ; partial  $\eta^2 = .51$ ) in that all participants demonstrated significant decreases in symptoms over time. This main effect was qualified by a significant group x time interaction indicating that PE participants experienced a greater decrease in HIV- and nonHIV-related PTSS than the controls. Post-hoc analyses revealed significant differences between baseline to post-intervention for HIV-related PTSS ( $F(1,63) = 8.54$ ,  $P < .01$ ) and nonHIV-related PTSS ( $F(1,62) = 9.98$ ,  $p < .01$ ). However, differences between baseline and 3-months were not significant.

A main effect of time was also revealed for depression symptoms, such that they decreased throughout the course of the study for all participants (Wilk's  $\lambda = .80$ ;  $F(2, 62) = 7.70$ ,  $P = .001$ ; partial  $\eta^2 = .20$ ). Results also revealed a trend towards significance for a group x time interaction, with PE participants experiencing a marginally greater decrease over time in depression symptoms. Post-hoc analyses revealed a significant reduction in depression symptoms from baseline to post-intervention ( $F(1,63) = 4.12$ ,  $P = .047$ ), but differences between baseline and 3-months were not significant.

Regarding posttraumatic cognitions, a significant main effect of time indicated that negative posttraumatic cognitions decreased throughout the study (Wilk's  $\lambda = .79$ ;  $F(2, 62) = 8.25$ ,  $P = .001$ ; partial  $\eta^2 = .21$ ). Further, a significant group x time interaction revealed that PE participants experienced a greater improvement in PTCI scores than control participants. Post-hoc analyses indicated significant differences from baseline to post-intervention ( $F(1,63) = 5.93$ ,  $P = .02$ ), but results were not significant through 3-months.

Results the outcome of substance use, a mixed model repeated measures ANOVA conducted on the baseline and the 3-month follow-up assessment revealed no main effect of time (Wilk's  $\lambda = .10$ ;  $F(1, 63) = .23$ ,  $P = .63$ ; partial  $\eta^2 = .00$ ) or group x time interaction.

### Mixed Model Repeated Measures ANOVAs: Completer analysis

The following analyses were performed on the 43 participants who were retained throughout all phases of the study. Inferential and descriptive statistics for the group x time interactions are displayed in table 4. Results from mixed model repeated measures ANOVAs replicated the ITT findings regarding PTSS such that reductions in HIV-related (Wilk's  $\lambda = .34$ ;  $F(2, 40) = 38.94$ ,  $P < .001$ ; partial  $\eta^2 = .66$ ) and nonHIV-related PTSS (Wilk's  $\lambda = .20$ ;  $F(2, 39) = 77.99$ ,  $P < .001$ ; partial  $\eta^2 = .80$ ) occurred for all participants throughout the course of the study. Further, significant group x time interactions revealed that PE participants

experienced a greater decrease in HIV- and nonHIV-related PTSS than control participants. Post-hoc analyses indicated significantly larger reductions in HIV- and nonHIV-related PTSS between baseline and post-intervention ( $F(1,45) = 37.21, P < .001$ ;  $F(1,44) = 50.62, P < .001$ ) and between baseline and 3-month follow-up PTSS scores ( $F(1,41) = 16.51, P < .001$ ;  $F(1,40) = 19.70, P < .001$ ) in PE participants versus controls, respectively.

Results also revealed that depression symptoms were reduced throughout the duration of the study (Wilk's  $\lambda = .69$ ;  $F(2, 40) = 8.85, P = .001$ ; partial  $\eta^2 = .31$ ), and this main effect was qualified by a significant group x time interaction revealing that PE participants demonstrated greater improvements in depression symptoms over time as compared to control participants. Post-hoc analyses indicated larger decreases in depression for PE participants than for control participants from baseline to post-intervention ( $F(1,45) = 7.05, P = .011$ ). However, the change from baseline to the 3-month follow-up assessment was only marginally significant ( $F(1,42) = 3.11, P = .087$ ).

Also similar to the ITT findings, results revealed a main effect for PTCI scores to improve over time (Wilk's  $\lambda = .61$ ;  $F(2, 40) = 12.83, P < .001$ ; partial  $\eta^2 = .39$ ), and this main effect was qualified by a significant group x time interaction. Post-hoc analyses indicated greater reductions in PTCI for PE participants between baseline and post-intervention ( $F(1,45) = 12.16, p = .002$ ) and baseline and 3-month follow-up ( $F(1,42) = 16.51, P = .02$ ).

With regards to substance use, no exacerbation of substance use occurred during the PE sessions, and a one-way ANOVA conducted between groups on the post-intervention assessment supported the results from therapy sessions, in that no between group differences on substance use within the past week were present ( $F(1,42) = .09, P = .77$ ). The PE group reported an average of 2.58 (6.65) and the control group reported an average of 2.12 (3.15) instances of substance within the past seven days. A mixed model repeated measures ANOVA conducted on baseline and the 3-month follow-up assessment confirmed the ITT findings and revealed no main effect of time (Wilk's  $\lambda = .10$ ;  $F(1, 41) = .14, P = .71$ ; partial  $\eta^2 = .00$ ) or group x time interaction.

### **Within Subjects ITT Analyses – Through the 6-month Follow-up**

After applying the LOCF method, within subjects repeated measures ANOVAs were conducted on 59 participants to determine whether treatment gains persisted at the 6-month follow-up. Time of assessment (baseline, post-intervention, 3- and 6-months post-treatment) was the within subjects factor. Descriptive and inferential statistics are displayed in Table 5. Results revealed significant main effects of time for the outcomes of HIV-related PTSS, nonHIV-related PTSS, depression and negative posttraumatic cognitions, such that PE participants experienced a reduction in symptoms over the course of the study. Post-hoc analyses revealed significant mean differences between baseline, post-intervention, 3- and 6-month assessments (see Table 7), implying that the effects of the intervention were maintained through 6 months after the completion of therapy. No significant main effects of time emerged for substance use.

### Within subjects Completer Analyses – Through the 6-month Follow-up

Results from within subjects repeated measures ANOVAs conducted on 30 participants replicated the ITT findings (see table 6), in that PE participants experienced significant reductions in HIV-related and nonHIV-related PTSS, depressive symptoms, and negative posttraumatic cognitions throughout 6-months post-treatment. Post-hoc pairwise comparisons again revealed significant differences between baseline and all follow-up assessments (See table 7). No significant main effects of time emerged for substance use.

### End-State Functioning

Results from chi square analyses revealed that 10 PE participants (52.6%) compared to 2 control participants (8.3%) met criteria for good end state functioning ( $\chi^2(1, n = 47) = 10.43, P = .002$ ) post-intervention. Three-months post-treatment, 12 PE participants (63.2%) compared to 6 control participants (25%) met criteria for good end-state functioning ( $\chi^2(1, n = 43) = 6.34, P = .01$ ). Examination of the larger sample size due to providing PE to the control group revealed that 18 (58%), 19 (63%), and 15 (50%) met good end-state functioning at the post-intervention, 3- and 6-month follow-up assessments.

### Discussion

To our knowledge, the current study was the first randomized controlled trial to test the efficacy of PE therapy for PTSD in PLWH. Consistent with hypotheses, results supported the use of PE in this population; PE recipients demonstrated significant improvement in both HIV- and nonHIV-related PTSS and achieved good end-state functioning at higher rates than a weekly monitoring/wait list control group. PE was also successful at reducing negative posttraumatic cognitions and depressive symptoms, although this latter result was primarily supported in completer analyses as ITT analyses were at the trend level. Gains achieved in therapy for the outcomes of HIV- and nonHIV-related PTSS, and negative posttraumatic cognitions were maintained throughout 3-months in the completer analysis, but this pattern of results did not emerge for the ITT analyses. However, given that LOCF is a conservative approach to ITT analysis, failure to find significance with this analysis may simply reflect limited power due to a small sample size. Further, results from within subjects analyses suggest that the gains achieved from PE therapy were maintained throughout 6-months for PTSS, depression, and negative posttraumatic cognitions.

Though all group x time interaction effect sizes findings were large (partial  $\eta^2 \geq .14$ ), the intervention accounted for the largest proportion of variance in HIV- and nonHIV-related PTSS. Additionally, the magnitude of change for both types of PTSS in the completer analyses was robust—the decline in HIV-related PTSS for PE participants was 19.58 points compared to a reduction of 6.47 for control participants. The change in nonHIV-related PTSS was equally large—a 22.68 point reduction for PE participants compared to a 9.96 point reduction for control participants. It is important to keep in mind that although the largest reduction in PTSS occurred for the PE participants in regards to their HIV-related trauma, the PE therapy itself was aimed at treating participants' most distressing trauma. As mentioned before, only 34% of participants regarded their HIV-related trauma as being the most traumatic and thus targeted it in therapy, implying that the remaining 66% of

participants targeted a nonHIV-related trauma in PE therapy. Given the observed significant reductions in both HIV- and nonHIV-related PTSS, results suggest that participants may have learned skills allowing them to transfer the gains of therapy to other traumas. PE participants also experienced significant reductions in depressive symptoms that were maintained throughout 3-months for the completers, and reductions in negative posttraumatic cognitions which were maintained throughout 6-months in both sets of analyses, supporting the efficacy of PE at decreasing a range of posttraumatic sequelae. Consistent with prior research [77, 78], substance use did not worsen over the course of treatment which lends support to the continued use of PE in PLWH who may have comorbid substance use issues.

Although the dropout rate (32%) for PE participants in the current study was within the range of dropout rates reported in exposure therapies for treating PTSD in non-medical populations (20.5–34% [79 – 81]; for recent reviews, see [82 and 83]), differential drop-out rate was an issue for the present sample. A greater proportion of PE recipients versus controls dropped out by post-intervention. Given that differential drop-out can bias the outcome estimates and their corresponding significance, the present results warrant replication and should be viewed with caution until further investigations confirm these findings. Despite this differential dropout, only 5 participants withdrew from the therapy because they either lost interest in continuing PE or thought the therapy was too much to handle at the current time. Additionally, as the present results were significant using conservative LOCF method in the ITT analyses, this suggests that differential dropout did not bias the present findings.

The high rates of post-traumatic distress observed in PLWH combined with the success of the present pilot study would underscore the importance of screening for PTSS and depression symptoms in routine visits to health care professionals [57, 84 – 86]. Further, as prior research has suggested that addressing PTSD and mental health comorbidities may be a necessary step in the process of improving adherence in PLWH [30, 87, 88], perhaps PE could provide an efficient means by which to decrease post-traumatic distress and comorbid disorders and possibly increase the efficacy of subsequent adherence and substance use interventions.

Strengths of the present study include the heterogeneity of the sample (males, females, varying sexual orientations, varying amounts of time living with HIV), as the exclusionary criteria were limited which allowed for the implementation of a practical intervention in a “real-life” setting. Several prior studies in PLWH have been conducted in limited samples of only women [4, 11, 31], or homosexual/bisexual men [3, 89]. Further, the inclusion of PLWH with various comorbidities allowed for high external validity, as it is rare for PTSD to exist as an independent psychological disorder. PTSS were also assessed via interview rather than self-reported questionnaire.

Though the present results provide preliminary evidence for the efficacy of PE in PLWH, they should be viewed with caution in the presence of some limitations. The small sample size of the present study limits power in conducting mediation or moderation analyses, and the lack of a control group at the 6-month assessment excludes the possibility for

comparison of the long-term effects of therapy. Despite these limitations, results from this study provide support for the utility of PE therapy as an efficacious intervention for PLWH. The therapy was readily accepted by PLWH, with a drop-out rate comparable to other studies utilizing exposure therapy. The results expand and improve upon previous mental health interventions that have been offered to PLWH by specifically targeting PTSD with an evidence-based, first-line intervention for the disorder.

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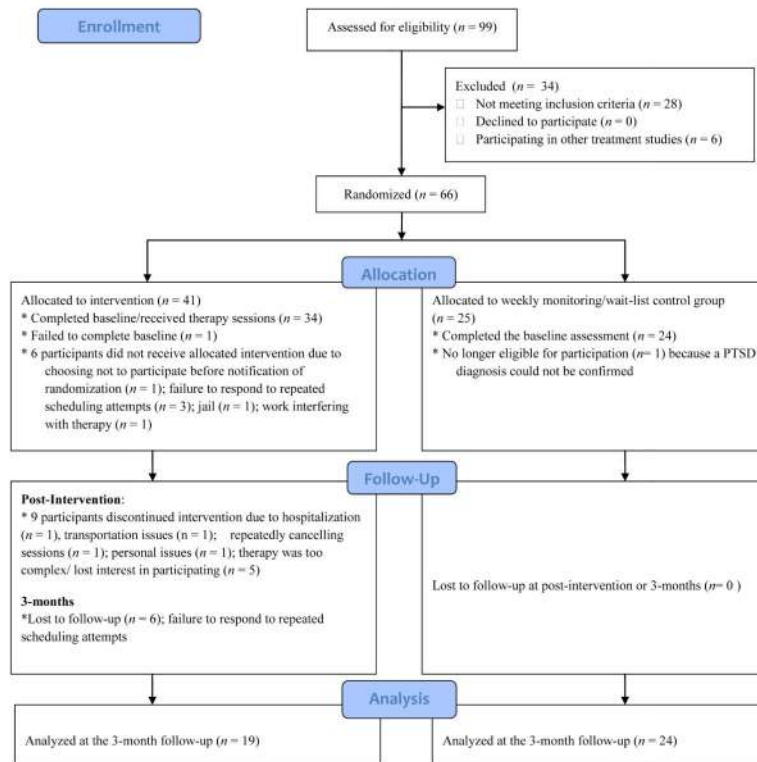
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**Figure 1.** Flow diagram of participant progress throughout the study.

**Table 1**

Means and Standard Deviations from the Full Sample for Continuous Level Demographic Variables

Demographics	Baseline ( <i>n</i> = 65)			Total Sample Mean (SD)
	Prolonged Exposure Mean (SD)	Wait-list/Control Mean (SD)	F test <sup>a</sup>	
Age	46 (5.8)	48(7.0)	1.92	46.37 (6.30)
Sexual Orientation <sup>b</sup>	5.12 (3.5)	5.76 (3.5)	.51	5.37 (3.49)
Months Living with HIV	157 (68)	163(55)	.70	159 (63)
HIV-related PTSS	25.30 (10.26)	26.00 (9.62)	.08	25.57 (9.95)
nonHIV-related PTSS <sup>c</sup>	27.45 (9.52)	30.42 (10.28)	1.37	28.56 (9.84)
Depressive symptoms	25.72 (10.96)	26.00 (10.58)	.01	25.83 (10.73)
Negative Posttraumatic Cognitions	115.66 (37.38)	111.32 (41.09)	.19	113.99 (38.59)
Substance Use	6.72 (11.49)	6.76 (10.70)	.00	6.74 (11.11)

(SD) = Standard deviation; PTSS = Posttraumatic Stress Symptoms.

<sup>a</sup>F test = F value from analyses examining group differences in demographic variables.<sup>b</sup>Sexual orientation = The mean score here reflects sexual orientation on a continuum from 1=9 (1 = completely homosexual; 5 = bisexual; 9 = completely heterosexual).<sup>c</sup>sample size for analyses regarding nonHIV-related PTSS is 64 (1 participant failed to report a nonHIV-related trauma).\*  $P < .05$ ,\*\*  $P < .01$ ,\*\*\*  $P < .001$ .

**Table 2**

Means and Standard Deviations from the Completer Sample for all Study Outcomes

Demographics	Post-Intervention ( <i>n</i> = 47)		3-month Follow-up ( <i>n</i> = 43)	
	PE ( <i>n</i> = 23) Mean (SD)	Control ( <i>n</i> = 24) Mean (SD)	PE ( <i>n</i> = 19) Mean (SD)	Control ( <i>n</i> = 24) Mean (SD)
HIV-related PTSS	8.30 (4.83)	24.13 (10.66)	7.32 (6.74)	20.46 (8.94)
nonHIV-related PTSS <sup>a</sup>	7.30 (3.98)	28.09 (11.13)	6.11 (5.48)	21.26 (7.80)
Depressive symptoms	16.00 (9.46)	27.50 (11.68)	13.53 (9.99)	22.08 (12.55)
Negative Posttraumatic Cognitions	83.70 (30.75)	115.08 (33.00)	78.26 (27.83)	100.71 (46.76)
Substance Use	--	--	4.53 (12.46)	7.21 (11.07)

(SD) = Standard deviation; PTSS = Posttraumatic Stress Symptoms.

<sup>a</sup> overall sample size for analyses regarding nonHIV-related PTSS is 63 (1 control participant failed to report a nonHIV-related trauma).

**Table 3**  
Group x Time Interactions: Intent-to-Treat Mixed Model Repeated Measures ANOVAs

Outcomes	Baseline Mean (SD)	Post-Intervention Mean (SD)	3-month follow-up Mean (SD)	Wilk's $\lambda$	F	Partial $\eta^2$
HIV-related PTSS ( <i>n</i> = 65)						
PE	25.30 (10.26)	14.90 (11.09)	14.43 (11.76)	.86	4.86***	.14
Control	26.00 (9.62)	23.28 (11.26)	19.76 (9.43)			
NonHIV-related PTSS ( <i>n</i> = 64)						
PE	27.45 (9.52)	14.60 (11.28)	13.98 (11.96)	.76	9.55***	.24
Control	30.42 (10.29)	26.96 (12.21)	20.42 (8.83)			
Depressive Symptoms ( <i>n</i> = 65)						
PE	25.72 (10.96)	19.79 (10.46)	18.56 (10.96)	.92	2.82 <sup>+</sup>	.09
Control	26.55 (10.57)	26.60 (12.29)	21.40 (12.75)			
Posttraumatic Cognitions ( <i>n</i> = 65)						
PE	115.66 (37.38)	97.25 (36.36)	94.28 (35.46)	.90	3.28*	.10
Control	111.32 (41.09)	112.56 (34.68)	98.76 (46.80)			
Substance Use ( <i>n</i> = 65)						
PE	6.73 (11.49)	---	7.75 (14.05)	.99	.12	.00
Control	6.76 (10.70)	---	6.92 (10.93)			

(SD) = Standard deviation; PTSS = Posttraumatic Stress Symptoms; PE = Prolonged Exposure Group; Control = Wait-list/Control Group.

\* *P* < .05,

\*\* *P* < .01,

\*\*\* *P* < .001.

**Table 4**  
Group x Time Interaction Results from Mixed Model Repeated Measures ANOVAs: Completer Sample

Outcomes	Baseline Mean (SD)	Post-Intervention Mean (SD)	3-month follow-up Mean (SD)	Wilk's $\lambda$	F	Partial $\eta^2$
HIV-related PTSS ( <i>n</i> = 43)						
PE	26.42 (9.76)	8.32 (5.15)	7.32 (6.74)	.55	16.35***	.43
Control	26.96 (8.52)	24.13 (10.66)	20.46 (8.94)			
NonHIV-related PTSS ( <i>n</i> = 42)						
PE	28.79 (8.87)	7.42 (4.11)	6.11 (5.48)	.45	23.99***	.55
Control	31.70 (8.34)	28.08 (11.13)	21.26 (7.80)			
Depressive Symptoms ( <i>n</i> = 43)						
PE	26.47 (11.38)	16.05 (10.07)	13.53 (9.99)	.85	3.44*	.15
Control	26.87 (9.84)	27.50 (11.68)	22.08 (12.55)			
Posttraumatic Cognitions ( <i>n</i> = 43)						
PE	117.00 (36.97)	84.53 (33.27)	78.26 (27.83)	.77	5.84**	.23
Control	113.79 (40.03)	115.08 (33.00)	100.71 (46.76)			
Substance Use ( <i>n</i> = 43)						
PE	3.37 (7.11)	---	4.53 (12.46)	.10	.08	.00
Control	7.04 (10.83)	---	7.21 (11.07)			

(SD) = Standard deviation; PTSS = Posttraumatic Stress Symptoms; PE = Prolonged Exposure Group; Control = Wait-list/Control Group.

\* *P* < .05,

\*\* *P* < .01,

\*\*\* *P* < .001.

**Table 5**  
 Results for Intent-to-Treat Within Subjects Repeated Measures ANOVA: Main Effects of Time

Outcomes	Baseline Mean (SD)	Post-Intervention Mean (SD)	3-month follow-up Mean (SD)	6-month follow-up Mean (SD)	Wilk's $\lambda$	F	Partial $\eta^2$
HIV-related PTSS ( <i>n</i> = 59)	24.21 (9.78) <sup>a,b,c</sup>	13.25 (10.19) <sup>a</sup>	13.51 (10.78) <sup>b</sup>	13.07 (11.16) <sup>c</sup>	.46	21.95 <sup>***</sup>	.54
NonHIV-related PTSS ( <i>n</i> = 58)	24.93 (9.74) <sup>a,b,c</sup>	13.50 (10.43) <sup>a</sup>	13.67 (11.11) <sup>b</sup>	13.20 (10.91) <sup>c</sup>	.49	18.76 <sup>***</sup>	.51
Depressive Symptoms ( <i>n</i> = 59)	24.24 (10.67) <sup>a,b,c</sup>	18.88 (11.10) <sup>a</sup>	18.64 (11.32) <sup>b</sup>	19.91 (11.89) <sup>c</sup>	.76	5.80 <sup>**</sup>	.24
Negative Posttraumatic Cognitions ( <i>n</i> = 59)	112.78 (41.84) <sup>a,b,c</sup>	95.85 (43.22) <sup>a</sup>	93.95 (40.03) <sup>b</sup>	93.14 (43.43) <sup>c</sup>	.70	7.90 <sup>***</sup>	.30
Substance Use ( <i>n</i> = 59)	7.66 (11.80) <sup>a,b,c</sup>	---	7.00 (12.86) <sup>b</sup>	7.14 (11.01) <sup>c</sup>	.99	.19	.07

(SD) = Standard deviation; PTSS = Posttraumatic Stress Symptoms.

<sup>a,b,c</sup> Mean(SD) = Means that share superscripts are significantly different from each other.

\* *P* < .05,

\*\* *P* < .01,

\*\*\* *P* < .001.

**Table 6**

Results for Within Subjects Repeated Measures ANOVA Completer Sample: Main Effects of Time ( $n = 30$ )

Outcomes	Baseline Mean (SD)	Post-Intervention Mean (SD)	3-month follow-up Mean (SD)	6-month follow-up Mean (SD)	Wilk's $\lambda$	F	Partial $\eta^2$
HIV-related PTSS	24.27 (8.87) <i>a,b,c</i>	8.43 (5.64) <i>a</i>	9.57 (7.54) <i>b</i>	8.80 (8.13) <i>c</i>	.19	39.65***	.82
NonHIV-related PTSS ( $n = 29$ )	25.62 (9.11) <i>a,b,c</i>	7.76 (5.07) <i>a</i>	8.62 (7.86) <i>b</i>	7.79 (6.57) <i>c</i>	.16	44.41***	.84
Depressive Symptoms	23.87 (11.31) <i>a,b,c</i>	16.47 (10.58) <i>a</i>	15.67 (11.68) <i>b</i>	18.02 (13.20) <i>c</i>	.62	5.47**	.38
Negative Posttraumatic Cognitions	107.84 (42.61) <i>a,b,c</i>	83.04 (40.46) <i>a</i>	81.72 (35.38) <i>b</i>	79.96 (41.53) <i>c</i>	.54	7.75**	.47
Substance Use	5.07 (9.79) <i>a,b,c</i>	---	4.10 (10.55) <i>b</i>	5.80 (11.15) <i>c</i>	.94	.89	.06

(SD) = Standard deviation; PTSS = Posttraumatic Stress Symptoms.

*a,b,c* Mean(SD) = Means that share superscripts are significantly different from each other.

\*  $P < .05$ ,

\*\*  $P < .01$ ,

\*\*\*  $P < .001$ .



**Table 7**

Post-hoc Pairwise Comparisons for Within Subjects Analyses

Outcomes	<i>t</i> Baseline to post-intervention	<i>t</i> Baseline to 3-month follow-up	<i>t</i> Baseline to 6-month follow-up
HIV-related PTSS: ITT	8.04***	6.80***	7.20***
NonHIV-related PTSS: ITT	7.58***	6.82***	7.07***
Depressive Symptoms: ITT	3.84***	3.54**	3.41**
Negative Posttraumatic Cognitions: ITT	4.67***	4.38***	4.73***
HIV-related PTSS: Completer Sample	10.55***	7.01***	7.80***
NonHIV-related PTSS: Completer Sample	11.46***	8.13***	9.00***
Depressive Symptoms: Completer Analysis	3.88**	3.00**	2.73*
Negative Posttraumatic Cognitions: Completer Analysis	4.75***	3.88**	4.35***

PTSS = Posttraumatic Stress Symptoms; ITT = Intent-to-Treat Analyses

\*  $P < .05$ ,\*\*  $P < .01$ ,\*\*\*  $P < .001$ .