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An Intensive Outpatient Program With Prolonged Exposure for Veterans With Posttraumatic Stress Disorder: Retention, Predictors, and Patterns of Change

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High rates of drop-out from treatment of PTSD have challenged implementation. Care models that integrate PTSD focused psychotherapy and complementary interventions may provide benefit in retention and outcome. The first 80 veterans with chronic PTSD enrolled in a 2-week intensive outpatient program combining Prolonged Exposure (PE) and complementary interventions completed symptom and biological measures at baseline and posttreatment. We examined trajectories of symptom change, mediating and moderating effects of a range of patient characteristics. Of the 80 veterans, 77 completed (96.3%) treatment and pre- and posttreatment measures. Self-reported PTSD ($p < .001$), depression ($p < .001$) and neurological symptoms ($p < .001$) showed large reductions with treatment. For PTSD, 77% ($n = 59$) showed clinically significant reductions. Satisfaction with social function ($p < .001$) significantly increased. Black veterans and those with a primary military sexual trauma (MST) reported higher baseline severity than white or primary combat trauma veterans respectively but did not differ in their trajectories of treatment change. Greater cortisol response to the trauma potentiated startle paradigm at baseline predicted smaller reductions in PTSD over treatment while greater reductions in this response

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from baseline to post were associated with better outcomes. Intensive outpatient prolonged exposure combined with complementary interventions shows excellent retention and large, clinically significant reduction in PTSD and related symptoms in two weeks. This model of care is robust to complex presentations of patients with varying demographics and symptom presentations at baseline.

Impact Statement
Intensive and integrative models of exposure-based treatment of PTSD show large reductions in PTSD and related mental health issues while greatly increasing retention over weekly PTSD standard models of care. Such models provide new options for PTSD care to improve outcomes, retention, and access through specialty PTSD care centers.

Keywords: posttraumatic stress disorder, treatment, prolonged exposure therapy, veterans

Prolonged Exposure (PE) therapy (Foa, Hembree, Rothbaum, & Rauch, 2019) is a first-line treatment for posttraumatic stress disorder (PTSD) in military veterans and service members (American Psychological Association, 2017; VA/DOD, 2017). Despite the existence of effective treatments and extensive efforts to support dissemination in VA and DOD, few veterans or others suffering with PTSD are able to access PE (Rosen, Matthieu, et al., 2016; Shiner, D'Avolio, et al., 2013). Shiner et al. (2013) found that just 6.8% of veterans in therapy for PTSD received PE or Cognitive Processing Therapy. One contributing factor for low access to PE is low rates of provider utilization (Finley et al., 2015; Shiner et al., 2013). In addition, even when veterans with PTSD access a provider trained in PE to start treatment, many do not complete a full treatment dose (Kehle-Forbes, Meis, Spoont, & Polusny, 2016; Mott et al., 2014). In clinical care, only about half of patients who start PTSD treatment complete an adequate course of care, regardless of whether it is psychotherapy or medication (Kehle-Forbes et al., 2016; Mott et al., 2014). Conventional outpatient PE (weekly sessions for up to 12 weeks) may not match the preferences of many patients with PTSD, who are challenged by logistic barriers, financial costs, uncertain calendars, avoidance symptoms, and mixed motivation.

Massed or intensive treatment models for PTSD based on evidence-based psychotherapies have emerged with encouraging results (e.g., Beidel, Frueh, Neer, & Lejuez, 2017; Foa et al., 2018; Harvey et al., 2019; Hendriks, de Kleine, Broekman, Hendriks, & van Minnen, 2018; Tanev, Federico, Terry, Clark, & Iverson, 2019; Zalta et al., 2018). Massed models refer to provision of therapy sessions more frequently than standard weekly formats. All models described as massed in our paper include at least daily exposure sessions and several have more than a single exposure session each day. A randomized controlled trial comparing massed vs. conventional delivery of PE and a case study of intensive PE have demonstrated changes in PTSD and depression similar to outpatient treatment studies from the same site but with much higher retention (80–90%) (Blount, Cigrang, Foa, Ford, & Peterson, 2014; Foa et al., 2018). Thus, they are getting more veterans through treatment without impacting the amount of symptom reduction. Available effectiveness data suggest that short-term (2–3 week) treatment programs combining massed trauma-focused psychotherapy with adjunctive and supportive services result in large reductions in PTSD at least comparable in magnitude to standard care with very high retention rates (Beidel et al., 2017; Harvey et al., 2019; Tanev et al., 2019; Zalta et al., 2018). In addition, there is evidence that these treatment effects are maintained over time (Beidel et al., 2017; Hendriks et al., 2018). Intensive programs offering massed treatment promise many benefits. First, high retention of veterans allows providers to have confidence that their patient had the opportunity for a full course of effective psychotherapy (Harvey, Petersen, et al., 2019; Zalta, Held, et al., 2018). Second, these programs often employ expert providers who focus specifically on evidence-based care for PTSD such as PE, which may allow for greater treatment fidelity and in turn greater magnitude of patient improvements even when comorbidities are present (Kehle-Forbes, Meis, et al., 2016; Rosen, Matthieu, et al., 2016). Third, the multidisciplinary nature of most of these intensive programs provides the added benefit of reducing PTSD symptoms while simultaneously working to increase positive coping and skills to reconnect with the veteran's family and community. The expectation is that this combined programming may lead to greater maintenance of gains over time though additional research is needed to specifically examine maintenance of gains. Closer examination of these massed models of evidence-based trauma-focused therapies is required to determine whether these potential benefits are realized in new models of care provided both inside and outside VA.

The current study examines outcomes from the Emory Healthcare Veterans Program (EHVP), a 2-week intensive outpatient program offering massed PE to post9/11 military veterans and servicemembers. Standard PTSD symptom assessments focus on report of symptoms over the past month or the past week creating a problem for 2- or 3-week treatment protocols as the treatment period is overlapped with the recall period. Thus, examination of change over time can be difficult and use of additional measurement strategies that are not dependent on recall is warranted. Given high rates of comorbidity of PTSD and depression (Knowles, Sripada, Defever, & Rauch, 2019), measures to capture both are presented.

In addition to symptom report measures, we also examined key biological correlates of change established in previous research studies and not dependent on recall. Our chosen low patient burden measures with previous established relationships to PTSD severity and treatment response included physiological and cortisol reactivity to trauma reminders (Jovanovic, Rauch, Rothbaum, & Rothbaum, 2017; Orr et al., 2012; Orr, Metzger, & Pitman, 2002; Pitman, Orr, Forgue, de Jong, & Claiborn, 1987; Shalev, Orr, &

Pitman, 1993). PTSD treatment studies have shown that heart rate reactivity to trauma reminders decreases with successful treatment of PTSD symptoms (Wangelin & Tuerk, 2015). In addition, treatment responders show an initial increase followed by a decrease in trauma potentiated startle in PE compared to nonresponders (Robison-Andrew et al., 2014). Examination of trauma potentiated startle in a massed program may provide guidance at pretreatment for those patients who are less likely to fully respond providing an opportunity for augmentation to facilitate change.

Finally, assessment of cortisol reactivity to an acute stress exposure may also be informative for predicting treatment response (Galatzer-Levy et al., 2014; Norrholm et al., 2016; Rauch et al., 2015). Research on hypothalamic-pituitary-adrenal (HPA) axis activity in PTSD is somewhat inconsistent but disruption is apparent and negative feedback inhibition may best describe the disruption (Elzinga, Schmahl, Vermetten, van Dyck, & Bremner, 2003; Liberzon, Abelson, Flagel, Raz, & Young, 1999; Yehuda, Yang, Buchsbaum, & Golier, 2006). Normalization of HPA axis activity may be associated with symptom improvement (Olff, Güzelcan, de Vries, Assies, & Gersons, 2006). Despite some contradiction, PTSD is best described as resulting in HPA axis dysfunction including generally low levels and reduced negative feedback inhibition-resulting in a system that is quick to activate and slow to shut down. Examination of how cortisol response to provocation paradigm may predict response to massed PE can also provide guidance in treatment selection and planning as noted above.

In the current retrospective effectiveness study, we examined massed PE outcomes among the first 80 veterans with chronic PTSD enrolled in EHVP. Of these 80, only 77 completed all pre- and posttreatment measures due to one veteran choosing to leave early, one veteran who admitted to malingering, and one veteran who received Cognitive Processing Therapy rather than PE. We examined effect size, trajectories of symptom change, and moderating effects on outcome.

Method

Participants and Procedure

Veterans were referred to the program from multiple sources including the VA providers, community providers, Wounded Warrior Project, and self-referral. Veteran Outreach Coordinators in our program facilitated awareness of our services through outreach events and our program advertised in radio and social media outlets. All patients completed a phone screen to determine whether they have experienced trauma, have served at least one day post 9/11/2001, were not imminently suicidal or homicidal and in need of a higher level of care, or abusing substances that required a higher level of care for detoxification. All then received a comprehensive evaluation [Mini International Neuropsychiatric Interview (Sheehan et al., 1998), Clinical Administered PTSD Scale-5 (CAPS-5; Weathers et al., 2013) and medical record review], and self-report measures of PTSD, mood disorders, anxiety disorders, substance use disorders, and traumatic brain injury (TBI) at intake. All assessors were masters or PhD level clinical psychology trainees under the supervision of a licensed psychologist or clinical psychologists. All were fully CAPS5 and MINI trained to criterion and with monthly meetings to continually maintain rating fidelity. Self-report measures were administered on Day 1 of treatment ("baseline"), and again on Days 3, 5, 8, and 10 of treatment. Cases were presented in multidisciplinary case conference to determine eligibility of the program and establish an initial individual treatment plan. Inclusion criteria were service members or veterans who served at least one day post 9/11with current PTSD based on clinical structured interview. Exclusion criteria were (a) current, imminent risk of suicide or homicide,(b) unmanaged psychosis, (c) alcohol or substance dependence severe enough to interfere with care or needing clinical attention (past 8 weeks), (d) inability to attend for the treatment period, (e) medical illness likely to result in imminent hospitalization or contraindication to study treatments, (f) serious cognitive impairment (e.g., confusion, inability to track discussion), and (g) no current treatment team for ongoing care following the program. Veterans with mild TBI were not excluded. Since this is a clinical program and not a clinical trial, standard CONSORT data is not available, but we did track relevant information for clinical processes. During the period of recruitment covered by the current cohort (12/03/2015–04/25/2017), we completed 685 phone screens with 421 completed intakes. Of completed intakes, 243 were accepted and 178 were not accepted. Of those not accepted, the most common reasons were (a) 88 required a higher level of care for physical or psychiatric reasons (due to exclusions noted above), (b) 36 were unable to be reached, (c) 34 continued with their current care team following intake, (d) 20 were for other reasons that were not detailed. Of the 243 accepted, 169 had a primary diagnosis of PTSD and of those 80 arrived for the PTSD IOP during our period of examination. Others were scheduled for additional cohorts outside of our window per availability. Seventy-seven of the first 80 veterans who met criteria and enrolled in our program were included in analyses, as these were the veterans who had both pre- and posttreatment self-report measures available. We did include all 80 to determine completion rate.

Treatment

The EHVP Intensive Outpatient Program (EHVP IOP) is a 2-week PTSD and comorbid conditions treatment program for veterans and service members. PE is provided by PE-trained doctoral level licensed clinical psychologists and postdoctoral fellows. Providers follow a standardized EHVP IOP treatment manual. To ensure treatment fidelity, the treatment team meets twice weekly for supervision of current cases and once weekly to review therapy video recordings. These meetings are supervised by the study's first and last author. See Table 1 for sample schedule of active treatment (individual PE sessions and in vivo group sessions), auxiliary services, and research assessments.

Prolonged exposure (PE) therapy. The active treatment components are based on PE (Foa et al., 2019) and adapted from group-based PE (Smith et al., 2015). The main goal of PE is to facilitate emotional processing of the trauma via systematic confrontation of trauma-related cues (Foa et al., 2019). PE consists of three key components: psychoeducation, repeated imaginal exposure in which veterans revisit their trauma memories in a therapeutic context and emotional processing, and in vivo exposure to places and situations that are avoided because they elicit anxiety.

At EHVP IOP, veterans receive seven daily individual 90-min PE sessions in which they engage in imaginal exposure and pro-

Table 1
EHVP IOP Structure and Session Content: Example Schedule

Day	Individual session (90 minutes)	Group/In Vivo session (120 minutes)	Auxiliary services	Assessments
1	Not provided	Psychoeducation	Orientation Case management Nutrition education Acupuncture	Pretreatment assessment (PCL5, PHQ9, psychophysiological assessment, saliva collection)
2	Psychoeducation Imaginal exposure Processing	Psychoeducation In vivo exposure planning Therapist-assisted practice	Case Management Sleep education Yoga	Not provided
3	Imaginal exposure Processing	In vivo exposure	Case management Yoga	Midtreatment assessment (PCL5, PHQ9)
4	Imaginal exposure Processing	In vivo exposure	Case management Finance/employment Acupuncture Yoga	Not provided
5	Imaginal exposure Processing	In vivo exposure	Case management Finance/employment Family session Yoga	Midtreatment assessment (PCL5, PHQ9)
6, 7	Weekend activities	Group activities	Baseball Festivals Music	Not provided
8	Imaginal exposure Processing	In vivo exposure	Case Management Nutrition Education Acupuncture	Midtreatment assessment (PCL5, PHQ9)
9	Imaginal exposure Processing	In vivo exposure	Case Management Sleep education Yoga	Not provided
10	Imaginal exposure Processing Transition planning	In vivo exposure Transition planning	Case Management Family Session Yoga	Midtreatment assessment (PCL5, PHQ9)
11	Imaginal Exposure Processing Transition planning	In vivo exposure Transition planning	Case Management Family session Finance/Employment Yoga	Not provided
12	Imaginal Exposure Processing Transition Planning	Not provided	Not provided	Post-treatment assessment (PCL5, PHQ9, psychophysiological assessment, saliva collection)

Note. PCL-5 = PTSD Checklist for the Fifth Edition of the Diagnostic and Statistical Manual 5 (DSM-5); PHQ-9 = Patient Health Questionnaire–9.

cessing of the traumatic memory. Additionally, they participate in nine daily 120-min long in vivo exposure group. In the first in vivo group, the two group coleaders provide psychoeducation on common reactions to trauma and rationale for engaging in exposures to address these symptoms. In the second in vivo group, patients engage in a therapist-assisted in vivo exposure and are given feedback regarding any safety behaviors. All following in vivo groups consist of (a) the initial 15-min check-in with the group and the coleaders to review homework and identify in vivo exposure for the day, (b) a 60–75 min period in which veterans complete individualized exposures on their own, and (c) a final 15-min check-in during which veterans report on their exposure and identify an in vivo exposure for homework.

All EHVP clinicians have received extensive training in PE. They also engage in weekly supervision meetings, one in which a PE expert informally reviews tapes of the sessions and provides feedback, and another in which each veteran's treatment is discussed with the senior EHVP clinicians and subject matter experts.

Integrative services. In addition to the active treatment described above and consistent with most of the previous studies reviewed above (Beidel et al., 2017; Harvey et al., 2019; Hendriks, et al., 2018), veterans receive a number of other services based on their interest and treatment plan, including daily case management, medication management, relapse prevention, skills training in family/relationship management (FOCUS), recreational activities; career/financial support, and promotion of physical health and wellness through sleep education, nutrition education, yoga, massage, and acupuncture. These services are not considered active components of the exposure treatment. Instead, they are intended to provide a holistic and individualized approach to support engagement in PE and preparedness to maintain skills after discharge. The veterans are expected to attend these sessions and are enrolled in these activities prior to their arrival to the EHVP IOP. On average, over the course of the 2-week EHVP IOP, veterans completed nine case management sessions (daily), one medication management session, two FOCUS sessions, one recreational activity, two career/financial education sessions, two sleep education sessions,

two nutrition education sessions, four yoga sessions, two relapse prevention sessions (if indicated in treatment plan), and two acupuncture or massage sessions. No study to date has broken apart these integrative elements from massed PE to determine the unique contribution of each. As a clinical retrospective analysis, we are not able to this in our sample.

Assessment. Veterans completed self-report measures at baseline (Day 1), at various points midtreatment (Days 3, 5, 8, and 10), and at the end of treatment (Day 12). At baseline and end of treatment, veterans also completed the psychophysiological assessments. All research data collection was administered by the trained research staff who interacted with the veterans only in the context of research data collection. To minimize the effect of demand characteristics, veterans' clinical providers were not present during any of the assessments while in EHVP IOP.

Measures

PTSD Checklist for the Fifth Edition of the Diagnostic and Statistical Manual (*DSM–5* (PCL-5). The PCL-5 (Weathers, Litz, Keane, Palmieri, Marx, & Schnurr, 2013) is a 20-item self-report *DSM–5* PTSD questionnaire. The PCL-5 has excellent psychometrics and a clinical cutoff of 33 (Bovin, Marx, Weathers, Gallagher, Rodriguez, Schnurr, & Keane, 2016; Blevins, Weathers, Davis, Witte, & Domino, 2015; Wortmann et al., 2016). Internal consistency in the current sample was high (α = .93–.98). PCL-5 was collected across treatment as the primary outcome measure. PCL-5 past month version was administered at baseline and PCL-5 past week was administered during (every other day) and at posttreatment.

Clinician-Administered PTSD Scale for *DSM–5* (CAPS-5). The CAPS-5 (Weathers et al., 2013) is a structured diagnostic interview for PTSD. The CAPS-5 total severity, subscale, diagnostic status, and item scores demonstrate excellent psychometrics (Weathers et al., 2018). Symptoms are rated as present based on a severity of at least 2. Diagnostic status is based on meeting *DSM–5* criteria meeting presence on CAPS5. CAPS5 was only collected at intake to establish PTSD diagnostic status.

Patient Health Questionnaire—9 (PHQ-9). The PHQ-9 (Kroenke, Spitzer, & Williams, 2001) is a nine-item self-report measure of depressive symptoms. Several studies support excellent psychometrics and a clinical cutoff of 11 (Löwe, Unützer, Callahan, Perkins, & Kroenke, 2004; Manea, Gilbody, & McMillan, 2012). Internal consistency in the current sample was high (α = .83–.91). PHQ-9 was collected across treatment as a measure of depression.

Alcohol Use Disorders Identification Test—Consumption (AUDIT-C). The AUDIT-C (Bradley, McDonell, Bush, Kivlahan, Diehr, & Fihn, 1998) is a brief validated self-report screen for risky drinking and alcohol abuse and dependence (alcohol misuse) including the frequency and amount of alcohol consumed. The AUDIT-C was only administered at intake.

Neurobehavioral Symptom Inventory (NSI). The NSI (Benge, Pastorek, & Thornton, 2009) is a 22-item self-report of common symptoms of postconcussive syndrome. NSI was collected at pre- and posttreatment based on high rates of TBI in this population and interest in examining change in these symptoms across treatment. Internal consistency in the current sample was high (α = .92–.93). Given that this is a clinical program for PTSD, additional in-depth neuropsychological assessment and more burdensome tests for cognitive function were not possible. The NSI was administered at pre- and posttreatment.

Patient-Reported Outcomes Measurement Information System—Short Form Version 1.0 – Physical Function 8A (8A). The PROMIS 8A (National Institute of Health, 2008) item bank assesses satisfaction with performing one's usual social roles and activities. Higher scores indicate greater satisfaction. Internal consistency in the current sample was high (α = .96). The PROMIS 8A was administered at pre- and posttreatment.

Trauma Potentiated Startle Paradigm

Psychophysiological assessments were completed according to previously published methods (e.g., (Norrholm et al., 2016)). Heart rate was quantified from R-peaks detected during electrocardiogram (ECG) recordings from two 5-mm Ag/AgCl electrodes placed on the upper right torso and left wrist. Participants viewed three, 2-min standardized virtual reality (VR)-based video segments using an eMagin Z800 head mounted display with audio stimuli presented binaurally with headphones. The paradigm was administered at pre- and posttreatment.

Cortisol Response to Trauma Potentiated Startle Paradigm

As in our previous studies (Rothbaum et al., 2014), we collected saliva samples at three timepoints (prior to VR, right after and 15 min later) as part of a trauma potentiated startle paradigm described above. Saliva was collected via Salivette (Sarsedt Inc, Newton, NC), and immediately frozen and batch-processed using a chemiluminescent immunoassay (Salimetrics, State College, PA) on a Beckman Access analyzer. The inter- and the intraassay coefficients of variance were under 11%, reflecting adequate precision and reproducibility of the salivary assay. The area under the curve (AUC) with respect to ground (AUCg) and AUC with respect to increase (AUCi) for cortisol response to the trauma potentiated startle paradigm overtime were calculated to determine whether total cortisol output (AUCg) and sensitivity of the cortisol response (AUCi) are predictive of treatment response (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). Cortisol was collected at pre- and posttreatment.

Data Analysis Plan

Trajectories of PCL-5 and PHQ-9 scores over treatment and potential moderators of these trajectories were analyzed using multilevel growth models with HLM Version 7.02 (Raudenbush, Bryk, Cheong, Congdon, & du Toit, 2011), such that assessment timepoint (level-1) was nested within person (level-2). Prepost change in all variables other than the PCL-5 and PHQ-9 were analyzed using paired-samples *t* tests in SPSS. Cohen's *d* type effect size estimates were also calculated. In each multilevel model, intake scores on each respective measure were included as control variables on both level-1 and level-2, to account for the effects of initial severity on intercept and slope. First, linear change was modeled by adding assessment timepoint as a predictor, followed by quadratic change (time point squared) and cubic change (time point cubed) to determine the best fitting shape of

change over treatment. Then moderators or predictors were added on level-2 as predictors of the intercept and linear change, respectively. All predictor variables (except categorical variables) were grand-mean centered so that intercepts represented the expected value of the outcome at the mean of each included predictor. AUCg and AUCi measures were log transformed. The time variable was coded such that baseline = 0 and posttreatment = 1, so that the coefficient estimate for the intercept represented the predicted value of PCL-5 or PHQ-9 at baseline and the slope of linear time (i.e., the relationship between time and the outcome variable) represented the total expected change in that variable over the course of treatment. Models were estimated using restricted maximum likelihood (RML). For each model, deviance likelihood ratio tests (LRTs) were used to assess whether adding parameters improved model fit. Intercepts and slopes were allowed to vary randomly only if this improved model fit. All predictor variables were examined in separate models. Fixed effects using robust standard errors are reported.

Results

Demographics

This retrospective study was approved by the Emory Human Subjects committee. Of 80 veterans with PTSD, 77 (96.3%) completed treatment. All 80 had pre- and 77 had posttreatment measures. Two participants were dismissed for not following program policy (e.g., active substance use and misconduct) and one withdrew voluntarily. All data analyses use the 77 participants who received a full course of PE to examine predictors of change. Of those veterans who received a full course of PE, 72 (93.5%) had at least one comorbid diagnosis. The most common psychiatric comorbidities were current major depressive disorder (77.9%), panic disorder (15.6%), generalized anxiety disorder (9.1%), alcohol abuse or dependence (9.1%), substance abuse or dependence (11.7%), social phobia (11.7%), and obsessive–compulsive disorder (2.6%). A total of 69 (89.6%) reported concurrent use of prescribed medications. The most common medications reported were antidepressants (e.g., sertraline; 74.0%), antihypertensives (e.g., prazosin; 22.1%), NSAIDs and salicylates (e.g., ibuprofen; 22.1%), anticonvulsants (e.g., lamotrigine; 20.1%), antihistamines (e.g., hydroxyzine; 20.1%), benzodiazepines (e.g., clonazepam; 18.2%), antipsychotics (e.g., quetiapine; 16.9%), beta-adrenergic blockers (e.g., propranolol; 14.3%), opioids (e.g., hydrocodone; 14.3%), and muscle relaxants (e.g., cyclobenzaprine; 13.0%). Veterans prescribed potentially interfering medications (e.g., benzodiazepines) were advised not to take these immediately before or after completing exposures. A total of 10 veterans (13.0%) were prescribed a change in medication during the course of treatment; of these, 5 (6.5%) initiated an antidepressant, 4 (5.2%) increased the dosage of an existing antidepressant, and 1 (1.3%) initiated an anticonvulsant. See Table 2 for patient demographics.

Table 2
Completer Sample Demographics (N = 77)

Measure	*M* (*SD*) or *N* (%)
Age in years *M* (*SD*)	41.19
Gender Female *N* (%)	23 (29.9%)
Race *N* (%)	
White	36 (46.8%)
Black	30 (39.0%)
Native Hawaiian	1 (1.3%)
More than one race	1 (1.3%)
Unknown	9 (11.7%)
Ethnicity *N* (%)	
Hispanic	12 (15.6%)
Non-Hispanic	62 (80.5%)
Unknown	3 (3.9%)
# of OIF, OND, or OEF deployments	
0	9 (11.7%)
1	31 (40.3%)
2	22 (28.6%)
3 or more	14 (18.2%)
Unknown	1 (1.3%)
Trauma Type N %	
Combat	56 (72.7%)
Military sexual trauma	17 (22.1%)
Other military-related trauma*	4 (5.2%)
Military Branch	
US Air Force	5 (6.5%)
US Army	52 (67.5%)
US Coast Guard	1 (1.3%)
US Marine Corps	10 (13.0%)
US Navy	6 (7.8%)
Multiple branches of service	2 (2.6%)
Unknown	1 (1.3%)

* such as training related accidents or car accidents during military duties.

Baseline to Post-Treatment Change in Symptoms

We conducted paired samples *t* tests to examine baseline to posttreatment change in PTSD and depression and additional indicators of functioning. Posttreatment scores were not available for 9 of the 77 completers on the PCL-5 due to administrations error, so baseline to posttreatment change in PCL-5 was calculated based on 68 veterans. $N = 77$ for all other measures. We examined those with and without posttreatment measures to determine if they differed on any pretreatment measures and found no significant differences. See Table 3 for symptom means and standard deviations. *T* tests for all other measures included all 77 completers. There was a significant decrease in both PTSD (PCL-5: $t(67) = 10.20$, $p < .001$, $d = 1.20$) and depression symptoms (PHQ-9: $t(76) = 10.17$, $p < .001$, $d = 1.12$) from baseline (PCL-5: $M = 54.41$, $SD = 13.78$; PHQ-9: $M = 17.82$, $SD = 5.36$) to posttreatment (PCL-5: $M = 32.01$, $SD = 21.60$; PHQ-9: $M = 10.94$, $SD = 6.12$). Similarly, 92% of had probable PTSD (defined as PCL-5 ≥ 33) at baseline and only 48% had probable PTSD at posttreatment. Additionally, there was a significant decrease in neurological symptoms (NSI: $t(76) = 7.64$, $p < .001$, $d = 0.75$) from baseline ($M = 46.48$, $SD = 13.75$) to posttreatment ($M = 34.97$, $SD = 14.59$), and a significant increase in satisfaction with social function (Promis8a: $t(76) = -5.05$, $p < .001$, $d = 0.68$) from baseline ($M = 7.84$, $SD = 3.83$) to posttreatment ($M = 10.56$, $SD = 4.35$).

Multilevel Growth Curve Analyses

Two unconditional models were conducted to determine the percentage of variance on level 1 (within-person) versus level 2 (between person) for the PCL-5 and PHQ-9, respectively. 81.91% of the variance in PCL-5 scores (level-1 ICC = 0.82) and 78.10% of the

Table 3
Descriptive Statistics for Primary Outcome Measures at Baseline and Post EHVP IOP

	Baseline		Completion	
Measure	*M*	*SD*	*M*	*SD*
PCL-5	54.00	13.96	32.01	21.59
PHQ-9	17.81	5.36	10.94	6.12
NSI	48.48	13.75	34.97	14.59
PROMIS 8A	7.84	3.82	10.56	4.35

Note. N = 77 for all measures, except for PCL-5 at baseline where n = 68. PCL-5 = PTSD Checklist for the Fifth Edition of the Diagnostic and Statistical Manual 5 (DSM-5); PHQ-9 = Patient Health Questionnaire–9; NSI = Neurobehavioral Symptom Inventory; PROMIS 8A = Patient-Reported Outcomes Measurement Information System-Short Form version 1.0–Physical Function 8A; EHVP = Emory Health care Veterans Program; IOP = Intensive Outpatient Program.

variance in PHQ-9 scores (level-1 ICC = 0.78) was accounted for by within-person differences, whereas the remaining percentages of variance were accounted for by between-person differences.

Linear Symptom Change

Linear change in PCL-5 and PHQ-9 over treatment were separately modeled, controlling for intake severity of each respective measure. All 77 completing participants could be included regardless of posttreatment PCL-5 availability, as all had at least three within-treatment PCL-5 administrations that could be modeled. PTSD severity (PCL-5) showed a significant linear decrease, $\gamma_{10} = -22.65$, $SE = 2.15$, $t = -10.56$, $p < .001$. The coefficient of the slope suggested that for a participant with a mean intake PCL-5 score, an average reduction of 22.65 points on the PCL-5 occurred. Depression severity (PHQ-9) also showed a significant linear decrease, $\gamma_{10} = -7.31$, $SE = 0.72$, $t = -10.10$, $p < .001$, indicating that for participants with a mean intake PHQ-9 score, an average reduction of 7.31 points on the PHQ-9 occurred.

Nonlinear Symptom Change

Quadratic time and cubic time were added to each model. The quadratic term did not significantly predict outcome in either model, but the cubic term significantly predicted outcome in both models (PCL-5 model cubic effect: $\gamma_{10} = 59.48$, $SE = 15.60$, $t = 3.81$, $p < .001$; PHQ-9 model cubic effect: $\gamma_{10} = 11.08$, $SE = 5.18$, $t = 2.14$, $p = .036$) and added significantly to model fit above and beyond linear change (PCL-5 model: $\chi^2(7) = 75.26$, $p < .001$; PHQ-9 model: $\chi^2(7) = 41.54$, $p < .001$). Examination of the graphed cubic effects for both models suggested that the shape of change was characterized by the fastest rate of change occurring in the middle of treatment (approximately Sessions 2 through 6) with slower rates of change at the beginning and end of treatment (see Figure 1A and 1B). Examination of the random effects showed that the cubic term significantly varied across participants when predicting PCL-5, suggesting significant differences in this shape of change across veterans, but not when predicting PHQ-9.

Predictors of Symptom Change

We examined moderating effect of intake demographic and symptom variables on linear symptom change over treatment. For models including symptom variables as moderators, PCL-5 or PHQ-9 scores were included to control for the effect of overall symptom severity. For models including demographic and psychophysiological variables, control variables were not included so that the effect of these predictors on intercept (i.e., baseline symptom severity) could be examined. All predictor variables were examined in separate models.

Demographics. Demographic variables examined as moderators were: gender, race (white vs. black)[1], trauma type (combat vs. military sexual trauma (MST)), and number of deployments. For the PCL-5, race and trauma type were both found to predict the intercept, but not the linear slope. These effects indicated that black veterans and those with a primary MST trauma began treatment reporting more severe symptoms than white or primary combat trauma veterans respectively but did not differ in the amount of benefit (i.e., symptom reduction). Importantly, the addition of race as a predictor did not significantly improve model fit ($\chi^2 = 510.07$, $p > .500$). No other demographics were found to be significant predictors of PCL-5 intercept or slope and none were found to predict PHQ-9 intercept or slope.

Intake symptoms and functioning. Intake symptom measures examined as moderators were: neuropsychological symptoms (NSI), drinking behavior (AUDIT-C), quality of life (PROMIS 8A), PTSD symptom severity as measured by the CAPS-5, PTSD symptom severity (PCL-5) and depression severity (PHQ-9). None of these measures were found to be significantly associated with the slope of PCL-5 over treatment (see Table 4). Intake PHQ-9 was negatively associated with the slope of PHQ-9 over treatment at a trend level, suggesting that those with higher depression severity at baseline experienced marginally greater reductions in depression symptoms. The PROMIS 8A was found to significantly predict the slope of PHQ-9 over treatment, indicating that those with lower quality of life at intake reported greater reductions in depression symptoms than those with higher quality of life (see Figure 1C). However, the addition of the PROMIS 8A as a predictor did not add significantly to model fit beyond the effects of linear time and intake PHQ-9 ($\chi^2 = 79.83$, $p > .500$). No other intake measures significantly predicted the intercept or linear slope of the PHQ-9.

Impact of baseline and change in psychophysiology and cortisol on PTSD and depression. Baseline psychophysiological measures were examined as predictors of intercept (baseline) and linear slope of PCL-5 and PHQ-9 change. Heart rate response (HRR) was available for 43 participants, and cortisol reactivity (AUCi and AUCg) was available for 52 participants at baseline, and 46 participants at both baseline and posttreatment.[2] Results showed baseline heart rate response (HRR) was associated with the slope of depression symptoms at a trend level but not PTSD symptoms (see Table 4)

[1] Other races and ethnicities did not participate in high enough numbers to allow additional comparisons.

[2] T-test and chi-square analyses were run comparing those who completed at least one psychophysiological assessment to those who completed none. The only significant difference found was that a higher percentage of veterans with MST had psychophysiological data (53%) than veterans with combat traumas (27%) although the actual numbers of veterans with psychophysiological data were similar across types (combat = 12; MST = 9). No other differences in demographics or outcome measures (baseline or completion) were found across groups.

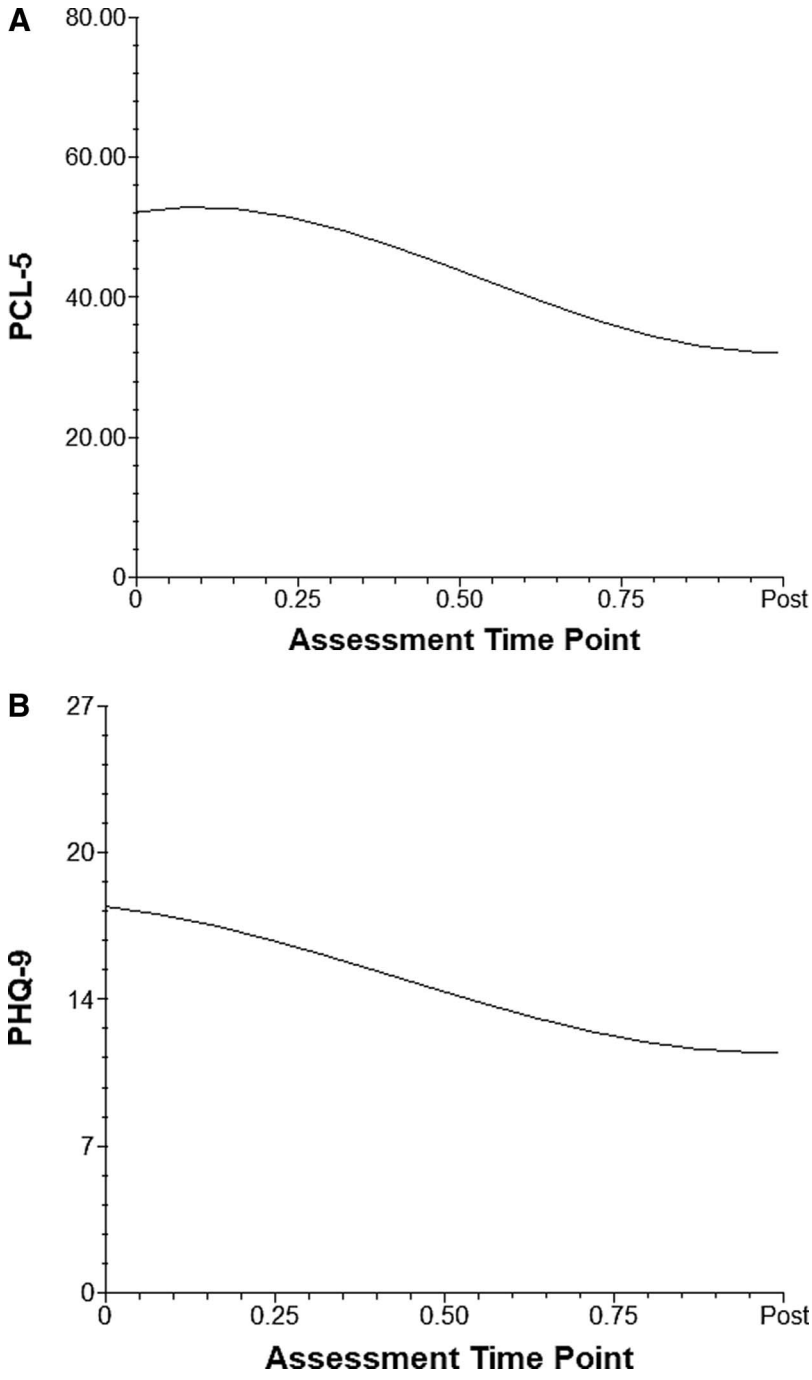

Figure 1. Average cubic trajectories of PTSD symptom (PTSD Checklist for *DSM–5*; PCL-5) change (A) and depression symptom (Patient Health Questionnaire 9; PHQ-9) change (B) over EHVP IOP; The effects of (C) low and high quality of life (PROMIS8A at Intake) on the linear slope of the PHQ-9 over EHVP IOP. The effects of (D) high and low cortisol response (AUCGPRE) on PTSD symptom change (PCL-5) over EHVP IOP. High and low scores represent the average of the highest and lowest quartile of observed scores in the sample. (*Figure continues on next page.*)

indicating that higher HRR at baseline predicted marginally greater reductions of depression symptoms over EHVP IOP. When examining cortisol, AUCg was significantly positively associated with the slope of the PCL-5, but not associated with the slope of the PHQ-9 (see Table 4), suggesting that greater cortisol output in response to the startle paradigm is related to less reduction in PTSD symptoms over EHVP IOP participation (see Figure 1D). AUCi was not associated with the intercept or slope of the PCL-5 or PHQ-9 (see Table 4).

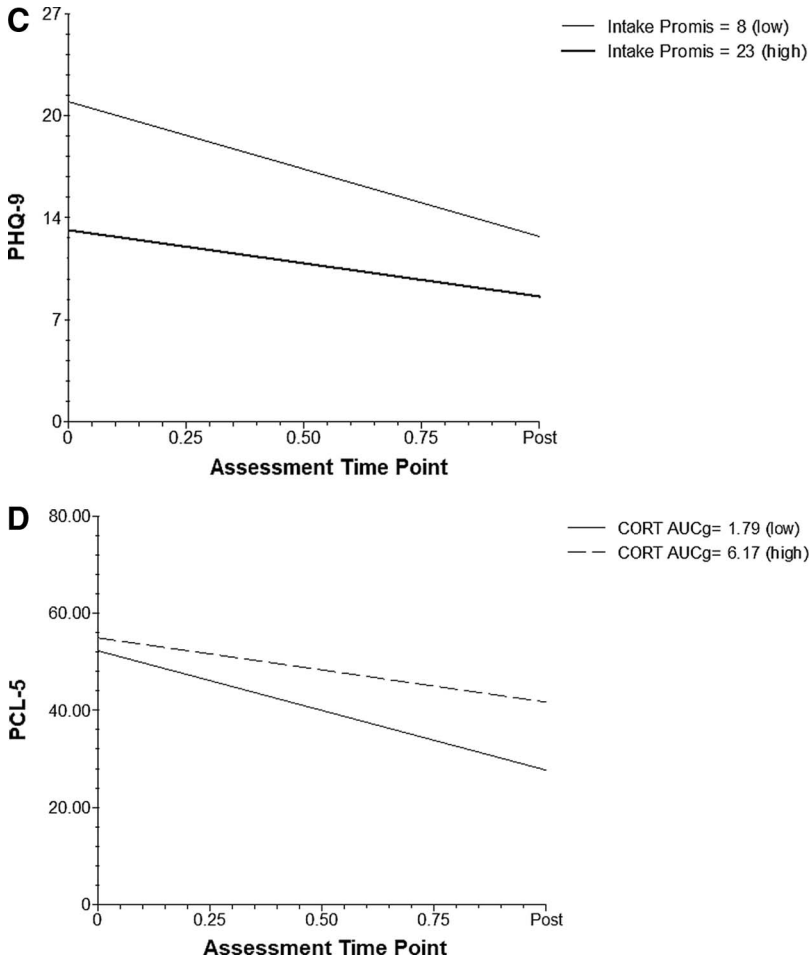

Figure 1. (*continued*)

Residualized change scores in the cortisol and HRR measures from baseline to post treatment were also examined as predictors of intercept and slope of PTSD and depression symptoms. Change in HRR was not significantly associated with PHQ-9 or PCL-5 scores at baseline (the intercept), or with the slope of these measures over treatment. AUCg change was significantly positively associated with the linear slope of PTSD symptoms, ($\gamma_{11} = 4.93$, $SE = 2.19$, $t = 2.26$, $p = .030$), but AUCi was not, suggesting that greater reductions in cortisol response (AUCg) over treatment were associated with greater reductions on the PCL-5. Neither AUCi nor AUCg change were associated with baseline symptom levels (i.e., the intercept). There were also no significant associations between either measure of cortisol change and the PHQ-9.

Discussion

The current study provides additional support for the effectiveness of integrative and intensive outpatient models of care for PTSD. Specifically, the EHVP IOP model of intensive outpatient prolonged exposure therapy combined with integrative services demonstrates significant and large reductions in PTSD and depression over two weeks with high acceptability and retention. The effect size for change in PTSD symptoms in this study ($d = 1.26$) was similar to that found in a previous effectiveness study for traditional PE in a VA setting ($d = 1.19$; Tuerk et al., 2011) which are comparable to meta-analyzed effect sizes for clinical trials of traditional PE (e.g., Powers, Halpern, Ferenschak, Gillihan, & Foa, 2010). The retention of over 95% of patients in the current model is noteworthy given that dropout rate is much higher (28%) for traditional PE for veterans delivered in VA settings (Eftekhari et al., 2013). Immersion in a new environment centered on approaching rather than avoiding trauma memories and reminders may be beneficial. Whereas standard outpatient treatment requires the patient to immerse and engage in a session and then go back to life between sessions, an intensive model allows patients to fully focus on processing traumatic events with support and few distractions. Moving toward intensive and integrative outpatient models may be a good fit for this avoidance-based disorder.

Consistent with previous studies (e.g., Rauch et al., 2015; Sripada et al., 2013), baseline severity of PTSD was not related to the magnitude of change. However, there was a trend toward higher baseline depression severity being related to greater reduction in depression over treatment and higher depression did not impede PTSD symptom change. Those reporting lower quality of life at intake reported significantly more change in depression. In line

Table 4
Growth Curve Models Examining Moderators of Symptom Change Over the Course of EHVP IOP

	Outcome: PCL-5			Outcome: PHQ-9		
Independent variable	B	*SE*	*t*	B	*SE*	*t*
NSI						
Effect on linear slope	−0.09	0.12	−0.75	−0.05	0.04	−1.13
AUDIT-C						
Effect on linear slope	0.89	0.70	1.28	0.42	0.26	1.59
PROMIS8A						
Effect on linear slope	0.63	0.40	1.56	0.30	0.11	2.74**
PHQ-9						
Effect on linear slope	−0.44	0.38	−1.16	−0.26	0.14	−1.86†
PCL-5						
Effect on linear slope	0.00	0.13	0.00	−0.03	0.04	−0.67
CAPS-5						
Effect on linear slope	0.20	0.21	0.96	0.02	0.08	0.28
Gender						
Effect on intercept	−2.36	3.59	−0.66	−0.01	1.35	−0.01
Effect on linear slope	−3.60	4.28	−0.84	−1.90	1.66	−1.15
Race						
Effect on intercept	7.75	3.28	2.36*	1.78	1.33	1.34
Effect on linear slope	7.23	4.63	1.56	1.34	1.62	0.83
Trauma Type						
Effect on intercept	8.55	3.58	2.39*	2.30	1.48	1.56
Effect on linear slope	−5.46	5.59	−0.98	0.82	1.88	0.44
Number of deployments						
Effect on intercept	0.01	1.06	0.01	−0.62	0.50	−1.23
Effect on linear slope	0.13	1.56	0.09	0.43	0.55	0.77
Heart rate reactivity						
Effect on intercept	−0.13	0.45	−0.30	0.08	0.17	0.47
Effect on linear slope	−0.35	0.65	−0.54	−0.36	0.18	−1.98†
Cortisol AUCg						
Effect on intercept	0.60	1.23	0.49	0.38	0.46	0.83
Effect on linear slope	2.60	1.08	2.41*	0.66	0.44	1.51
Cortisol AUCi						
Effect on intercept	2.41	1.84	1.31	0.97	0.78	1.24
Effect on linear slope	−3.42	2.60	−1.32	−0.86	0.55	−1.57

Note. Each moderator variable was entered in a separate multilevel model. PCL-5 = PTSD Checklist for the Fifth Edition of the Diagnostic and Statistical Manual 5 (DSM-5); PHQ-9 = Patient Health Questionnaire–9; NSI = Neurobehavioral Symptom Inventory; PROMIS 8A = Patient-Reported Outcomes Measurement Information System-Short Form version 1.0 –Physical Function 8A; EHVP = Emory Health care Veterans Program; IOP = Intensive Outpatient Program; CAPS-5 = Clinical Administered PTSD Scale-5.
† $p < .10$. * $p < .05$. ** $p < .01$.

with these findings, previous research shows no impact of depression on PTSD symptom change during PE (Hagenaars et al., 2010; Van Minnen, Arntz, & Keijsers, 2002). Further meta-analyses show that evidence-based treatments for PTSD reduce depression and PTSD at similar rates (Ronconi, Shiner, & Watts, 2015). Our findings extend this literature by demonstrating similar trends for depression symptoms over intensive PE for PTSD. Additionally, while many demographic variables were examined to determine impact on patterns of symptom change, only black veterans and those who identified MST as their target trauma showed higher severity of PTSD throughout the program but *did not* differ in the magnitude of change. Pretreatment depression, neurobehavioral symptom severity, alcohol use, quality of life, and PTSD *did not*moderate PTSD change. Together, these results suggest that intensive treatment programs like EHVP may be effective across demographically diverse veterans with a range of presenting concerns. When examining patterns of change in depression, those reporting lower quality of life showed larger gains.

In addition to symptom predictors, we also examined biological measures as predictors of change as well as change in biological measures and patterns of symptom change over treatment. Neither heart rate response nor cortisol response at baseline was associated with PTSD or depression severity at baseline. Greater baseline heart rate response was related to more change in depression at a trend level, but not to change in PTSD over treatment. Since our sample had only patients with PTSD, this may be due to more variance in depression severity in our sample than PTSD severity. However, examination of this result for replication in noneffectiveness samples is warranted.

Baseline cortisol response (AUCg) to the startle paradigm showed a positive and significant relationship with symptom change such that those people with higher cortisol response across the startle paradigm showed less change in PTSD over treatment, in line with previous findings examining cortisol reactivity during the same startle paradigm in a randomized clinical trial of VR exposure therapy for veterans with PTSD

(Norrholm et al., 2016). However, reduction in AUCg across treatment was significantly related to reduction in PTSD with treatment. Thus, those veterans who show a responsive HPA axis at baseline are less responsive to treatment, but those veterans who show reductions in HPA axis responsivity across treatment also show the largest symptom gains. Of note, response rates remain high even in those who are less responsive at baseline. As such, baseline assessment may be able to identify those veterans who require modifications to exposure to ensure they get the most out of treatment while still expecting therapeutic change even in the less responsive patients.

Limitations are apparent. First, effectiveness data from clinical care do not support causative interpretations as there is not randomization. Second, these veterans do not represent the spectrum of PTSD outpatients, as they did not include those who were unable to attend for two weeks or nonveteran patients. Third, we did not examine the effect of medication and as such cannot speak to the influence of medication on response or outcomes. A majority of participants were taking psychiatric medications prior to program entry and throughout treatment. Fourth, we did not present long-term follow-up as it is ongoing. Preliminary examinations suggest they changes were maintained. Fifth, we examined the EHVP IOP model as a whole and not what each of the component parts (massed PE and integrative) contributed. We would suspect that the effects on PTSD were driven by the massed PE, but dismantling study designs are needed to accurately make that claim. Finally, our sample size for the biological measures was smaller and requires replication.

In conclusion, integrative PTSD treatment including intensive outpatient PE and positive coping and wellness is a compelling model of PTSD care with highly promising outcomes in both depression and PTSD symptom reductions and retention in care across complex patient presentations. Additional study to establish maintenance of gains over time and focused on extending this model for use with other trauma populations beyond veterans is needed. Further, examination of who is using these models compared to standard outpatient care is needed to ensure we are reaching those people suffering with PTSD who need care.

References

American Psychological Association. (2017). *Clinical practice guideline for the treatment of PTSD*. Retrieved from http://www.apa.org/ptsd-guideline/ptsd.pdf

Beidel, D. C., Frueh, B. C., Neer, S. M., & Lejuez, C. W. (2017). The efficacy of trauma management therapy: A controlled pilot investigation of a three-week intensive outpatient program for combat-related PTSD. *Journal of Anxiety Disorders, 50,* 23–32. http://dx.doi.org/10.1016/j.janxdis.2017.05.001

Benge, J. F., Pastorek, N. J., & Thornton, G. M. (2009). Postconcussive symptoms in OEF-OIF veterans: Factor structure and impact of posttraumatic stress. *Rehabilitation Psychology, 54,* 270–278. http://dx.doi.org/10.1037/a0016736

Blevins, C. A., Weathers, F. W., Davis, M. T., Witte, T. K., & Domino, J. L. (2015). The Posttraumatic Stress Disorder Checklist for *DSM–5* (PCL-5): Development and initial psychometric evaluation. *Journal of Traumatic Stress, 28,* 489–498. http://dx.doi.org/10.1002/jts.22059

Blount, T. H., Cigrang, J. A., Foa, E. B., Ford, H. L., & Peterson, A. L. (2014). Intensive outpatient prolonged exposure for combat-related PTSD: A case study. *Cognitive and Behavioral Practice, 21,* 89–96. http://dx.doi.org/10.1016/j.cbpra.2013.05.004

Bovin, M. J., Marx, B. P., Weathers, F. W., Gallagher, M. W., Rodriguez, P., Schnurr, P. P., & Keane, T. M. (2016). Psychometric properties of the PTSD Checklist for Diagnostic and Statistical Manual of Mental Disorder—Fifth Edition (PCL-5) in veterans. *Psychological Assessment, 28,* 1379–1391. http://dx.doi.org/10.1037/pas0000254

Bradley, K. A., McDonell, M. B., Bush, K., Kivlahan, D. R., Diehr, P., & Fihn, S. D. (1998). The AUDIT alcohol consumption questions: Reliability, validity, and responsiveness to change in older male primary care patients. *Alcoholism: Clinical and Experimental Research, 22,* 1842–1849. http://dx.doi.org/10.1097/00000374-199811000-00034

Eftekhari, A., Ruzek, J. I., Crowley, J. J., Rosen, C. S., Greenbaum, M. A., & Karlin, B. E. (2013). Effectiveness of National Implementation of Prolonged Exposure Therapy in Veterans Affairs Care. *JAMA Psychiatry, 70,* 949–955. http://dx.doi.org/10.1001/jamapsychiatry.2013.36

Elzinga, B. M., Schmahl, C. G., Vermetten, E., van Dyck, R., & Bremner, J. D. (2003). Higher cortisol levels following exposure to traumatic reminders in abuse-related PTSD. *Neuropsychopharmacology, 28,* 1656–1665. http://dx.doi.org/10.1038/sj.npp.1300226

Finley, E. P., Garcia, H. A., Ketchum, N. S., McGeary, D. D., McGeary, C. A., Stirman, S. W., & Peterson, A. L. (2015). Utilization of evidence-based psychotherapies in Veterans Affairs posttraumatic stress disorder outpatient clinics. *Psychological Services, 12,* 73–82. http://dx.doi.org/10.1037/ser0000014

Foa, E. B., Hembree, E. A., Rothbaum, B. O., & Rauch, S. A. M. (2019). *Prolonged exposure therapy for PTSD: Therapist guide* (2nd ed.). New York, NY: Oxford University Press. http://dx.doi.org/10.1093/med-psych/9780190926939.001.0001

Foa, E. B., McLean, C. P., Zang, Y., Rosenfield, D., Yadin, E., Yarvis, J. S., . . . the STRONG STAR Consortium. (2018). Effect of prolonged exposure therapy delivered over 2 weeks vs 8 weeks vs present-centered therapy on PTSD symptom severity in military personnel: A randomized clinical trial. *Journal of the American Medical Association, 319,* 354–364. http://dx.doi.org/10.1001/jama.2017.21242

Galatzer-Levy, I. R., Steenkamp, M. M., Brown, A. D., Qian, M., Inslicht, S., Henn-Haase, C., . . . Marmar, C. R. (2014). Cortisol response to an experimental stress paradigm prospectively predicts long-term distress and resilience trajectories in response to active police service. *Journal of Psychiatric Research, 56,* 36–42. http://dx.doi.org/10.1016/j.jpsychires.2014.04.020

Hagenaars, M. A., Van Minnen, A., & Hoogduin, K. A. (2010). The impact of dissociation and depression on the efficacy of prolonged exposure treatment for PTSD. *Behaviour Research and Therapy, 48,* 19–27. http://dx.doi.org/10.1016/j.brat.2009.09.001

Harvey, M. M., Petersen, T. J., Sager, J. C., Makhija-Graham, N. J., Wright, E. C., Clark, E. L., . . . Simon, N. M. (2019). An intensive outpatient program for veterans with posttraumatic stress disorder and traumatic brain injury. *Cognitive and Behavioral Practice.* Advance online publication. http://dx.doi.org/10.1016/j.cbpra.2018.07.003

National Institute of Health (Producer). (2008, 06/01/2018). Patient Reported Outcomes Measurement Information System (PROMIS) [online]. Retrieved from http://www.nihpromis.org

Hendriks, L., de Kleine, R. A., Broekman, T. G., Hendriks, G. J., & van Minnen, A. (2018). Intensive prolonged exposure therapy for chronic PTSD patients following multiple trauma and multiple treatment attempts. *European Journal of Psychotraumatology, 9,* 1425574. http://dx.doi.org/10.1080/20008198.2018.1425574

Jovanovic, T., Rauch, S. A., Rothbaum, A. O., & Rothbaum, B. O. (2017). Using experimental methodologies to assess posttraumatic stress. *Current Opinion in Psychology, 14,* 23–28. http://dx.doi.org/10.1016/j.copsyc.2016.10.001

Kehle-Forbes, S. M., Meis, L. A., Spoont, M. R., & Polusny, M. A. (2016). Treatment initiation and dropout from prolonged exposure and cognitive

processing therapy in a VA outpatient clinic. *Psychological Trauma: Theory, Research, Practice and Policy, 8,* 107–114. http://dx.doi.org/10.1037/tra0000065

Knowles, K. A., Sripada, R. K., Defever, M., & Rauch, S. A. M. (2019). Comorbid mood and anxiety disorders and severity of posttraumatic stress disorder symptoms in treatment-seeking veterans. *Psychological Trauma: Theory, Research, Practice and Policy, 11,* 451–458. http://dx.doi.org/10.1037/tra0000383

Kroenke, K., Spitzer, R. L., & Williams, J. B. W. (2001). The PHQ-9: Validity of a brief depression severity measure. *Journal of General Internal Medicine, 16,* 606–613. http://dx.doi.org/10.1046/j.1525-1497.2001.016009606.x

Liberzon, I., Abelson, J. L., Flagel, S. B., Raz, J., & Young, E. A. (1999). Neuroendocrine and psychophysiologic responses in PTSD: A symptom provocation study. *Neuropsychopharmacology, 21,* 40–50. http://dx.doi.org/10.1016/S0893-133X(98)00128-6

Löwe, B., Unützer, J., Callahan, C. M., Perkins, A. J., & Kroenke, K. (2004). Monitoring depression treatment outcomes with the patient health questionnaire-9. *Medical Care, 42,* 1194–1201. http://dx.doi.org/10.1097/00005650-200412000-00006

Manea, L., Gilbody, S., & McMillan, D. (2012). Optimal cut-off score for diagnosing depression with the Patient Health Questionnaire (PHQ-9): A meta-analysis. *Canadian Medical Association Journal, 184,* E191–E196. http://dx.doi.org/10.1503/cmaj.110829

Mott, J. M., Mondragon, S., Hundt, N. E., Beason-Smith, M., Grady, R. H., & Teng, E. J. (2014). Characteristics of U.S. veterans who begin and complete prolonged exposure and cognitive processing therapy for PTSD. *Journal of Traumatic Stress, 27,* 265–273. http://dx.doi.org/10.1002/jts.21927

Norrholm, S. D., Jovanovic, T., Gerardi, M., Breazeale, K. G., Price, M., Davis, M., . . . Rothbaum, B. O. (2016). Baseline psychophysiological and cortisol reactivity as a predictor of PTSD treatment outcome in virtual reality exposure therapy. *Behaviour Research and Therapy, 82,* 28–37. http://dx.doi.org/10.1016/j.brat.2016.05.002

Olff, M., Güzelcan, Y., de Vries, G.-J., Assies, J., & Gersons, B. P. R. (2006). HPA- and HPT-axis alterations in chronic posttraumatic stress disorder. *Psychoneuroendocrinology, 31,* 1220–1230. http://dx.doi.org/10.1016/j.psyneuen.2006.09.003

Orr, S. P., Lasko, N. B., Macklin, M. L., Pineles, S. L., Chang, Y., & Pitman, R. K. (2012). Predicting post-trauma stress symptoms from pre-trauma psychophysiologic reactivity, personality traits and measure of psychopathology. *Biology of Mood and Anxiety, 2,* 1–12. http://dx.doi.org/10.1186/2045-5380-2-8

Orr, S. P., Metzger, L. J., & Pitman, R. K. (2002). Psychophysiology of post-traumatic stress disorder. *Psychiatric Clinics of North America, 25,* 271–293. http://dx.doi.org/10.1016/S0193-953X(01)00007-7

Pitman, R. K., Orr, S. P., Forgue, D. F., de Jong, J. B., & Claiborn, J. M. (1987). Psychophysiologic assessment of posttraumatic stress disorder imagery in Vietnam combat veterans. *Archives of General Psychiatry, 44,* 970–975. http://dx.doi.org/10.1001/archpsyc.1987.01800230050009

Powers, M. B., Halpern, J. M., Ferenschak, M. P., Gillihan, S. J., & Foa, E. B. (2010). A meta-analytic review of prolonged exposure for posttraumatic stress disorder. *Clinical Psychology Review, 30,* 635–641. http://dx.doi.org/10.1016/j.cpr.2010.04.007

Pruessner, J. C., Kirschbaum, C., Meinlschmid, G., & Hellhammer, D. H. (2003). Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology, 28,* 916–931. http://dx.doi.org/10.1016/S0306-4530(02)00108-7

Rauch, S. A., King, A. P., Abelson, J., Tuerk, P. W., Smith, E., Rothbaum, B. O., . . . Liberzon, I. (2015). Biological and symptom changes in posttraumatic stress disorder treatment: A randomized clinical trial. *Depression and Anxiety, 32,* 204–212. http://dx.doi.org/10.1002/da.22331

Raudenbush, S. W., Bryk, A. S., Cheong, Y. F., Congdon, R. T., & du Toit, M. (2011). *HLM7 hierarchical linear and nonlinear modeling user manual: User guide for Scientific Software International's (S.S.I.) Program*. Skokie, IL: Scientific Software International, Inc.

Robison-Andrew, E. J., Duval, E. R., Nelson, C. B., Echiverri-Cohen, A., Giardino, N., Defever, A., . . . Rauch, S. A. M. (2014). Changes in trauma-potentiated startle with treatment of posttraumatic stress disorder in combat veterans. *Journal of Anxiety Disorders, 28,* 358–362. http://dx.doi.org/10.1016/j.janxdis.2014.04.002

Ronconi, J. M., Shiner, B., & Watts, B. V. (2015). A Meta-Analysis of Depressive Symptom Outcomes in Randomized, Controlled Trials for PTSD. *Journal of Nervous and Mental Disease, 203,* 522–529. http://dx.doi.org/10.1097/nmd.0000000000000322

Rosen, C. S., Matthieu, M. M., Wiltsey Stirman, S. J. M., Cook, J. M., Landes, S., Bernardy, N. C., . . . M. H. S. Research. (2016). A review of studies on the system-wide implementation of evidence-based psychotherapies for posttraumatic stress disorder in the Veterans Health Administration. *Administration and Policy in Mental Health and Mental Health Services Research, 43,* 957–977.

Rothbaum, B. O., Price, M., Jovanovic, T., Norrholm, S. D., Gerardi, M., Dunlop, B., . . . Ressler, K. J. (2014). A randomized, double-blind evaluation of D-cycloserine or alprazolam combined with virtual reality exposure therapy for posttraumatic stress disorder in Iraq and Afghanistan War veterans. *The American Journal of Psychiatry, 171,* 640–648. http://dx.doi.org/10.1176/appi.ajp.2014.13121625

Shalev, A. Y., Orr, S. P., & Pitman, R. K. (1993). Psychophysiologic assessment of traumatic imagery in Israeli civilian patients with posttraumatic stress disorder. *The American Journal of Psychiatry, 150,* 620–624. http://dx.doi.org/10.1176/ajp.150.4.620

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., . . . Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (M. I. N. I.): The development and validation of a structured diagnostic psychiatric interview for *DSM–IV* and ICD-10. *The Journal of Clinical Psychiatry, 59*(Suppl. 20), 22–33.

Shiner, B., D'Avolio, L. W., Nguyen, T. M., Zayed, M. H., Young-Xu, Y., Desai, R. A., . . . Watts, B. V. (2013). Measuring use of evidence based psychotherapy for posttraumatic stress disorder. *Administration and Policy in Mental Health and Mental Health Services Research, 40,* 311–318. http://dx.doi.org/10.1007/s10488-012-0421-0

Smith, E. R., Porter, K. E., Messina, M. G., Beyer, J. A., Defever, M. E., Foa, E. B., & Rauch, S. A. (2015). Prolonged Exposure for PTSD in a Veteran group: A pilot effectiveness study. *Journal of Anxiety Disorders, 30,* 23–27. http://dx.doi.org/10.1016/j.janxdis.2014.12.008

Sripada, R. K., Rauch, S. A., Tuerk, P. W., Smith, E., Defever, A. M., Mayer, R. A., . . . Venners, M. (2013). Mild traumatic brain injury and treatment response in prolonged exposure for PTSD. *Journal of Traumatic Stress, 26,* 369–375. http://dx.doi.org/10.1002/jts.21813

Tanev, K. S., Federico, L. E., Terry, D. P., Clark, E. L., & Iverson, G. L. (2019). Cognitive impairment and predicting response to treatment in an intensive clinical program for post-9/11 veterans with posttraumatic stress disorder. *The Journal of Neuropsychiatry and Clinical Neurosciences, 31,* 337–345. Advance online publication. http://dx.doi.org/10.1176/appi.neuropsych.18090208

Tuerk, P. W., Yoder, M., Grubaugh, A., Myrick, H., Hamner, M., & Acierno, R. (2011). Prolonged exposure therapy for combat-related posttraumatic stress disorder: an examination of treatment effectiveness for veterans of the wars in Afghanistan and Iraq. *Journal of Anxiety Disorders, 25,* 397–403. http://dx.doi.org/10.1016/j.janxdis.2010.11.002

Van Minnen, A., Arntz, A., & Keijsers, G. P. (2002). Prolonged exposure in patients with chronic PTSD: predictors of treatment outcome and dropout. *Behaviour Research and Therapy, 40,* 439–457. http://dx.doi.org/10.1016/s0005-7967(01)00024-9

VA/DOD. (2017). *Veterans Affairs and Department of Defense clinical practice guideline for management of post-traumatic stress*. Retrieved from https://www.healthquality.va.gov/guidelines/MH/ptsd/

Wangelin, B. C., & Tuerk, P. W. (2015). Taking the Pulse of Prolonged Exposure therapy: Psychiological Reactivity to Trauma Imagery as an Objective Measure of Treatment Response. *Depression and Anxiety, 32,* 927–934. http://dx.doi.org/10.1002/da.22449

Weathers, F. W., Blake, D. D., Schnurr, P. P., Kaloupek, D. G., Marx, B. P., & Keane, T. M. (Producer). (2013, 06/01/2016). The Clinician-Administered PTSD Scale for DSM–5 (CAPS-5). Retrieved from http://www.ptsd.va.gov/professional/assessment/adult-int/caps.asp

Weathers, F. W., Bovin, M. J., Lee, D. J., Sloan, D. M., Schnurr, P. P., Kaloupek, D. G., . . . Marx, B. P. (2018). The Clinician-Administered PTSD Scale for *DSM–5* (CAPS-5): Development and initial psychometric evaluation in military veterans. *Psychological Assessment, 30,* 383–395. http://dx.doi.org/10.1037/pas0000486

Weathers, F. W., Litz, B. T., Keane, T. M., Palmieri, P. A., Marx, B. P., & Schnurr, P. P. (2013). The PTSD Checklist for *DSM–5* (PCL-5). Scale available from the National Center for PTSD at www.ptsd.va.gov

Wortmann, J. H., Jordan, A. H., Weathers, F. W., Resick, P. A., Dondanville, K. A., Hall-Clark, B., . . . Litz, B. T. (2016). Psychometric analysis of the PTSD Checklist-5 (PCL-5) among treatment-seeking military service members. *Psychological Assessment, 28,* 1392–1403. http://dx.doi.org/10.1037/pas0000260

Yehuda, R., Yang, R.-K., Buchsbaum, M. S., & Golier, J. A. (2006). Alterations in cortisol negative feedback inhibition as examined using the ACTH response to cortisol administration in PTSD. *Psychoneuroendocrinology, 31,* 447–451. http://dx.doi.org/10.1016/j.psyneuen.2005.10.007

Zalta, A. K., Held, P., Smith, D. L., Klassen, B. J., Lofgreen, A. M., Normand, P. S., . . . Karnik, N. S. (2018). Evaluating patterns and predictors of symptom change during a three-week intensive outpatient treatment for veterans with PTSD. *BMC Psychiatry, 18,* 242. http://dx.doi.org/10.1186/s12888-018-1816-6

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Correction to Rauch et al. (2021)

In the article "An Intensive Outpatient Program With Prolonged Exposure for Veterans With Posttraumatic Stress Disorder: Retention, Predictors, and Patterns of Change," by Sheila A. M. Rauch, Carly W. Yasinski, Loren M. Post, Tanja Jovanovic, Seth Norrholm, Andrew M. Sherrill, Vasiliki Michopoulos, Jessica L. Maples-Keller, Kathryn Black, Liza Zwiebach, Boadie W. Dunlop, Laura Loucks, Brittany Lannert, Monika Stojek, Laura Watkins, Mark Burton, Kelsey Sprang, Lauren McSweeney, Katie Ragsdale, and Barbara O. Rothbaum (*Psychological Services*, 2021, Vol. 18, No. 4, pp. 606–618, https://doi.org/10.1037/ser0000422), in the second sentence of the paragraph under "Baseline to Post-Treatment Change in Symptoms" in the Results section, changes were needed to match the information given in Table 3. The sentence "Posttreatment scores were not available for 11 of the 77 completers on the PCL-5 and one of the 77 completers on the PHQ-9 due to administrations error, so baseline to posttreatment change in PCL-5 was calculated based on 68 veterans and for the PHQ-9 on 76 patients" should have said "Posttreatment scores were not available for 9 of the 77 completers on the PCL-5 due to administrations error, so baseline to posttreatment change in PCL-5 was calculated based on 68 veterans. $N = 77$ for all other measures." These changes do not alter the conclusions of this article. The online version of this article has been corrected.

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