

Efficacy of Integrated Exposure Therapy vs Integrated Coping Skills Therapy for Comorbid Posttraumatic Stress Disorder and Alcohol Use Disorder

A Randomized Clinical Trial

Sonya B. Norman, PhD; Ryan Trim, PhD; Moira Haller, PhD; Brittany C. Davis, PhD; Ursula S. Myers, PhD; Peter J. Colvonen, PhD; Erika Blanes, MA; Robert Lyons, BS; Emma Y. Siegel, BA; Abigail C. Angkaw, PhD; Gregory J. Norman, PhD; Tina Mayes, PhD

[+ Supplemental content](#)

IMPORTANCE Co-occurrence of posttraumatic stress disorder (PTSD) and alcohol use disorder (AUD) is common and associated with psychiatric and functional problems. Understanding whether exposure therapy is tolerable and efficacious for treating PTSD and AUD is critical to ensure that best practice treatments are available.

OBJECTIVE To compare the efficacy of integrated (ie, targeting both PTSD and alcohol use) prolonged exposure (I-PE) therapy with present-centered integrated coping skills (I-CS) therapy, a more commonly available treatment, in reducing PTSD symptoms and alcohol use.

DESIGN, SETTING, AND PARTICIPANTS This prospective randomized clinical trial with masked assessments considered 186 veterans seeking Veterans Affairs mental health services. A total of 119 veterans with PTSD and AUD were randomized. Data were collected from February 1, 2013, to May 31, 2017, before treatment, after treatment, and at 3- and 6-month follow-ups. Intention-to-treat analyses were performed.

INTERVENTIONS Veterans underwent I-PE (Concurrent Treatment of PTSD and Substance Use Disorder Using Prolonged Exposure) or I-CS (Seeking Safety) therapy.

MAIN OUTCOMES AND MEASURES A priori planned outcomes were PTSD symptoms (Clinician Administered PTSD Scale for *DSM-5*) and percentage of heavy drinking days (Timeline Follow-Back) before treatment, after treatment, and at 3- and 6-month follow-ups.

RESULTS A total of 119 veterans (mean [SD] age, 41.6 [12.6] years; 107 [89.9%] male) were randomized. Linear mixture models found that PTSD symptoms decreased in both conditions, with a significantly greater decrease for I-PE treatment compared with I-CS treatment (treatment \times time interaction, -2.83 ; $F_{3,233.1} = 4.92$; Cohen $d = 0.41$; $P = .002$). The percentage of heavy drinking days improved in both conditions but was not statistically different between I-PE and I-CS treatment (treatment \times time interaction, 1.8% ; $F_{3,209.9} = 0.18$; Cohen $d = 0.04$; $P = .91$).

CONCLUSIONS AND RELEVANCE The I-PE arm had a greater reduction in PTSD symptoms than the I-CS arm and comparable drinking decreases. The study provides evidence that exposure therapy is more efficacious in treating PTSD than a more commonly available integrated treatment without exposure for comorbid PTSD and AUD.

TRIAL REGISTRATION ClinicalTrials.gov identifier: NCT01601067

JAMA Psychiatry. 2019;76(8):791-799. doi:10.1001/jamapsychiatry.2019.0638
Published online April 24, 2019.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Sonya Norman, PhD, VA San Diego Healthcare System, 3350 La Jolla Village Dr, MC116B, San Diego, CA 92161 (snorman@ucsd.edu).

Posttraumatic stress disorder (PTSD) frequently co-occurs with alcohol use disorders (AUDs) in the general population¹ and among veterans.² Individuals with PTSD and AUD exhibit briefer abstinence periods, greater risk of suicidality and homelessness, and more medical, legal, and psychosocial problems than individuals with either disorder alone.³⁻⁷

Trauma-focused exposure psychotherapies, such as prolonged exposure therapy,⁸ are the first line of treatment of PTSD based on numerous studies and clinical practice guidelines.⁹⁻¹⁷ Several studies¹⁸⁻²¹ have found that, for patients with PTSD and AUD or PTSD comorbid with alcohol and/or other substance use disorders (A/SUDs), exposure therapy is more efficacious in reducing PTSD symptoms than A/SUD-only treatment. However, individuals with PTSD and AUD are often not offered exposure therapy because of concerns that exposure to trauma memories may lead to increased drinking and crises.²² Furthermore, treatment attendance is sometimes lower with exposure therapy than in A/SUD-only treatment.¹⁸ Psychotherapy for PTSD and AUD that focuses on improving coping skills is well accepted and highly disseminated.²³ Such therapy posits that establishing safety through better coping is the first priority for patients with PTSD and A/SUD and that eliciting trauma memories too early in treatment may be harmful.²⁴ Although session attendance is comparable to A/SUD-only treatment, questions remain about whether coping skills therapy is more efficacious than A/SUD-only care.¹⁸ To date, no randomized clinical trials (RCTs) have directly compared the efficacy and tolerability of 2 active integrated PTSD and AUD interventions, specifically, exposure and coping skills therapies. In addition, many studies of PTSD and AUD treatment have been limited by narrow inclusion and exclusion criteria and methodologic problems, such as low recruitment, leading to risk of bias and low power to detect differences among treatments.¹⁸ Understanding which interventions are the most efficacious and tolerable for treating PTSD and AUD and, in particular, whether exposure therapy is tolerable and more efficacious than coping skills therapy even when AUD is present is critical to improving outcomes and ensuring best practice treatments are available to patients with comorbid conditions.

The current trial was designed to address these critical gaps. The objective was to compare integrated prolonged exposure (I-PE) therapy, using the Concurrent Treatment for PTSD and Substance Use Disorder Using Prolonged Exposure (COPE)²⁵ protocol, with the most widely used¹⁸ integrated coping skills (I-CS) therapy, Seeking Safety (SS).²⁶ We hypothesized that I-PE treatment would produce greater reductions in PTSD symptoms after treatment and at follow-ups and that both arms would have reductions in the percentage of heavy drinking days (PHDD) after treatment but that the I-PE therapy arm would have a significantly lower PHDD at 3- and 6-month follow-ups. The PHDD variable was selected as the primary alcohol use outcome because many participants chose harm reduction rather than abstinence as their treatment goal. In addition to the primary outcomes of PTSD symptoms and PHDD, we examined the percentage of days abstinent (PDA) from al-

Key Points

Question Is integrated prolonged exposure therapy tolerable and more efficacious than present-centered integrated coping skills therapy for reducing posttraumatic stress disorder symptoms and alcohol use in patients with comorbid posttraumatic stress disorder and alcohol use disorder?

Findings In this randomized clinical trial of 119 patients, exposure therapy reduced posttraumatic stress disorder symptoms significantly more than coping skills therapy after treatment and at 3- and 6-month follow-ups. Participants in both treatment arms had reductions in heavy drinking days over time.

Meaning Integrated prolonged exposure therapy was well tolerated and had greater efficacy for reducing posttraumatic stress disorder symptoms than present-centered integrated coping skills therapy.

cohol and PTSD remission at each time point. Discontinuations attributable to serious adverse events and treatment satisfaction were examined as markers of tolerability and satisfaction.

Methods

Design

The study was an RCT of 2 active treatments, I-PE and I-CS therapy, for PTSD and AUD. Participants gave written informed consent before enrollment by the study coordinator (E.B.). Independent evaluators were masked to treatment assignment for study duration. Details of methods are published elsewhere.²⁷ The study was approved by the VA San Diego Research Review Board. The trial protocol can be found in [Supplement 1](#).

Participants

Demographic characteristics are given in [Table 1](#). Participants were 119 adult veterans (107 male) seeking treatment at a large urban veterans affairs (VA) facility. Patients who potentially had PTSD and AUD based on medical record review were referred to the study by mental health practitioners. Patients also responded to flyers posted around the VA facility. Eligible participants had current full or subthreshold PTSD (up to 1 symptom missing)²⁸ and current AUD with at least 20 days of heavy alcohol use in the past 90 days not in a restricted environment and wanted to reduce or abstain from alcohol use. Exclusion criteria were acute suicidality, unmanaged psychosis or mania, and intravenous drug use. Participants were asked not to engage in other PTSD psychotherapy during study treatment. Participation in other mental health treatment (medications and psychotherapy) was tracked.

Procedures

Recruitment took place from February 1, 2013, to May 31, 2017. After a telephone screen, participants were scheduled to provide written informed consent and complete baseline assessments. The Clinician Administered PTSD Scale for *DSM-5*

Table 1. Demographic Characteristics of the Intention-to-Treat Sample^a

Characteristics	Total (N = 119)	I-PE Treatment (n = 63)	I-CS Treatment (n = 56)	P Value
Age, mean (SD), y	41.6 (12.6)	43.2 (13.5)	39.7 (11.3)	.13
Sex				
Men	107 (89.9)	56 (88.9)	51 (91.1)	.69
Women	12 (10.1)	7 (11.1)	5 (8.9)	
Marital status				
Not married	87 (73.1)	45 (71.4)	42 (75.0)	.54
Married	32 (26.9)	18 (28.6)	14 (25.0)	
Educational level				
High school graduate or GED	11 (9.2)	6 (9.5)	5 (8.9)	.62
Some college	65 (54.6)	33 (52.4)	32 (57.1)	
College graduate	36 (30.2)	21 (33.3)	15 (26.8)	
Ethnicity				
Hispanic	35 (29.4)	18 (28.6)	17 (30.4)	.70
Non-Hispanic	83 (69.7)	44 (69.8)	39 (69.6)	
Race				
White	78 (65.5)	41 (65.1)	37 (66.1)	.44
Black	16 (13.4)	8 (12.7)	8 (14.3)	
Asian	6 (5.0)	3 (4.8)	3 (5.4)	
Other	18 (15.1)	11 (17.5)	7 (12.5)	
Subthreshold PTSD	5 (4.2)	2 (3.2)	3 (5.4)	.82
Lifetime trauma exposure, mean (SD), No. of events	8.3 (2.7)	8.5 (2.6)	7.9 (2.8)	.20
Event type				
Combat trauma	100 (84.0)	51 (81.0)	49 (87.5)	.33
Sexual trauma	28 (23.5)	15 (23.8)	13 (23.2)	.94
Physical assault	98 (82.4)	53 (84.1)	45 (80.4)	.74
Disaster exposure	83 (69.7)	43 (68.2)	40 (71.4)	.71
Serious incident	60 (50.4)	30 (47.6)	30 (53.6)	.52
Life-threatening illness or injury	34 (28.6)	19 (30.2)	15 (26.8)	.73
Taking psychotropic medication ^b	78 (65.5)	49 (77.8)	29 (51.8)	.003
Baseline assessment scores, mean (SD) ^b				
Interviewer-rated PTSD severity, CAPS-5 score, mean (SD) ^c	42.7 (9.5)	43.2 (8.8)	42.0 (10.3)	.55
Substance use, TLFB score, mean (SD) ^c				
Days drinking alcohol in past 90 d, %	67.2 (22.9)	65.7 (24.5)	68.8 (21.1)	.45
Days of heavy drinking in past 90 d, % ^d	51.5 (26.1)	52.5 (25.6)	50.4 (26.9)	.66
Days of drug use in past 90 d, %	16.6 (30.9)	16.4 (31.2)	16.8 (30.9)	.94
No. of total sessions attended, mean (SD)	9.8 (4.9)	8.4 (4.6)	11.4 (4.8)	.001
Mean No. of weeks in treatment	13.61 (6.46)	12.21 (6.46)	15.19 (6.40)	.02
Treatment satisfaction, CSQ-8 score, mean (SD) ^c	29.1 (2.7)	28.9 (2.7)	29.4 (2.8)	.40

Abbreviations: CAPS-5, Clinician Administered PTSD Scale for *DSM-5*; CSQ-8, Client Satisfaction Questionnaire 8; GED, General Educational Development; I-CS, integrated coping skills; I-PE, integrated prolonged exposure; PTSD, posttraumatic stress disorder; TLFB, Timeline Follow-Back.

^a Data are presented as number (percentage) unless otherwise indicated.

^b For descriptions of score ranges, see the Methods section of the text.

^c Scoring details are given in the Measures subsection of the Methods section.

^d Heavy drinking was defined as at least 5 drinks per day for men and 4 drinks per day for women.

(CAPS-5),²⁹ the Structured Clinical Interview for *DSM-IV-TR* (SCID-IV) Module E,³⁰ and the Timeline Follow-Back³¹ confirmed study criteria for PTSD, AUD, and alcohol use, respectively. Participants then met with a study practitioner (M.H., B.C.D., U.S.M., P.J.C., T.M., and others) to learn more about both therapies and ask any remaining questions about the treatment process. Balanced block randomization (variable blocks of 8-12 individuals) with masked allocation was stratified by sex. A statistician not otherwise involved in the study used SAS Institute's³² random number generator for randomization. Participants were informed of their treatment condition at their first therapy session. Participants engaged in 12 to 16 sessions

of psychotherapy and then completed measures after treatment and at 3- and 6-month posttreatment follow-ups. Compensation was \$20 at baseline, \$30 after treatment, and \$50 per follow-up.

Masked independent evaluators completed training and achieved at least 90% agreement on CAPS-5 item scores before conducting assessments. Interrater reliability, conducted on 11% of randomly selected CAPS-5 assessments, was excellent ($\kappa = 0.94$ for diagnosis; intraclass correlation coefficient, 0.99; 95% CI, 0.98-0.99).^{29,33} Study therapists were 13 licensed psychologists, postdoctoral fellows, clinical psychology interns, and doctoral students. Most participants were seen

by therapists who administered both treatments (to control for therapist effects). The exception was doctoral students, who were only able to see ¹ to 3 participants during their training rotation (a parallel set of analyses were conducted that excluded 11 participants treated by doctoral students to ensure robustness of the findings). Therapists received training in study protocols through didactics, videos, and practice sessions with a supervisor before treating a participant. The first time that therapists administered each intervention, all sessions were rated for fidelity. Henceforth, all sessions were recorded and 10% were rated. Therapists received weekly individual and group supervision.

Measures

The CAPS-5 (score range, 0-80, with 0 indicating no PTSD symptoms and 80 indicating extreme ratings across all symptoms), a 30-item structured interview²⁹ considered to be the criterion standard for PTSD, was the primary measure of PTSD symptoms and diagnosis. Diagnosis was determined using the rule of a severity score of 2 or higher, which follows DSM-5 PTSD criteria. A CAPS-5 diagnosis using this rule displayed strong interrater reliability ($\kappa = 0.78$), and severity scores had strong internal consistency ($\alpha = .88$) in the development sample.²⁹ Internal consistency in the current sample was strong ($\alpha = .83$). At each time point, PTSD remission was defined as a total score less than 12 because it is not possible to have a diagnosis of PTSD with a score less than 12. This optimally conservative cut-off was recommended by CAPS developers (P. P. Schnurr, PhD, and B. P. Marx, PhD, written communication, April 2018).

Frequency and quantity of alcohol use were assessed using the Timeline Follow-Back, a calendar-assisted structured clinical interview³¹ that displays good psychometric properties.³⁴ The PHDD was calculated by dividing the number of days in which 5 or more drinks for men or 4 or more drinks for women were consumed by the total number of days in the reference period. Toxicology screens were completed during a randomly selected week each month, and Breathalyzer tests were administered if there was indication that a participant came to an appointment after consuming alcohol.

The Modified Interview of Antiretroviral Medication Use³⁵ was used to assess past week adherence to psychotropic medications. The Client Satisfaction Questionnaire (score range, 8-32, with 8 indicating extremely poor satisfaction and 32 indicating extremely high satisfaction), a widely used measure of psychotherapy satisfaction,³⁶ was administered every other therapy session. The mean across-treatment sessions were computed to ascertain satisfaction.

Treatments

The I-PE and I-CS treatments were delivered in 90-minute individual sessions. Therapy was 12 sessions, with the option of completing up to 16 sessions if the participant and therapist agreed that treatment goals were not yet met. Participants were encouraged to attend therapy 1 to 2 times per week on consecutive weeks but allowed up to 6 months to finish treatment.

COPE²⁵ is an integrated PTSD and SUD treatment that augments prolonged exposure with cognitive behavioral relapse

prevention skills for SUD in each session. COPE includes in vivo exposures to trauma reminders (starting in session 3) and repeated imaginal exposures to the trauma memory (starting in session 4). The COPE manual includes 12 sessions. For participants who completed 13 to 16 sessions, up to 4 SUD skills were repeated (S. E. Back, PhD, oral communication, November 2012).

The SS treatment²⁶ is a present-focused, PTSD and SUD integrated therapy that teaches cognitive behavioral and interpersonal techniques and case management. It consists of 24 modules. Each module includes safe coping skills. Trauma is discussed in the context of how it is currently affecting the patient's life. For this study, session topics were predetermined for sessions 1 through 12 based on previous research.³⁷ Participants completing 13 to 16 sessions selected from the remaining topics.

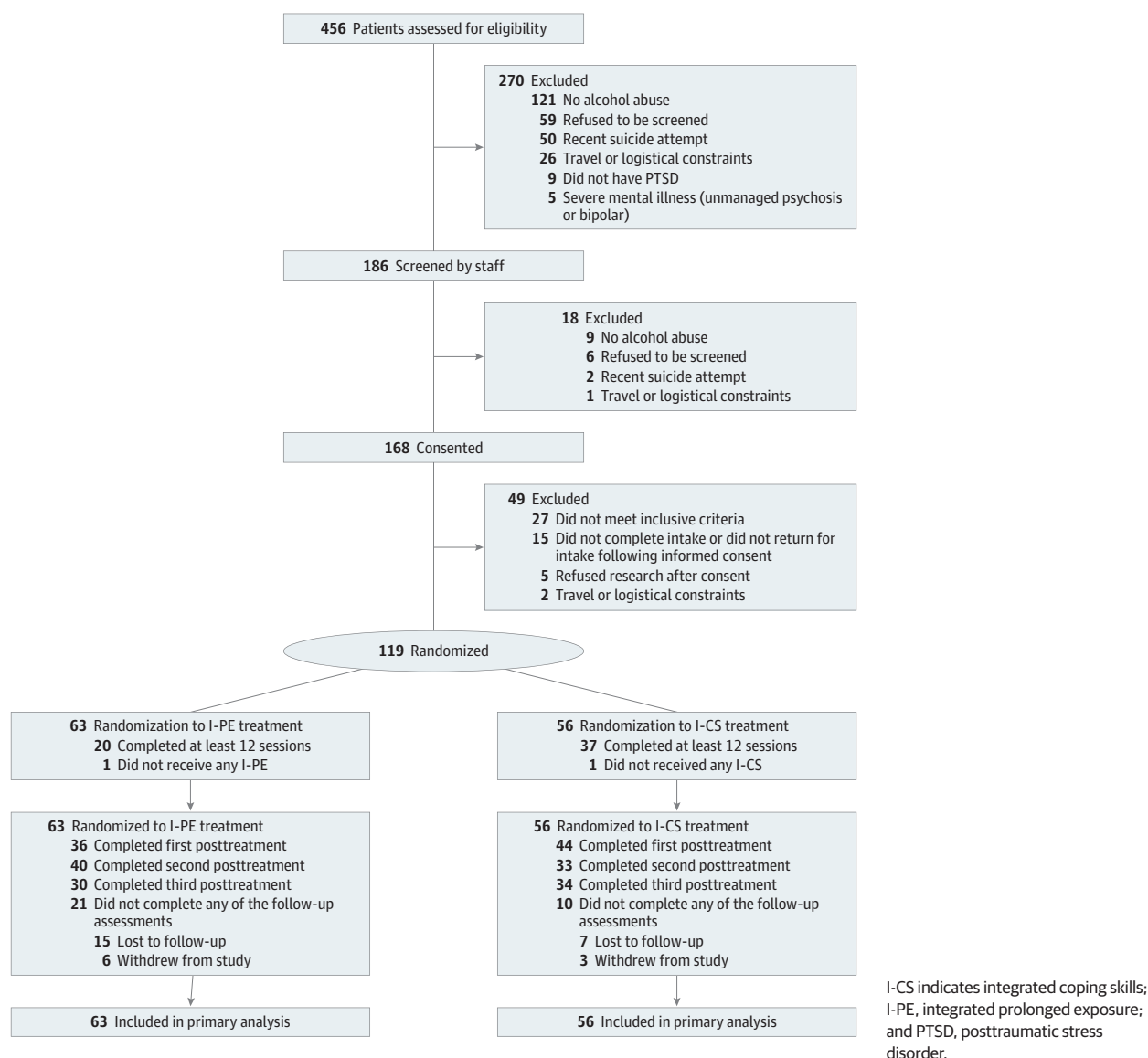
Forty-seven I-PE and 59 I-CS therapy session recordings were rated for fidelity. A score of 2 or higher (range, 0-4, with 0 indicating no fidelity and 4 indicating excellent fidelity) on the COPE fidelity scale indicated adequate adherence and competence with I-PE therapy.^{11,20} Strong adherence (mean [SD], 3.18 [0.48]) and competency were maintained (mean [SD], 3.65 [0.42]). The SS adherence scale,³⁸ a 4-point scale (range, 0-3, with 0 indicating not done or harmful and 3 indicating done thoroughly or extremely helpful), was used for I-CS therapy. Strong adherence (mean [SD], 2.45 [0.27]) and competency (mean [SD], 2.59 [0.26]) were maintained.

Statistical Analysis

Sample size was determined to ensure adequate statistical power to detect between-group differences in PTSD and alcohol use after treatment. We anticipated a large between-group effect size for PTSD based on findings of studies evaluating I-PE and I-CS treatment for PTSD¹⁸; thus, the sample size was based on alcohol use. We estimated the between-group standardized effect for alcohol use to be 0.58 based on an earlier trial conducted by our team.³⁹ Ninety-six participants (48 in each condition) were needed to have 80% power with a 2-tailed test with α at .05 to detect this estimated effect size using intention to treat. The final sample size of 119 exceeded the target by 24%.

Linear mixed models were used to analyze the continuous outcomes (CAPS, PHDD, and PDA) using SPSS, version 21 (SPSS).⁴⁰ These models allow for an intention-to-treat analysis in which all available data from randomized participants are included to estimate unbiased variable estimates under the missing at random assumption. Treatment condition, time, and their interaction were treated as fixed effects, and the intercept was specified as a random effect to account for the repeated observations within participants. Analyses were conducted using an identity covariance matrix for the random effects and an autoregressive covariance for the repeated effect of time. Between-group effect sizes were computed according to Cohen d using estimated data from these procedures. Rates of PTSD remission (CAPS score <12) were compared for participants for whom data were available at each time point using χ^2 tests. A 1-sided $P < .05$ was considered to be statistically significant.

Figure 1. Consort Flow Diagram



Results

A total of 119 veterans (mean [SD] age, 41.6 [12.6] years; 107 [89.9%] male) were randomized. **Figure 1** shows the flow of the patients through the study. The I-PE and I-CS arms did not significantly differ on background variables or on baseline measures of the primary outcomes (Table 1). The I-PE arm had higher rates than the I-CS arm of taking psychotropic medication (77.8% vs 51.8%; $t_{117} = 3.07$; $P = .003$). Number of sessions completed was higher in the I-CS arm than the I-PE arm (11.4 vs 8.4; $t_{117} = 3.47$; $P = .001$). Session attendance was comparable between the 2 treatments through session 5, but the proportion attending I-PE treatment was lower than the proportion attending I-CS treatment at subsequent sessions.

The estimated marginal means from the mixed models for outcomes over time are given in **Table 2**. The CAPS scores de-

creased in both arms, with a significantly greater decrease in CAPS scores for the I-PE arm compared with the I-CS arm (treatment \times time interaction, -2.83 ; $F_{3,233.1} = 4.92$; Cohen $d = 0.41$; $P = .002$) (**Figure 2**). The PHDD decreased in both arms, but these changes were not statistically different between arms (treatment \times time interaction, 1.8% ; $F_{3,209.9} = 0.18$; Cohen $d = 0.04$; $P = .91$). The PDA had the same pattern of results as the PHDD.

The I-PE arm had significantly higher rates of PTSD remission than the I-CS arm after treatment (8 of 36 [22.2%] vs 3 of 44 [6.8%]; $\chi^2 = 3.96$; $P = .047$) and 3-month follow-up (10 of 40 [25%] vs 2 of 33 [6.1%]; $\chi^2 = 4.72$; $P = .03$); there was a marginal group difference in favor of I-PE treatment at 6-month follow-up (10 of 30 [33.3%] vs 5 of 34 [14.7%]; $\chi^2 = 3.08$; $P = .08$) (**Figure 3**).

No participants were discharged from the study because of serious adverse events. Satisfaction in I-PE (mean [SD], 28.9 [2.7])

Table 2. Continuous Outcomes at All Time Points

Outcome and Time Point	Marginal Mean From Linear Mixed Models (95% CI)	
	I-PE Treatment	I-CS Treatment
PTSD severity (CAPS) ^a		
Baseline	43.2 (40.0-46.4)	42.1 (38.7-45.5)
After treatment	25.8 (22.1-29.6)	32.9 (29.3-36.6)
3-mo Follow-up	26.4 (22.6-30.3)	31.0 (27.0-35.1)
6-mo Follow-up	22.5 (18.2-26.8)	29.8 (25.6-33.9)
Heavy drinking days, % ^b		
Baseline	52.5 (46.5-58.6)	50.4 (44.1-56.7)
After treatment	21.0 (13.4-28.6)	17.4 (10.4-24.5)
3-mo Follow-up	14.2 (6.9-21.4)	15.0 (7.1-22.8)
6-mo Follow-up	20.2 (11.9-28.5)	19.9 (12.1-27.6)
Days abstinent, % ^c		
Baseline	34.3 (27.1-41.6)	31.2 (23.5-38.8)
After treatment	67.5 (58.9-76.1)	63.1 (54.9-71.4)
3-mo Follow-up	65.6 (57.0-74.2)	68.4 (59.3-77.4)
6-mo Follow-up	66.2 (56.5-75.9)	64.0 (54.8-73.3)

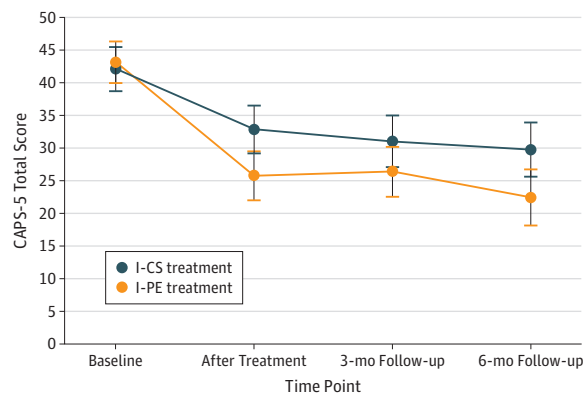
Abbreviations: CAPS, Clinician Administered PTSD Scale for *DSM-5*; I-CS, integrated coping skills; I-PE, integrated prolonged exposure; PTSD, posttraumatic stress disorder.

^a Slope = -4.03 (95% CI, -5.38 to -2.68); group × time interaction = -2.83 (95% CI, -4.75 to -0.91).

^b Slope = -10.49 (95% CI, -13.54 to -7.44).

^c Slope = 10.80 (95% CI, 7.66 to 13.95).

Figure 2. Posttraumatic Stress Disorder Symptom Severity Estimated Means by Treatment Condition at Each Time Point



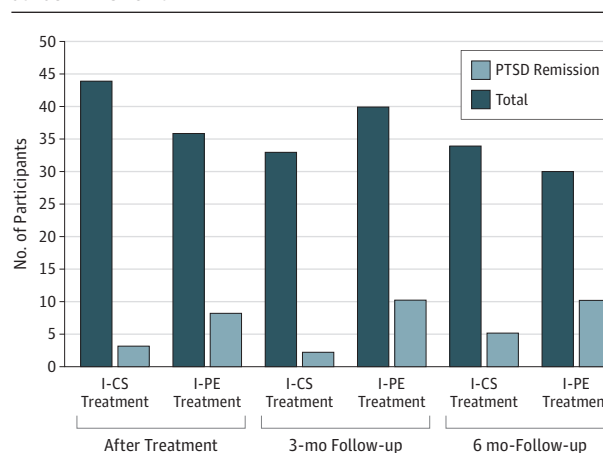
Error bars indicate 95% CIs. CAPS-5 indicates Clinician Administered PTSD Scale for *DSM-5*. I-CS indicates integrated coping skills; I-PE, integrated prolonged exposure.

and I-CS (mean [SD], 29.4 [2.8]) treatment was high and did not differ between arms. A parallel set of analyses that excluded the 11 participants seen by doctoral students found no meaningful differences from the estimates using the full sample.

Discussion

The aim of this study was to compare the relative efficacy of 2 promising psychotherapies for PTSD and AUD. The 2 treat-

Figure 3. Exploratory Completer Analysis of Rates of Posttraumatic Stress Disorder (PTSD) Remission by Treatment Condition at Each Time Point



PTSD remission was defined as a Clinician Administered PTSD Scale for *DSM-5* score less than 12. I-CS indicates integrated coping skills; I-PE, integrated prolonged exposure.

ments are based on vastly different models. Whereas I-PE treatment posits that exposure to trauma-related memories and emotions is critical, I-CS treatment posits that patients with PTSD and AUD may not be ready for exposure and that a focus on better coping is key to recovery. As hypothesized, participants in both conditions had significant reductions in PTSD symptoms with greater reductions in the I-PE arm over time. The PTSD remission rates were greater for the I-PE arm than the I-CS arm.

Contrary to our hypotheses, no statistically significant differences were found between conditions in alcohol use at follow-ups. This hypothesis was based on research suggesting that as PTSD resolves, individuals are more successful in reducing drinking.^{37,41-46} Our last follow-up was 6 months after treatment. It is possible that the effect we hypothesized would be seen further downstream. However, PTSD symptoms improved in both conditions, and participants in both conditions received cognitive behavioral interventions for AUD. Although I-PE and I-CS treatments differ greatly in how PTSD is treated, the cognitive behavioral AUD components may have been too similar for one condition to outperform the other.

Key implications of this novel direct comparison of 2 active integrated PTSD and AUD treatments are that patients with PTSD and AUD can tolerate and benefit from exposure therapy and, regarding PTSD, exposure therapy is more efficacious than therapy without exposure. This information is critical because having an AUD continues to be a barrier to receiving exposure therapy because of therapist perceptions of patients' fragility (ie, beliefs that patients will not be able to handle trauma-related memories and may have an increase in alcohol use).⁴⁷ Participants were not required to be abstinent and were not excluded for having additional SUDs (except intravenous drug use), and the mean number of trauma types experienced was more than 7, further reinforcing that patients with complicated, comorbid conditions can tolerate and benefit from exposure therapy.

Although I-PE treatment produced greater PTSD symptom reduction and remission rates, both treatments produced decreases in PTSD symptoms, reductions in alcohol use, and high treatment satisfaction. These findings raise questions regarding which treatment should be offered to whom and when. Findings of this study and a meta-analysis¹⁸ that found I-PE treatment to be more efficacious than AUD-only treatment suggest that I-PE treatment should be offered when possible. The I-CS treatment may be useful when exposure therapy is refused by a patient or is not available. The I-CS treatment may be less costly to implement in that it can be delivered in groups, in 45- to 60-minute sessions,²⁶ and by trained peers.⁴⁸ However, in the present study, therapists were doctoral psychology trainees and psychologists and sessions were individual and 90 minutes long. Results may not generalize to delivery using a group format or shorter sessions. Given the better PTSD outcomes with fewer sessions attended, I-PE treatment may ultimately be more cost effective. Future research is needed to investigate the cost effectiveness of I-PE treatment compared with I-CS treatment.

It is not clear whether some participants in the I-PE arm attended fewer sessions because they found I-PE treatment to be too difficult, if they completed treatment more quickly because they felt better, or for other reasons. Prolonged exposure is generally conducted in approximately 12 sessions.⁸ The mechanism of exposure (processing trauma-related distress, overcoming avoidance of trauma reminders, and challenging beliefs that one cannot handle trauma memories and reminders through exposure) may work more quickly and effectively than learning to cope better with current life difficulties. Future research is needed to understand why participants had better PTSD outcomes with I-PE treatment even though they attended significantly fewer sessions, and who is most likely to benefit from each treatment under which conditions.

To our knowledge, there has been little research on treating comorbid PTSD and A/SUD with trauma-focused treatments other than exposure. Preliminary studies suggest that cognitive processing therapy⁴⁹ and eye movement desensitization and reprocessing⁵⁰ are promising. Randomized clinical

trials with these psychotherapies would further expand treatment options for PTSD and A/SUD.

Strengths and Limitations

This study has several strengths. It is the first RCT of which we are aware to compare 2 active PTSD and AUD psychotherapies. Many previous treatment studies of PTSD and AUD have had underrecruitment and limitations associated with risk of bias.¹⁸ The study used a rigorous methodologic design and was powered to evaluate hypotheses. The study had minimal exclusion criteria, allowing for evaluation of a clinically complex, real-world comorbid population.

A limitation is that delivery of I-CS treatment in this study was different from how the SS treatment is typically delivered (in group or shorter individual sessions).^{18,26} We chose to deliver 90-minute individual sessions to match for dose (COPE uses 90-minute individual sessions) rather than have participants in the I-PE arm receive 30 to 45 minutes more of therapy per session. The trade-off of this choice is that findings regarding I-CS treatment may not generalize to other, more standard delivery formats. In general, group treatments for PTSD have lower effect sizes than individual treatments⁵¹⁻⁵³; thus, current findings may not generalize to I-CS treatment delivered in group format. Other limitations of the study included a mostly male veteran sample, potentially limiting generalizability. Attrition was high (73.9% completed at least 1 posttreatment assessment), although comparable with other RCTs of I-PE treatment (eg, 48%-79% completing at least 1 post-treatment assessment).^{19,20,54} Consistent with other studies of PTSD and AUD,¹⁸ the exposure therapy condition had fewer sessions attended and higher study dropout.

Conclusions

This study provides evidence that exposure therapy is more efficacious in treating PTSD among individuals with PTSD and AUD than a more commonly available integrated treatment without exposure. Exposure therapy did not worsen drinking outcomes, and both I-PE and I-CS treatment reduced heavy drinking.

ARTICLE INFORMATION

Accepted for Publication: March 29, 2019.

Published Online: April 24, 2019.

doi:10.1001/jamapsychiatry.2019.0638

Author Affiliations: VA San Diego Healthcare System, San Diego, California (S. B. Norman, Trim, Haller, Davis, Colvonen, Blanes, Lyons, Angkaw, Mayes); National Center for PTSD, White River Junction, Vermont (S. B. Norman, Angkaw); VA Center of Excellence for Stress and Mental Health, San Diego, California (S. B. Norman, Colvonen); Department of Psychiatry, University of California, San Diego, School of Medicine, La Jolla (S. B. Norman, Trim, Haller, Colvonen, Angkaw, G. J. Norman, Mayes); James A. Haley Veterans' Hospital, Tampa, Florida (Davis); Ralph H. Johnson VA Medical Center, Charleston, South Carolina (Myers); San Diego Joint Doctoral Program in Clinical Psychology, San Diego State University/

University of California, San Diego (Lyons, Angkaw); Department of Psychology, University of Texas, Austin (Siegel).

Author Contributions: Drs S.B. Norman and Trim had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: S.B. Norman, Trim, Davis, Colvonen, Mayes.

Acquisition, analysis, or interpretation of data: S.B. Norman, Trim, Haller, Myers, Colvonen, Blanes, Lyons, Siegel, Angkaw, G.J. Norman.

Drafting of the manuscript: S.B. Norman, Trim, Haller, Myers, Colvonen, Blanes, Lyons, G.J. Norman.

Critical revision of the manuscript for important intellectual content: Trim, Haller, Davis, Myers, Colvonen, Lyons, Siegel, Angkaw, G.J. Norman, Mayes.

Statistical analysis: Trim, Haller, Colvonen, Lyons, G.J. Norman.

Obtained funding: S.B. Norman, Myers.

Administrative, technical, or material support: Myers, Colvonen, Blanes, Lyons, Siegel.

Supervision: S.B. Norman, Trim, Colvonen, Angkaw, Mayes.

Conflict of Interest Disclosures: Drs S.B. Norman, Trim, Haller, Davis, Colvonen, Angkaw, and Mayes, Ms Siegel, and Ms Blanes reported receiving funding from the US Department of Veterans Affairs during the conduct of this study. Dr Myers and Mr Lyons reported receiving funding from the National Institute on Alcohol Abuse and Alcoholism during the conduct of this study. No other disclosures were reported.

Funding/Support: This study was supported by VA Clinical Science Research and Development Merit Grant 1I01CX000756 (Dr S. Norman, principal investigator). Other funding support included

training fellowships through the VA Office of Academic Affiliation (Drs Haller and Colvonen) and T32 fellowship T32AA013525 through the National Institute on Alcohol Abuse and Alcoholism (Dr Myers and Mr Lyons).

Role of the Funder/Sponsor: The funding source had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and the decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

Additional Contributions: Paula Schnurr, PhD, and Jessica Hamblen, PhD, National Center for PTSD, White River Junction, Vermont, and Dartmouth College, Hanover, New Hampshire, provided consultation regarding study design and implementation. They were not compensated for their work. We thank the therapists and research assistants involved in the study.

REFERENCES

- Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):617-627. doi:10.1001/archpsyc.62.6.617
- Seal KH, Cohen G, Waldrop A, Cohen BE, Maguen S, Ren L. Substance use disorders in Iraq and Afghanistan veterans in VA healthcare, 2001-2010: implications for screening, diagnosis and treatment. *Drug Alcohol Depend*. 2011;116(1-3):93-101. doi:10.1016/j.drugalcdep.2010.11.027
- Driessen M, Schulte S, Luedecke C, et al; TRAUMAB-Study Group. Trauma and PTSD in patients with alcohol, drug, or dual dependence: a multi-center study. *Alcohol Clin Exp Res*. 2008;32(3):481-488. doi:10.1111/j.1530-0277.2007.00591.x
- Tate SR, Norman SB, McQuaid JR, Brown SA. Health problems of substance-dependent veterans with and those without trauma history. *J Subst Abuse Treat*. 2007;33(1):25-32. doi:10.1016/j.jsat.2006.11.006
- Calabrese JR, Prescott M, Tamburrino M, et al. PTSD comorbidity and suicidal ideation associated with PTSD within the Ohio Army National Guard. *J Clin Psychiatry*. 2011;72(8):1072-1078. doi:10.4088/JCP.11m06956
- Edens EL, Kaspro W, Tsai J, Rosenheck RA. Association of substance use and VA service-connected disability benefits with risk of homelessness among veterans. *Am J Addict*. 2011;20(5):412-419. doi:10.1111/j.1521-0391.2011.00166.x
- Straus E, Norman SB, Haller M, Southwick SM, Hamblen JL, Pietrzak RH. Differences in protective factors among U.S. Veterans with posttraumatic stress disorder, alcohol use disorder, and their comorbidity: results from the National Health and Resilience in Veterans Study. *Drug Alcohol Depend*. 2019;194:6-12. doi:10.1016/j.drugalcdep.2018.09.011
- Foa E, Hembree E, Rothbaum BO. *Prolonged Exposure Therapy for PTSD: Emotional Processing of Traumatic Experiences Therapist Guide*. New York, NY: Oxford University Press; 2007. doi:10.1093/med:psych/9780195308501.001.0001
- Foa EB, Dancu CV, Hembree EA, Jaycox LH, Meadows EA, Street GP. A comparison of exposure therapy, stress inoculation training, and their combination for reducing posttraumatic stress disorder in female assault victims. *J Consult Clin Psychol*. 1999;67(2):194-200. doi:10.1037/0022-006X.67.2.194
- Institute of Medicine. *Treatment of Posttraumatic Stress Disorder: An Assessment of the Evidence*. Washington, DC: Institute of Medicine; 2007.
- Brady KT, Dansky BS, Back SE, Foa EB, Carroll KM. Exposure therapy in the treatment of PTSD among cocaine-dependent individuals: preliminary findings. *J Subst Abuse Treat*. 2001;21(1):47-54. doi:10.1016/S0740-5472(01)00182-9
- Coffey SF, Dansky BS, Brady KT. Exposure-based, trauma-focused therapy for comorbid posttraumatic stress disorder-substance use disorder. In: Ouimette P, Brown PJ, eds. *Trauma and Substance Abuse: Causes, Consequences, and Treatment of Comorbid Disorders*. Washington, DC: American Psychological Association; 2003:127-146. doi:10.1037/10460-007
- Riggs DS, Foa EB. Treatment for co-morbid posttraumatic stress disorder and substance use disorders. In: *Anxiety and Substance Use Disorders*. New York, NY: Springer; 2008:119-137. doi:10.1007/978-0-387-74290-8_7
- Triffleman E, Carroll K, Kellogg S. Substance dependence posttraumatic stress disorder therapy: an integrated cognitive-behavioral approach. *J Subst Abuse Treat*. 1999;17(1-2):3-14. doi:10.1016/S0740-5472(98)00067-1
- National Institute for Health and Clinical Practice. *Guideline for Post-traumatic Stress Disorder*. Bethesda, MD: National Institute for Health and Clinical Practice; 2018.
- American Psychological Association Guideline Development Panel for the Treatment of PTSD in Adults. *Clinical Practice Guideline for the Treatment of Posttraumatic Stress Disorder (PTSD) in Adults*. Washington, DC: American Psychological Association; 2017.
- National Institute of Health and Care Excellence (NICE). *Post-traumatic Stress Disorder: Management (Clinical Guideline)*. London, England: National Institute of Health and Care Excellence; 2005.
- Roberts NP, Roberts PA, Jones N, Bisson JI. Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: a systematic review and meta-analysis. *Clin Psychol Rev*. 2015;38:25-38. doi:10.1016/j.cpr.2015.02.007
- Mills KL, Teesson M, Back SE, et al. Integrated exposure-based therapy for co-occurring posttraumatic stress disorder and substance dependence: a randomized controlled trial. *JAMA*. 2012;308(7):690-699. doi:10.1001/jama.2012.9071
- Ruglass LM, Lopez-Castro T, Papini S, Killeen T, Back SE, Hien DA. Concurrent treatment with prolonged exposure for co-occurring full or subthreshold posttraumatic stress disorder and substance use disorders: a randomized clinical trial. *Psychother Psychosom*. 2017;86(3):150-161. doi:10.1159/000462977
- Persson A, Back SE, Killeen TK, et al. Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE): a pilot study in alcohol-dependent women. *J Addict Med*. 2017;11(2):119-125. doi:10.1097/ADM.0000000000000286
- Becker CB, Zayfert C, Anderson E. A survey of psychologists' attitudes towards and utilization of exposure therapy for PTSD. *Behav Res Ther*. 2004;42(3):277-292. doi:10.1016/S0005-7967(03)00138-4
- Brown VB, Najavits LM, Cadiz S, Finkelstein N, Heckman JP, Rechberger E; Seeking Safety Group. Implementing an evidence-based practice. *J Psychoactive Drugs*. 2007;39(3):231-240. doi:10.1080/02791072.2007.10400609
- Najavits LM. Seeking safety. In: Follette VM, Ruzek JI, eds. *Cognitive-Behavioral Therapies for Trauma*. New York, NY: Guilford Press; 2006.
- Back SE, Foa EB, Killeen TK, et al. *Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE): Therapist Guide*. Oxford, England: Oxford University Press; 2014.
- Najavits LM. *Seeking Safety: A Treatment Manual for PTSD and Substance Abuse*. New York, NY: Guilford Press; 2002.
- Norman SB, Haller M, Spadoni AD, et al. Maximizing the utility of a single site randomized controlled psychotherapy trial. *Contemp Clin Trials*. 2015;42:244-251. doi:10.1016/j.cct.2015.04.011
- Franklin CL, Raines AM, Chambliss JL, Walton JL, Maieritsch KP. Examining various subthreshold definitions of PTSD using the Clinician Administered PTSD Scale for DSM-5. *J Affect Disord*. 2018;234:256-260. doi:10.1016/j.jad.2018.03.001
- Weathers FW, Bovin MJ, Lee DJ, et al. The Clinician-Administered PTSD Scale for DSM-5 (CAPS-5): development and initial psychometric evaluation in military veterans. *Psychol Assess*. 2018;30(3):383-395. doi:10.1037/pas0000486
- First MB, Spitzer RL, Gibbon M, Williams JB. *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition*. Washington, DC: American Psychiatric Publishing; 2002.
- Sobell LC, Sobell MB. Timeline follow-back: a technique for assessing self-reported alcohol consumption. In: Litten R, Allen JP, eds. *Measuring Alcohol Consumption: Psychological and Biochemical Methods*. Clifton, NJ: Humana Press; 1992:41-72. doi:10.1007/978-1-4612-0357-5_3
- SAS Institute. *SAS/IML Studio 3.3 for SAS/STAT Users*. Cary, NC: SAS Institute; 2010.
- McHugh ML. Interrater reliability: the kappa statistic. *Biochem Med (Zagreb)*. 2012;22(3):276-282. doi:10.11613/BM.2012.031
- Sobell LC, Brown J, Leo GI, Sobell MB. The reliability of the Alcohol Timeline Followback when administered by telephone and by computer. *Drug Alcohol Depend*. 1996;42(1):49-54. doi:10.1016/0376-8716(96)01263-X
- Paterson DL, Swindells S, Mohr J, et al. Adherence to protease inhibitor therapy and outcomes in patients with HIV infection. *Ann Intern Med*. 2000;133(1):21-30. doi:10.7326/0003-4819-133-1-200007040-00004
- Attkisson CC, Zwick R. The client satisfaction questionnaire: psychometric properties and correlations with service utilization and psychotherapy outcome. *Eval Program Plann*. 1982;5(3):233-237. doi:10.1016/0149-7189(82)90074-X
- Hien DA, Jiang H, Campbell ANC, et al. Do treatment improvements in PTSD severity affect substance use outcomes? a secondary analysis

- from a randomized clinical trial in NIDA's Clinical Trials Network. *Am J Psychiatry*. 2010;167(1):95-101. doi:10.1176/appi.ajp.2009.09091261
38. Najavits L, Liese B. *Seeking Safety Adherence Scale*. Version 3. Boston, MA: Harvard Medical School/McLean Hospital; 2003.
39. Haller M, Norman SB, Cummins K, et al. Integrated cognitive behavioral therapy versus cognitive processing therapy for adults with depression, substance use disorder, and trauma. *J Subst Abuse Treat*. 2016;62:38-48. doi:10.1016/j.jsat.2015.11.005
40. IBM. *IBM SPSS statistics version 21*. Boston, MA: International Business Machines Corp; 2012:126.
41. Hien DA, Smith KZ, Owens M, López-Castro T, Ruglass LM, Papini S. Lagged effects of substance use on PTSD severity in a randomized controlled trial with modified prolonged exposure and relapse prevention. *J Consult Clin Psychol*. 2018;86(10):810-819. doi:10.1037/ccp0000345
42. Back SE, Brady KT, Jaanimägi U, Jackson JL. Cocaine dependence and PTSD: a pilot study of symptom interplay and treatment preferences. *Addict Behav*. 2006;31(2):351-354. doi:10.1016/j.addbeh.2005.05.008
43. Read JP, Brown PJ, Kahler CW. Substance use and posttraumatic stress disorders: symptom interplay and effects on outcome. *Addict Behav*. 2004;29(8):1665-1672. doi:10.1016/j.addbeh.2004.02.061
44. Myrick H, Brady K. Current review of the comorbidity of affective, anxiety, and substance use disorders. *Curr Opin Psychiatry*. 2003;16(3):261-270. doi:10.1097/01.yco.0000069080.26384.d8
45. Sharkansky EJ, Brief DJ, Peirce JM, Meehan JC, Mannix LM. Substance abuse patients with posttraumatic stress disorder (PTSD): identifying specific triggers of substance use and their associations with PTSD symptoms. *Psychol Addict Behav*. 1999;13(2):89-97. doi:10.1037/0893-164X.13.2.89
46. Dansky BS, Brady KT, Saladin ME. Untreated symptoms of PTSD among cocaine-dependent individuals: changes over time. *J Subst Abuse Treat*. 1998;15(6):499-504. doi:10.1016/S0740-5472(97)00293-6
47. van Minnen A, Harned MS, Zoellner L, Mills K. Examining potential contraindications for prolonged exposure therapy for PTSD. *Eur J Psychotraumatol*. 2012;3(1):18805. doi:10.3402/ejpt.v3i0.18805
48. Najavits LM, Hamilton N, Miller N, Griffin J, Welsh T, Vargo M. Peer-led seeking safety: results of a pilot outcome study with relevance to public health. *J Psychoactive Drugs*. 2014;46(4):295-302. doi:10.1080/02791072.2014.922227
49. Kaysen D, Schumm J, Pedersen ER, Seim RW, Bedard-Gilligan M, Chard K. Cognitive processing therapy for veterans with comorbid PTSD and alcohol use disorders. *Addict Behav*. 2014;39(2):420-427. doi:10.1016/j.addbeh.2013.08.016
50. Perez-Dandieu B, Tapia G. Treating trauma in addiction with EMDR: a pilot study. *J Psychoactive Drugs*. 2014;46(4):303-309. doi:10.1080/02791072.2014.921744
51. Sloan DM, Feinstein BA, Gallagher MW, Beck JG, Keane TM. Efficacy of group treatment for posttraumatic stress disorder symptoms: a meta-analysis. *Psychol Trauma*. 2013;5(2):176-183. doi:10.1037/a0026291
52. Resick PA, Wachen JS, Dondanville KA, et al; and the STRONG STAR Consortium. Effect of group vs individual cognitive processing therapy in active-duty military seeking treatment for posttraumatic stress disorder: a randomized clinical trial. *JAMA Psychiatry*. 2017;74(1):28-36. doi:10.1001/jamapsychiatry.2016.2729
53. Watts BV, Schnurr PP, Mayo L, Young-Xu Y, Weeks WB, Friedman MJ. Meta-analysis of the efficacy of treatments for posttraumatic stress disorder. *J Clin Psychiatry*. 2013;74(6):e541-e550. doi:10.4088/JCP.12r08225
54. Back SE, Killeen T, Badour CL, et al. Concurrent treatment of substance use disorders and PTSD using prolonged exposure: a randomized clinical trial in military veterans. *Addict Behav*. 2019;90:369-377. doi:10.1016/j.addbeh.2018.11.032