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ADVANCING SCIENCE AND PROMOTING UNDERSTANDING OF TRAUMATIC STRESS

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Behavioral Interventions for Comorbid PTSD and Substance Use Disorder

Prevalence and Associated Problems

Posttraumatic stress disorder (PTSD) and substance use disorders (SUD) often co-occur. According to one national epidemiologic study 46.4% of individuals with lifetime PTSD also met criteria for SUD (Pietrzak et al., 2011). Among Veterans these numbers are even higher, a substantial majority with PTSD have met criteria for comorbid SUD in their life time. The National Vietnam Veterans Readjustment Study, conducted in the 1980s found 74% of Vietnam Veterans with PTSD had comorbid SUD (Kulka et al., 1990). Among treatment seeking Veterans who served in Operations Enduring Freedom (OEF) / Iraqi Freedom (OIF) / New Dawn (OND), 63% of those diagnosed with Alcohol Use Disorder (AUD) or other SUD also had a diagnosis of PTSD (Seal et al., 2011). For those diagnosed with AUD and another SUD, the rate of PTSD diagnosis was 76%.

Although PTSD and SUD (PTSD+SUD) are each associated with functional impairment, on average, individuals who have both disorders have more additional psychiatric and functional problems across multiple domains, including medical, legal, financial, and social (McDevitt-Murphy et al., 2010; Tate et al., 2007). In a nationally representative sample of US Veterans, the co-occurrence of PTSD and AUD was associated with higher rates of attempted suicide (46%) and suicidal ideation (39.1%) when compared to AUD alone (attempts = 4.1%; ideation = 7.0%), and greater suicide attempts when compared to PTSD alone (22.8%) (Norman et al., 2018).

Behavioral Intervention Research

Historically, treatments for PTSD+SUD were sequential, with SUD treated first, due in part to prevailing, although unsubstantiated concerns that

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patients had to be abstinent from substances in order to effectively address trauma and PTSD symptoms. In addition, it was commonly assumed that patients with SUD who were still using substances were too fragile to deal with trauma memories and PTSD and that doing so may lead to clinical worsening such as relapse or worse use, symptom exacerbation, and increased risk of suicidal intent and behaviors (Becker et al., 1991). At the Department of Veterans Affairs (VA) and in the community, it was common for patients to be turned away from PTSD treatments if they had not achieved some length of abstinence from substances.

Given these concerns, it is not surprising that early efforts to treat PTSD+SUD concurrently or in an integrated fashion (i.e., addressing both PTSD and SUD within one protocol) approached PTSD using present focused, skills based approaches that did not include trauma processing or exposure to trauma reminders (Najavits, 2006; McGovern, 2015). The *Seeking Safety* protocol (Najavits, 2006), was among the first integrated treatments to be studied. *Seeking Safety* is a present centered coping skills therapy that helps patients develop skills in interpersonal, cognitive, and behavioral domains. *Seeking Safety* has been evaluated in over 10 randomized controlled trials with a variety of populations (e.g., women, Veterans) with comparisons that included health education and evidence-based SUD treatments such as relapse prevention (Garland et al., 2016; Hien et al., 2009; Roberts et al., 2015; Schäfer et al., 2019). These studies have generally found that *Seeking Safety* improves PTSD+SUD comparably to comparison conditions and provided the first evidence that PTSD+SUD could be treated in an integrated fashion without clinical worsening. Another skills based model, *Integrated Cognitive Behavioral Therapy for PTSD and SUD*, uses cognitive restructuring and other cognitive behavioral

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strategies to address both PTSD and SUD. Initial studies have shown the treatment to be comparably effective to SUD treatment alone for reducing PTSD symptoms (Capone et al., 2018; McGovern et al., 2015). At the same time, numerous studies demonstrated that the most effective treatments for PTSD-alone were trauma focused psychotherapies (therapies where a primary focus of each session involves processing trauma related memories and distress) (Watts et al., 2013). However, concerns that patients with SUDs could not handle trauma processing continued to be a barrier to comorbid patients receiving such treatments. It was not until the past decade that studies of trauma focused therapies for those with PTSD+SUD began to emerge in larger numbers. These studies primarily evaluated prolonged exposure (PE) therapy concurrently or integrated with evidence based SUD treatment. In PE, patients process trauma through in-vivo (real life) and imaginal (retelling and listening to recorded accounts of the trauma memory) exposure to trauma reminders. The most studied integrated treatment has been the *Concurrent Treatment of PTSD and Substance Use Disorder Using Prolonged Exposure* (COPE) protocol which blends PE with relapse prevention for SUD. Contrary to beliefs that patients with PTSD+SUD could not handle trauma focused therapies, these studies have shown consistently that PE with SUD treatment as usual leads to better PTSD outcomes, and in some studies better SUD outcomes, than present focused or SUD only treatment (e.g., Norman et al., 2019; Roberts et al., 2015; Ruglass et al., 2017). Mills and colleagues (Mills et al., 2012) compared COPE to SUD treatment in the Australian healthcare system and found that COPE had significantly greater reductions in PTSD symptom severity at the end of nine months post-baseline. Ruglass and colleagues (Ruglass et al., 2017) compared COPE to relapse prevention and to active monitoring in a community sample. Among those with full PTSD, participants who received COPE had better PTSD outcomes than those in the other two conditions.

Three recent studies evaluating PE or COPE with Veterans with PTSD+SUD largely support the community findings. Back and colleagues (Back et al., 2019) compared COPE to relapse prevention among Veterans who served post-9/11 and found that COPE resulted in greater PTSD symptom reduction and greater likelihood of remission. Kehle-Forbes and colleagues (Kehle-Forbes et al., 2019) compared PE integrated with motivational enhancement therapy (MET) to sequential treatment where PE followed MET. Both conditions had clinically and significant reductions in substance use and PTSD symptom severity, but did not significantly differ from each other. The first study to directly compare integrated PE (COPE) to integrated present focused coping skills therapy (*Seeking Safety*) was with a Veteran sample. The study found that improvement in PTSD symptom severity and remission rates were better in the PE condition than in *Seeking Safety* (Norman et al., 2019).

Studies that have looked at processes or symptom change within treatment are helping to inform whether effective PTSD treatment such as PE or COPE should be delayed until substance use is reduced or stopped. Several studies have shown that within treatment for PTSD+SUD, PTSD symptom improvement is associated with greater subsequent substance use improvement, but the reverse relationship (substance use predicting subsequent PTSD symptoms) is not as strong (Hien et al., 2010, 2018; Kaczurkin et al., 2016; Tripp et al., in press), suggesting that effective PTSD treatment should not be delayed.

Studies have also examined whether clinical worsening (e.g., PTSD or depression symptom exacerbation, increased substance use, increased suicidal ideation) occurs when exposure is first initiated in COPE (Lancaster et al., 2020; Tripp et al., 2020). These studies have shown low rates of clinical worsening overall and that worsening rates were no higher in COPE than in the control condition (relapse prevention in one study, *Seeking Safety* in the other). These studies further document that introducing exposure is not adverse to comorbid PTSD+SUD patients, even in the short term when patients first initiate imaginal exposure. No evidence from these studies shows worsening of substance use or other adverse events in patients who have received trauma processing treatments, even while using up to 4 times per week (i.e., Hien et al., 2018). Taken together, these findings underscore that treating PTSD effectively using PE or COPE is important to both PTSD and SUD outcomes and serve to contradict fears and unsubstantiated beliefs that effective PTSD treatment should be delayed until improvement in substance use is achieved.

Other evidence-based trauma focused treatments for PTSD such as Cognitive Processing Therapy (CPT) and Eye Movement Desensitization and Reprocessing (EMDR) have thus far been less studied for comorbid PTSD+SUD, although early results are promising and generally follow the findings reported on PE above demonstrating positive direct impacts on PTSD and well tolerated trauma processing with respect to SUD outcomes and treatment dropout. A retrospective chart review of Veterans who had received at least one session of CPT showed that Veterans with and without current and past alcohol use disorder did not differ in number of sessions attended and all showed PTSD symptom reduction (Kaysen et al., 2014). In a sample of 73 American Indian/Native American women with full or subthreshold PTSD and recent alcohol or substance use, a culturally modified version of CPT led to greater reductions in PTSD symptoms and substance use than six weeks of waitlist control (Pearson et al., 2019). A small pilot study of 12 participants showed that patients randomized to EMDR plus SUD treatment as usual showed greater PTSD symptom reduction than those randomized to SUD treatment as usual only (Perez-Dandieu & Tapia, 2014). Further studies of CPT and EMDR with randomized controlled trial designs are critical as these trauma focused therapies are highly recommended for the treatment of PTSD in all (in the case of CPT) or most (in the case of EMDR) clinical practice guidelines for the treatment of PTSD (Hamblen et al., 2019).

Promising Directions and Gaps

Research over the past decade has moved the field of treating comorbid PTSD+SUD forward significantly, especially the documented effectiveness of PE concurrent or integrated with evidence based SUD treatment. However, many gaps and questions remain about how best to treat this comorbidity. While PE offered concurrently with SUD treatment is more effective than other treatment options for PTSD+SUD, attendance at any treatment among patients with PTSD+SUD is often low, treatment dropout in general is high, and effect sizes for PE for PTSD+SUD are smaller than in studies of PE for primary PTSD. A meta-analysis of PTSD+SUD treatment studies found dropout to range between 50 and 70% (it is important to note that this meta-analysis included early studies that included highly modified exposure protocols). While in PTSD treatment studies effect sizes for PE are generally large (Watts et al., 2013), for studies of

PTSD+SUD, effects in favor of PE have been small to moderate (Roberts et al., 2015). Boosting PE session attendance is a potential method by which to optimize the effects of PE on PTSD for patients who also have SUD. Therefore, strategies to improve treatment attendance and effectiveness remain a priority. There are several promising directions.

Combined Behavioral Interventions with Medication

Combining behavioral interventions and medication is one approach to improving treatment outcomes that has received less research attention, even though in clinical practice many patients receive both. Thus far, studies of medication to treat comorbid PTSD+SUD suggest that medications targeting PTSD (e.g., sertraline) tend to improve PTSD but not substance use outcomes, while medications targeting substance use (e.g., naltrexone for alcohol use) tend to improve substance use but not PTSD outcomes (Petrakis & Simpson, 2017). In a study of PE and naltrexone for PTSD and alcohol use disorder, the condition that received both had the smallest increases from post-treatment in percent days drinking at six month follow-up (Foa et al., 2013). A study of *Seeking Safety* and sertraline showed that the condition that received both had greater decreases in PTSD symptom severity than the condition that received *Seeking Safety* and placebo (Hien et al., 2015). In a sample of patients with Opioid Use Disorder (OUD) those who received PTSD treatment had better retention in buprenorphine maintenance treatment than those who were not in PTSD treatment (Meshberg-Cohen et al., 2019). Further research is needed to understand if the synergy of behavioral intervention and medication may help comorbid patients engage in and benefit from treatment.

Massed Treatment

Offering PE or other trauma focused therapy in a massed format (i.e., multiple sessions per week where patients finish PE in 2–4 weeks instead of 3–5 months, M-PE) in intensive outpatient (IOP) or residential SUD treatment is another promising method to improve the effectiveness of PE for patients with PTSD+SUD. Residential treatment for SUD is associated with much higher rates of treatment attendance overall (SAHMSA, Office of Applied Studies, 2008). In IOP or residential care, patients are in treatment multiple days per week in a structured environment to help with the challenges of early recovery. Patients whose PTSD improves in residential treatment have longer subsequent abstinence periods (Manhapra et al., 2015), whereas untreated PTSD is linked to dropout from residential SUD treatment (Tull et al., 2013). During outpatient treatment, the instability in functioning associated with PTSD+SUD and frequent substance use can make it difficult for these patients to complete the homework that is a critical part of PE. PE offered in a massed format is effective, session attendance is higher, and drop out is lower than in weekly treatment (Foa et al., 2018; Rauch et al., 2018; Van Woudenberg et al., 2018). Pilot studies show near perfect attendance and completion rates for PE in residential SUD settings (Berenz et al., 2012; Norman et al., 2016). Increasing PE attendance through delivering M-PE in residential setting, therefore, may be an effective method to improve PTSD+SUD treatment outcomes.

Incentives

A study of patients with PTSD and OUD compared PE with and without incentives for attending PE and found that the condition that received incentives had better attendance and greater PTSD

symptom reduction (Schacht et al., 2017). More research on incentives and interventions that include incentives such as contingency management may help identify methods to improve treatment outcomes for PTSD+SUD.

Examining Potential Differences among SUDs

Most research to date has been with participants with alcohol use disorder or with any substance use disorder. In the latter, samples have been too small to examine potential differences in treatment response by primary substance used. Therefore, it is not yet known if different SUDs may respond best to different treatment types.

OUD and cannabis use disorder (CUD) are two SUDs that are of particular interest given that, among other factors, overprescription of opioids and changing laws creating easier access to cannabis have led to increases in addiction to both of these substances over the past decade. OUD and CUD are also complicated by the fact that opioids and cannabis may be prescribed or recommended for common co-occurring conditions (and for the treatment of PTSD in the case of CUD, even though efficacy data from clinical trials showing cannabis as an effective PTSD treatment is lacking (e.g., Hindocha et al., 2019). Clinicians report that it can be more challenging to raise patients' motivation to change when patients believe the substances have prescribed beneficial effects. Preliminary studies with comorbid PTSD+OUD suggest that getting PTSD treatment improves retention in buprenorphine maintenance treatment for OUD (Meshberg-Cohen et al., 2019), and that a modified version of PE helps reduce PTSD symptoms and opioid cravings more than non-trauma focused treatment (Peck et al., 2018). More research on how to raise awareness of problematic use and addiction to opioids and cannabis and how to treat patients who have these SUDs comorbid with PTSD is needed.

Cultural, Ethnic, Racial Differences and Disparities

Another area where little is known is variability in cultural, ethnic, racial and other differences in response to treatment, as well as what treatment disparities may exist. To date, given small sample sizes and high rates of attrition, studies have been underpowered to examine health disparities in treatment responses for PTSD+SUD. A promising approach for addressing these gaps will involve integrative data analyses, such as National Institute on Alcohol Abuse and Alcoholism- (NIAAA-) funded Project Harmony (AA025853 <https://www.projectharmonyvct.com/>) which applies innovative meta-analytic techniques to pool individual patient data from over 30 PTSD+SUD clinical trials with Veteran and community populations totaling over 3,500 participants. These studies will allow examination of individual differences in treatment outcomes including comparisons of gender and race/ethnicity.

Implementation and Dissemination

Although the evidence is strongly in favor of applying a trauma focused approach for treating PTSD in patients with PTSD+SUD, the norm in many substance use settings remains not to treat the PTSD or to treat it using present focused approaches. Across the country, depending upon the state, limited mental health funding for those in substance use treatment provides further barriers for PTSD care. Dissemination and implementation efforts and research are needed to make best practice treatments available to this vulnerable patient population.

Back, S. E., Killeen, T., Badour, C. L., Flanagan, J. C., Allan, N. P., Ana, E. S., Lozano, B., Korte, K. J., Foa, E. B., & Brady, K. T. (2019). **Concurrent treatment of substance use disorders and PTSD using prolonged exposure: A randomized clinical trial in military veterans.** *Addictive Behaviors, 90*, 369–377. doi:10.1016/j.addbeh.2018.11.032 *Objective:* A substantial amount of individuals with substance use disorders (SUD) also meet criteria for posttraumatic stress disorder (PTSD). Prolonged Exposure (PE) is an effective, evidence-based treatment for PTSD, but there is limited data on its use among individuals with current alcohol or drug use disorders. This study evaluated the efficacy of an integrated treatment that incorporates PE (Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure or COPE) among veterans. *Method:* Military veterans ($N = 81$, 90.1% male) with current SUD and PTSD were randomized to 12 sessions of COPE or Relapse Prevention (RP). Primary outcomes included the Clinician Administered PTSD Scale (CAPS), PTSD Checklist-Military version (PCL-M), and the Timeline Follow-back (TLFB). *Results:* On average, participants attended 8 out of 12 sessions and there were no group differences in retention. Intent-to-treat analyses revealed that COPE, in comparison to RP, resulted in significantly greater reductions in CAPS ($d = 1.4$, $p < .001$) and PCL-M scores ($d = 1.3$, $p = .01$), as well as higher rates of PTSD diagnostic remission ($OR = 5.3$, $p < .01$). Both groups evidenced significant and comparable reductions in SUD severity during treatment. At 6-months follow-up, participants in COPE evidenced significantly fewer drinks per drinking day than participants in RP ($p = .05$). *Conclusions:* This study is the first to report on the use of an integrated, exposure-based treatment for co-occurring SUD and PTSD in a veteran sample. The findings demonstrate that integrated, exposure-based treatments are feasible and effective for military veterans with SUD and PTSD. Implications for clinical practice are discussed.

Foa, E. B., Yusko, D. A., McLean, C. P., Suvak, M. K., Bux, D. A., Oslin, D., O'Brien, C. P., Imms, P., Riggs, D. S., & Volpicelli, J. (2013). **Concurrent naltrexone and prolonged exposure therapy for patients with comorbid alcohol dependence and PTSD: A randomized clinical trial.** *JAMA, 310*, 488–495. doi:10.1001/jama.2013.8268 *Importance:* Alcohol dependence comorbid with posttraumatic stress disorder (PTSD) has been found to be resistant to treatment. In addition, there is a concern that prolonged exposure therapy for PTSD may exacerbate alcohol use. *Objective:* To compare the efficacy of an evidence-based treatment for alcohol dependence (naltrexone) plus an evidence-based treatment for PTSD (prolonged exposure therapy), their combination, and supportive counseling. *Design, Setting, and Participants:* A single-blind, randomized clinical trial of 165 participants with PTSD and alcohol dependence conducted at the University of Pennsylvania and the Philadelphia Veterans Administration. Participant enrollment began on February 8, 2001, and ended on June 25, 2009. Data collection was completed on August 12, 2010. *Interventions:* Participants were randomly assigned to (1) prolonged exposure therapy plus naltrexone (100 mg/d), (2) prolonged exposure therapy plus pill placebo, (3) supportive counseling plus naltrexone (100 mg/d), or (4) supportive counseling plus pill placebo. Prolonged exposure therapy was composed of 12 weekly 90-minute sessions followed by 6 biweekly sessions. All

participants received supportive counseling. *Main Outcomes and Measures:* The Timeline Follow-Back Interview and the PTSD Symptom Severity Interview were used to assess the percentage of days drinking alcohol and PTSD severity, respectively, and the Penn Alcohol Craving Scale was used to assess alcohol craving. Independent evaluations occurred prior to treatment (week 0), at posttreatment (week 24), and at 6 months after treatment discontinuation (week 52). *Results:* Participants in all 4 treatment groups had large reductions in the percentage of days drinking (mean change, -63.9% [95% CI, -73.6% to -54.2%] for prolonged exposure therapy plus naltrexone; -63.9% [95% CI, -73.9% to -53.8%] for prolonged exposure therapy plus placebo; -69.9% [95% CI, -78.7% to -61.2%] for supportive counseling plus naltrexone; and -61.0% [95% CI, -68.9% to -53.0%] for supportive counseling plus placebo). However, those who received naltrexone had lower percentages of days drinking than those who received placebo (mean difference, 7.93%; $P = .008$). There was also a reduction in PTSD symptoms in all 4 groups, but the main effect of prolonged exposure therapy was not statistically significant. Six months after the end of treatment, participants in all 4 groups had increases in percentage of days drinking. However, those in the prolonged exposure therapy plus naltrexone group had the smallest increases. *Conclusions and Relevance:* In this study of patients with alcohol dependence and PTSD, naltrexone treatment resulted in a decrease in the percentage of days drinking. Prolonged exposure therapy was not associated with an exacerbation of alcohol use disorder.

Hien, D. A., Jiang, H., Campbell, A. N. C., Hu, M.-C., Miele, G. M., Cohen, L. R., Brigham, G. S., Capstick, C., Kulaga, A., Robinson, J., Suarez-Morales, L., & Nunes, E. V. (2010). **Do treatment improvements in PTSD severity affect substance use outcomes? A secondary analysis from a randomized clinical trial in NIDA's clinical trials network.** *American Journal of Psychiatry, 167*, 95–101. doi:10.1176/appi.ajp.2009.09091261 *Objective:* The purpose of the analysis was to examine the temporal course of improvement in symptoms of posttraumatic stress disorder (PTSD) and substance use disorder among women in outpatient substance abuse treatment. *Method:* Participants were 353 women randomly assigned to 12 sessions of either trauma-focused or health education group treatment. PTSD and substance use assessments were conducted during treatment and posttreatment at 1 week and after 3, 6, and 12 months. A continuous Markov model was fit on four defined response categories (nonresponse, substance use response, PTSD response, or global response [improvement in both PTSD and substance use]) to investigate the temporal association between improvement in PTSD and substance use symptom severity during the study's treatment phase. A generalized linear model was applied to test this relationship over the follow-up period. *Results:* Subjects exhibiting nonresponse, substance use response, or global response tended to maintain original classification; subjects exhibiting PTSD response were significantly more likely to transition to global response over time, indicating maintained PTSD improvement was associated with subsequent substance use improvement. Trauma-focused treatment was significantly more effective than health education in achieving substance use improvement, but only among those who were heavy substance users at baseline and had achieved significant PTSD reductions. *Conclusions:* PTSD severity reductions

were more likely to be associated with substance use improvement, with minimal evidence of substance use symptom reduction improving PTSD symptoms. Results support the self-medication model of coping with PTSD symptoms and an empirical basis for integrated interventions for improved substance use outcomes in patients with severe symptoms.

Hien, D. A., Smith, K. Z., Owens, M., López-Castro, T., Ruglass, L. M., & Papini, S. (2018). **Lagged effects of substance use on PTSD severity in a randomized controlled trial with modified prolonged exposure and relapse prevention.** *Journal of Consulting and Clinical Psychology, 86*, 810–819. doi:10.1037/ccp0000345

Objective: To advance understanding of the effectiveness of evidence-based treatments for comorbid posttraumatic stress disorder (PTSD) and substance use disorder (SUD), research must provide a more nuanced picture of how substance use affects change in PTSD symptoms over the course of treatments and whether prolonged exposure techniques can be efficacious during active substance use. A data set that included patients with PTSD/subthreshold-PTSD and SUD treated with an exposure-based intervention provided an opportunity to conduct a secondary analysis to test how patients' substance use impacted PTSD change over treatment. **Method:** We applied growth models to week-to-week PTSD symptom and substance use changes during treatment and follow-up of a randomized controlled trial of two cognitive-behavioral treatments for PTSD and SUD: Concurrent Treatment of PTSD and SUD Using Prolonged Exposure (COPE) and Relapse Prevention Therapy (RPT). Cross-lagged analyses were used to determine whether prior week substance use impacted subsequent PTSD symptom severity. **Results:** Both treatments evidenced significant reductions in PTSD symptom severity. In the context of continued substance use, results suggest that individuals still benefit from exposure-based treatment. **Conclusion:** Results provide evidence that RPT and COPE both led to significant reductions in PTSD, providing further support that exposure-based techniques tailored for SUD can be conducted without jeopardizing PTSD or SUD outcomes. Implications for clinical decision making around treatment selection are discussed.

Hien, D. A., Wells, E. A., Jiang, H., Suarez-Morales, L., Campbell, A. N. C., Cohen, L. R., Miele, G. M., Killeen, T., Brigham, G. S., Zhang, Y., Hansen, C., Hodgkins, C., Hatch-Maillette, M., Brown, C., Kulaga, A., Kristman-Valente, A., Chu, M., Sage, R., Robinson, J. A., Liu, D. & Nunes, E. V. (2009). **Multisite randomized trial of behavioral interventions for women with co-occurring PTSD and substance use disorders.** *Journal of Consulting and Clinical Psychology, 77*, 607–619. doi:10.1037/a0016227 The authors compared the effectiveness of the *Seeking Safety* group, cognitive-behavioral treatment for substance use disorder and posttraumatic stress disorder (PTSD), to an active comparison health education group (Women's Health Education [WHE]) within the National Institute on Drug Abuse's Clinical Trials Network. The authors randomized 353 women to receive 12 sessions of *Seeking Safety* ($M = 6.2$ sessions) or WHE ($M = 6.0$ sessions) with follow-up assessment 1 week and 3, 6, and 12 months posttreatment. Primary outcomes were the Clinician Administered PTSD Scale (CAPS), the PTSD Symptom Scale–Self Report (PSS-SR), and a substance use inventory (self-reported abstinence and percentage of days of use over 7 days). Intention-to-treat analysis showed

large, clinically significant reductions in CAPS and PSS-SR symptoms ($d = 1.94$ and 1.12 , respectively) but no reliable difference between conditions. Substance use outcomes were not significantly different over time between the two treatments and at follow-up showed no significant change from baseline. Study results do not favor *Seeking Safety* over WHE as an adjunct to substance use disorder treatment for women with PTSD and reflect considerable opportunity to improve clinical outcomes in community-based treatments for these co-occurring conditions.

Kaczurkin, A. N., Asnaani, A., Alpert, E., & Foa, E. B. (2016). **The impact of treatment condition and the lagged effects of PTSD symptom severity and alcohol use on changes in alcohol craving.** *Behaviour Research and Therapy, 79*, 7–14. doi:10.1016/j.brat.2016.02.001

Given the high rates of comorbidity between posttraumatic stress disorder (PTSD) and substance use disorder (SUD), we investigated an integrated treatment for these disorders. Individuals with comorbid PTSD and alcohol dependence were randomized to receive naltrexone or placebo, with or without prolonged exposure (PE). All participants also received BRENDA (supportive counseling). The naltrexone plus PE group showed a greater decline in alcohol craving symptoms than those in the placebo with no PE group. The PE plus placebo and the naltrexone without PE groups did not differ significantly from the placebo with no PE group in terms of alcohol craving. No treatment group differences were found for percentage of drinking days. Alcohol craving was moderated by PTSD severity, with those with higher PTSD symptoms showing faster decreases in alcohol craving. Both PTSD and alcohol use had a lagged effect on alcohol craving, with changes in PTSD symptoms and percentage of days drinking being associated with subsequent changes in craving. These results support the relationship between greater PTSD symptoms leading to greater alcohol craving and suggest that reducing PTSD symptoms may be beneficial to reducing craving in those with co-occurring PTSD/SUD.

Kaysen, D., Schumm, J., Pedersen, E. R., Seim, R. W., Bedard-Gilligan, M., & Chard, K. (2014). **Cognitive processing therapy for veterans with comorbid PTSD and alcohol use disorders.**

Addictive Behaviors, 39, 420–427. doi:10.1016/j.addbeh.2013.08.016 Posttraumatic stress disorder (PTSD) and alcohol-use disorders (AUD) frequently present comorbidly in veteran populations. Traditionally those with alcohol dependence have been excluded from PTSD treatment outcome studies, thus we do not know how those with alcohol dependence may tolerate or respond to PTSD-specific interventions; no studies to date have examined the extent to which cognitive PTSD interventions are tolerated or effective for those with comorbid PTSD/AUD. The present study examines the extent to which CPT is tolerated by and effective in treating PTSD symptoms for veterans with PTSD and AUD, as compared to veterans with PTSD only in an outpatient treatment setting. Data were obtained through chart review of 536 veterans diagnosed with PTSD who had received at least 1 session of CPT at a Midwestern US Veterans Affairs hospital. Nearly half ($n = 264$, 49.3%) of the veterans in the study exhibited a current or past AUD diagnosis. Participants were grouped into the following diagnostic groups: current AUD (past 12 months), past AUD (prior to 12 months), and no AUD. Participants completed an average of 9 sessions of CPT with no significant difference between AUD diagnostic groups on the

number of CPT sessions completed. Individuals with past AUD had higher initial symptoms of self-reported PTSD symptoms than those with no AUD. All groups reported significant reductions in PTSD symptoms and depression over time. Overall, the results suggest that CPT appears well tolerated among veterans with comorbid AUD and is associated with significant reductions in symptoms of PTSD and depression in an outpatient treatment setting.

Kehle-Forbes, S. M., Chen, S., Polusny, M. A., Lynch, K. G., Koffel, E., Ingram, E., Foa, E. B., Van Horn, D. H. A., Drapkin, M. L., Yusko, D. A., & Oslin, D. W. (2019). **A randomized controlled trial evaluating integrated versus phased application of evidence-based psychotherapies for military veterans with comorbid PTSD and substance use disorders.** *Drug and Alcohol Dependence, 205*, 107647. doi:10.1016/j.drugalcdep.2019.107647

Objective: Recent clinical practice guidelines recommend the delivery of evidence-based psychotherapies for both substance use disorder (SUD) and posttraumatic stress disorder (PTSD) within the same treatment episode for patients with SUD/PTSD comorbidity.

This randomized clinical trial evaluated the comparative effectiveness of integrating versus phasing evidence-based psychotherapies for SUD and PTSD among veterans with co-occurring SUD/PTSD. **Method:** 183 veterans with DSM-IV PTSD and SUD at two VA Medical Centers were randomized to one of two psychotherapies during which Motivational Enhancement Therapy [MET] for SUD and Prolonged Exposure [PE] for PTSD were either phased or integrated throughout treatment. Primary outcomes as evaluated by blinded assessors were percent days with drug use or heavy drinking and PTSD symptomology. We hypothesized integrated MET/PE ($n = 95$) would yield better SUD and PTSD-related outcomes at posttreatment than phased MET/PE ($n = 88$). **Results:** In intent-to-treat analyses ($n = 183$), both treatment groups achieved clinically ($d = 0.46 - 1.06$) and statistically significant reductions in SUD ($p < 0.01$) and PTSD ($p < 0.01$) symptomology; the time by treatment interactions were not significant. Post-hoc analyses could not confirm statistical non-inferiority; between-group effect sizes suggest a lack of clinically-meaningful differences between the two treatment approaches ($d = 0.08 - 0.27$).

Conclusions: Our hypothesis that integrated MET/PE would result in better outcomes than phased MET/PE across a range of PTSD and SUD measures was not supported; both strategies for combining two single-disorder treatments for co-occurring SUD/PTSD yielded significant symptom reduction.

Lancaster, C., Gros, D., Mullarkey, M., Badour, C., Killeen, T., Brady, K., & Back, S. (2020). **Does trauma-focused exposure therapy exacerbate symptoms among patients with comorbid PTSD and substance use disorders?** *Behavioural and Cognitive Psychotherapy, 48*(1), 38–53. doi:10.1017/S1352465819000304

Background: Although exposure-based therapy is a well-established, effective treatment for post-traumatic stress disorder (PTSD), some practitioners report reluctance to implement it due to concerns that it may exacerbate symptoms of PTSD and commonly comorbid disorders, such as substance use disorders (SUD). **Aim:** This study compared the exacerbation of psychological symptoms among participants with comorbid PTSD and SUD who received either SUD treatment alone or SUD treatment integrated with exposure therapy for PTSD. **Method:** Participants ($N = 71$) were

treatment-seeking, military Veterans with comorbid PTSD and SUD who were randomized to 12 individual sessions of either (1) an integrated, exposure-based treatment (Concurrent Treatment of PTSD and Substance Use Disorders using Prolonged Exposure; COPE); or (2) a non-exposure-based, SUD-only treatment (Relapse Prevention; RP). We examined between-group differences in the frequency of statistically reliable exacerbations of PTSD, SUD and depression symptoms experienced during treatment. **Results:** At each of the 12 sessions, symptom exacerbation was minimal and generally equally likely in either treatment group. However, an analysis of treatment completers suggests that RP participants experienced slightly more exacerbations of PTSD symptoms during the course of treatment. **Conclusions:** This study is the first to investigate symptom exacerbation throughout trauma-focused exposure therapy for individuals with comorbid PTSD and SUD. Results add to a growing literature which suggests that trauma-focused, exposure-based therapy does not increase the risk of symptom exacerbation relative to non-exposure-based therapy.

Meshberg-Cohen, S., Black, A. C., DeViva, J. C., Petrakis, I. L., & Rosen, M. I. (2019). **Trauma treatment for veterans in buprenorphine maintenance treatment for opioid use disorder.** *Addictive Behaviors, 89*, 29–34. doi:10.1016/j.addbeh.2018.09.010

Introduction: Opioid use disorder (OUD) rates are high among veterans. PTSD is also prevalent among veterans; those with comorbidity have worse outcomes than those without comorbidity. This study assessed buprenorphine retention rates in veterans initiating OUD treatment, comparing veterans without PTSD to veterans with PTSD who were receiving versus not receiving concurrent trauma treatment. **Methods:** This retrospective chart review examined consecutive referrals to buprenorphine maintenance ($N = 140$). PTSD diagnosis was identified by chart review and retention was defined as continuous buprenorphine maintenance 6-months post-admission. Logistic regression analyses compared buprenorphine retention for veterans without PTSD and PTSD-diagnosed veterans who received concurrent trauma treatment to a reference group of PTSD-diagnosed veterans who did not receive trauma treatment. Models adjusted for opioid type, age, and service-connected status. **Results:** Sixty-seven (47.9%) buprenorphine-seeking veterans carried a PTSD diagnosis; only 31.3% ($n = 21$) received trauma treatment while in buprenorphine maintenance, with 11.9% ($n = 8$) receiving evidence-based psychotherapy for PTSD. Among PTSD-diagnosed veterans who received trauma treatment, 90.5% ($n = 19/21$) were in buprenorphine maintenance at 6-months, compared to 23.9% ($n = 11/46$) of PTSD-diagnosed veterans without trauma treatment, and 46.6% ($n = 34/73$) of veterans without PTSD. In the full model, veterans with trauma treatment had 43.36 times greater odds of remaining in buprenorphine treatment than the reference group. **Conclusions:** Most PTSD-diagnosed veterans in buprenorphine treatment were not receiving trauma treatment. Those receiving concurrent trauma treatment had better retention, suggesting OUD and trauma can be simultaneously addressed. Future clinical trials should investigate trauma-focused treatment for veterans with comorbid PTSD who are seeking buprenorphine for OUD.

Norman, S. B., Davis, B. C., Colvonen, P. J., Haller, M., Myers, U. S., Trim, R. S., Bogner, R., & Robinson, S. K. (2016). **Prolonged**

exposure with veterans in a residential substance use treatment program. *Cognitive and Behavioral Practice, 23*, 162–172.

[doi:10.1016/j.cbpra.2015.08.002](https://doi.org/10.1016/j.cbpra.2015.08.002) Prolonged exposure therapy (PE) is effective in reducing posttraumatic stress disorder (PTSD) symptoms among individuals with comorbid substance use disorder (SUD) and PTSD. However, concerns that PE will lead to negative outcomes such as dropout and relapse remain a barrier to high-risk individuals, such as those warranting residential SUD care, receiving PE. The goal of this study was to gather information on feasibility, acceptability, and efficacy of offering PE in residential SUD treatment. Study therapists conducted PE (3 times/week, up to 15 sessions) with 9 patients admitted to a residential SUD treatment program at a Veterans Affairs (VA) hospital. Participants completed the PTSD Symptom Checklist (PCL-S) and Patient Health Questionnaire (PHQ-9) at admission, at discharge from the 4- to 6-week program, and 3-months postdischarge follow-up. Patients who were offered PE tolerated and engaged in PE as indicated by completion of the protocol, high satisfaction scores, and clinically significant decreases in PTSD and depression symptom severity. Symptom reduction at follow-up was significantly greater among patients who received PE than those who did not ($n = 21$). This preliminary data provides initial support for further investigation of the efficacy of PE in residential SUD care.

Norman, S. B., Trim, R., Haller, M., Davis, B. C., Myers, U. S., Colvonen, P. J., Blanes, E., Lyons, R., Siegel, E. Y., Angkaw, A. C., Norman, G. J., & Mayes, T. (2019). **Efficacy of integrated exposure therapy vs integrated coping skills therapy for comorbid posttraumatic stress disorder and alcohol use disorder: A randomized clinical trial.** *JAMA Psychiatry, 76*, 791–799.

[doi:10.1001/jamapsychiatry.2019.0638](https://doi.org/10.1001/jamapsychiatry.2019.0638) *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.

Pearson, C. R., Kaysen, D., Huh, D., & Bedard-Gilligan, M. (2019). **Randomized control trial of culturally adapted cognitive processing therapy for PTSD substance misuse and HIV sexual risk behavior for Native American women.** *AIDS and Behavior, 23*, 695–706. [doi:10.1007/s10461-018-02382-8](https://doi.org/10.1007/s10461-018-02382-8) An overlooked sequela of HIV risk is trauma exposure, yet few HIV interventions address trauma exposure, mental health, and substance misuse. In a two-arm randomized controlled trial 73 Native American women were randomized to a culturally-adapted Cognitive Processing Therapy (CPT) or 6-weeks waitlist. Outcomes assessed: PTSD symptom severity, alcohol use frequency, substance abuse or dependence diagnosis, and high-risk sexual behavior defined as vaginal/anal intercourse (a) under the influence of alcohol and/or illicit substances, (b) with a partner who was concurrently sexually active with someone else, and/or (c) with more than one partner in the past 6 weeks. Among immediate intervention participants, compared to waitlist participants, there were large reductions in PTSD symptom severity, high-risk sexual behavior, and a medium-to-large reduction in the frequency of alcohol use. CPT appears to improve mental health and risk behaviors, suggesting that addressing PTSD may be one way of improving HIV-risk related outcomes.

Peck, K. R., Schumacher, J. A., Stasiewicz, P. R., & Coffey, S. F. (2018). **Adults with comorbid posttraumatic stress disorder, alcohol use disorder, and opioid use disorder: The effectiveness of modified prolonged exposure.** *Journal of Traumatic Stress, 31*, 373–382. [doi:10.1002/jts.22291](https://doi.org/10.1002/jts.22291) Opioid use disorders (OUDs) are a growing problem in the United States. When OUDs co-occur with problematic drinking and posttraumatic stress disorder (PTSD), negative drug-related mental and physical health outcomes may be exacerbated. Thus, it is important to establish whether PTSD treatments with established efficacy for dually diagnosed individuals also demonstrate efficacy in individuals who engage in problematic drinking and concurrent opioid misuse. Adults who met DSM-IV-TR criteria for PTSD and alcohol dependence were recruited from a substance use treatment facility and were randomly assigned to receive either modified prolonged exposure (mPE) therapy for PTSD or a non-trauma-focused comparison treatment. Compared to adults in a non-OUD comparison group ($n = 74$), adults with OUD ($n = 52$) were younger, reported more cravings for alcohol, were more likely to use amphetamines and sedatives, were hospitalized more frequently for drug- and alcohol-related problems, and suffered from more severe PTSD symptomatology, depressive symptoms, and anxiety, standardized mean differences = 0.36–1.81. For participants with OUD, mPE was associated with large reductions in PTSD symptomatology, sleep disturbances, and symptoms of anxiety and depression, $d_s = 1.08$ – 2.56 . Moreover, participants

with OUD reported decreases in alcohol cravings that were significantly greater than those reported by the non-OUD comparison group, $F(1, 71.42) = 6.37, p = .014$. Overall, our findings support the efficacy of mPE for PTSD among individuals who engage in problematic drinking and concurrent opioid misuse, despite severe baseline symptoms.

Ruglass, L. M., Lopez-Castro, T., Papini, S., Killeen, T., Back, S. E., & Hien, D. A. (2017). **Concurrent treatment with prolonged exposure for co-occurring full or subthreshold posttraumatic stress disorder and substance use disorders: A randomized clinical trial.** *Psychotherapy and Psychosomatics, 86*, 150–161. doi:10.1159/000462977

Background: To test whether an integrated prolonged exposure (PE) approach could address posttraumatic stress disorder (PTSD) symptoms effectively in individuals with co-occurring substance use disorders (SUD), we compared concurrent treatment of PTSD and SUD using PE (COPE) to relapse prevention therapy (RPT) for SUD and an active monitoring control group (AMCG). **Methods:** We conducted a randomized 12-week trial with participants ($n = 110$; 64% males; 59% African Americans) who met Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision criteria for full or subthreshold PTSD and SUD. Participants were randomly assigned to COPE ($n = 39$), RPT ($n = 43$), or AMCG ($n = 28$). **Results:** At the end-of-treatment, COPE and RPT demonstrated greater reduction in PTSD symptom severity relative to AMCG (COPE-AMCG = $-34.06, p < 0.001$; RPT-AMCG = $-22.58, p = 0.002$). Although the difference between COPE and RPT was not significant in the complete sample, the subset of participants with full (vs. subthreshold) PTSD demonstrated significantly greater reduction of PTSD severity in COPE relative to RPT. Both treatments were superior to AMCG in reducing the days of primary substance use (COPE-AMCG = $-0.97, p = 0.01$; RPT-AMCG = $-2.07, p < 0.001$). Relative to COPE, RPT showed significantly more improvement in SUD outcome at end-of-treatment (RPT-COPE = $-1.10, p = 0.047$). At 3-month follow-up, COPE and RPT maintained their treatment gains and were not significantly different in PTSD severity or days of primary substance use. **Conclusion:** COPE and RPT reduced PTSD and SUD severity in participants with PTSD + SUD. Findings suggest that among those with full PTSD, COPE improves PTSD symptoms more than a SUD-only treatment. The use of PE for PTSD was associated with significant decreases in PTSD symptoms without worsening of substance use.

Schacht, R. L., Brooner, R. K., King, V. L., Kidorf, M. S., & Peirce, J. M. (2017). **Incentivizing attendance to prolonged exposure for PTSD with opioid use disorder patients: A randomized controlled trial.** *Journal of Consulting and Clinical Psychology, 85*, 689–701. doi:10.1037/ccp0000208 **Objective:** To determine whether contingent monetary incentives increase opioid use disorder patients' attendance to Prolonged Exposure (PE) therapy and whether attendance is associated with improvement in posttraumatic stress disorder (PTSD) and substance use disorder (SUD) outcomes. **Method:** Patients ($N = 58$) with PTSD were offered PE or PE with incentives (PE + I; max \$480) to attend PE sessions. Participants were assessed at baseline and weeks 6, 12, and 24 postrandomization. **Results:** Participants were mostly women (79%) and Caucasian (71%); mean age 37.43 years ($SD = 11.33$). PE + I participants attended a median of 9 (of 12) sessions compared

to 1 session for PE participants ($p < .001$), which included more exposure sessions (PE + I $mdn = 6$; PE $mdn = 0$; $p < .001$). A Time \times treatment condition interaction indicated that PE + I participants exhibited a greater decrease in PTSD severity over time than PE participants (OR = 3.1; 95% CI = 0.4–5.7; $p = .024$). PE + I participants remained in substance use treatment longer than PE participants (mdn days = 262 vs. 192; $p = .039$). There were no group differences in drug use. **Conclusions:** Monetary incentives increased SUD patients' attendance to an otherwise poorly attended treatment for PTSD. Better attendance in the incentivized group was associated with greater PTSD improvement, better SUD treatment retention, and no increased drug use. Incentives are well supported for improving adherence to substance use treatment goals and promising as a means to improve therapy attendance, which may improve the effectiveness of existing psychotherapies in difficult-to-treat populations.

ADDITIONAL CITATIONS

Becker, C. B., Zayfert, C., & Anderson, E. (2004). **A survey of psychologists' attitudes towards and utilization of exposure therapy for PTSD.** *Behaviour Research and Therapy, 42*, 277–292. doi:10.1016/S0005-7967(03)00138-4 This study assessed psychologists' use of imaginal exposure. Among 852 psychologists, a large majority did not report using exposure therapy to treat PTSD. Psychologists also reported a large number of perceived barriers to implementing exposure. This study demonstrated the low utilization and negative perceptions of PE among many clinicians in the early 2000's.

Berenz, E. C., Rowe, L., Schumacher, J. A., Stasiewicz, P. R., & Coffey, S. F. (2012). **Prolonged exposure therapy for PTSD among individuals in a residential substance use treatment program: A case series.** *Professional Psychology, Research and Practice, 43*, 154–161. doi:10.1037/a0026138 This study described outcomes for four patients with PTSD in a residential substance use treatment program who received PE in addition to SUD treatment. Patients completed 9 biweekly 60-min sessions of PE. None of the clients met criteria for PTSD at the end of treatment, 3- and 6-months posttreatment, suggesting larger study of PE in SUD residential treatment is needed.

Capone, C., Pousseau, C., Saunders, E., Eaton, E., Hamblen, J., & McGovern, M. (2018). **Is integrated CBT effective in reducing PTSD symptoms and substance use in Iraq and Afghanistan veterans? Results from a randomized clinical trial.** *Cognitive Therapy and Research, 42*, 735–746. doi:10.1007/s10608-018-9931-8 This study was a randomized controlled trial of ICBT compared to SUD TAU in 44 military veterans with PTSD+SUD. There was a significant reduction in PTSD and SUD in both conditions, but there were no significant differences in PTSD or SUD symptom change by treatment condition. Consistent with other studies, this study did not find an integrated treatment that was not trauma focused to outperform SUD-only treatment.

Foa, E. B., McLean, C. P., Zang, Y., Rosenfield, D., Yadin, E., Yarvis, J. S., Mintz, J., Young-McCaughan, S., Borah, E. V., Dondanville, K. A., Fina, B. A., Hall-Clark, B. N., Lichner, T., Litz, B. T., Roache, J.,

Wright, E. C., Peterson, A. L. & for 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.** *JAMA*, *319*, 354–364. doi:10.1001/jama.2017.21242 This study was a randomized clinical trial comparing weekly PE, daily PE, weekly present centered therapy (PCT), or supportive weekly phone calls among 370 military personnel with PTSD who served in Iraq and/or Afghanistan. Massed PE reduced PTSD symptom severity more than supportive phone calls at 2-week follow-up and was noninferior to spaced therapy. There was no significant difference between spaced PE and PCT. This study shows the efficacy of massed PE.

Garland, E. L., Roberts-Lewis, A., Tronnier, C. D., Graves, R., & Kelley, K. (2016). **Mindfulness-Oriented Recovery Enhancement versus CBT for cooccurring substance dependence, traumatic stress, and psychiatric disorders: Proximal outcomes from a pragmatic randomized trial.** *Behaviour Research and Therapy*, *77*, 7–16. doi:10.1016/j.brat.2015.11.012 This study was a pragmatic randomized controlled trial comparing Mindfulness-Oriented Recovery Enhancement (MORE) to group Cognitive-Behavioral Therapy (*Seeking Safety*) and TAU for previously homeless men with SUD+psychiatric disorders residing in a therapeutic community. Participants were randomly assigned to 10 weeks of group treatment with MORE ($n = 64$), CBT ($n = 64$), or TAU ($n = 52$). MORE was associated with modest yet significantly greater improvements in substance craving, post-traumatic stress, and negative affect than cognitive behavioral therapy, and greater improvements in post-traumatic stress and positive affect than TAU.

Hammen, J. L., Norman, S. B., Sonis, J. H., Phelps, A. J., Bisson, J. I., Nunes, V. D., Megnin-Viggars, O., Forbes, D., Riggs, D. S., & Schnurr, P. P. (2019). **A guide to guidelines for the treatment of posttraumatic stress disorder in adults: An update.** *Psychotherapy*, *56*, 359–373. doi:10.1037/pst0000231 This paper compares and contrasts five recent clinical practice guidelines (CPGs) for the treatment of PTSD in adults. All of the guidelines gave the highest overall recommendations to trauma-focused psychotherapies that included PE and CPT (and in most cases EMDR), and all agreed that selective serotonin reuptake inhibitors (either specific ones or the whole class) were the most effective medications for PTSD.

Hien, D. A., Levin, F. R., Ruglass, L. M., López-Castro, T., Papini, S., Hu, M.-C., Cohen, L. R., & Herron, A. (2015). **Combining seeking safety with sertraline for PTSD and alcohol use disorders: A randomized controlled trial.** *Journal of Consulting and Clinical Psychology*, *83*, 359–369. doi:10.1037/a0038719 This study was the first randomized controlled trial to test the benefit of combining *Seeking Safety* with sertraline. Sixty-nine participants (81% female; 59% African American) with PTSD+AUD were randomized to receive a partial-dose (12 sessions) of *Seeking Safety* with either sertraline ($n = 32$) or placebo ($n = 37$). Both conditions demonstrated significant improvement in PTSD symptoms. The sertraline condition exhibited a significantly greater reduction in PTSD symptoms at end-of-treatment, 6- and 12-month follow-up. Both conditions improved significantly on AUD severity at all time points with no significant differences between conditions.

Hindocha, C., Cousijn, J., Rall, M., & Bloomfield, M. A. P. (2019). **The effectiveness of cannabinoids in the treatment of posttraumatic stress disorder (PTSD): A systematic review.** *Journal of Dual Diagnosis*, 1–20. doi:10.1080/15504263.2019.1652380 This study was a systematic review of cannabinoids for the treatment of PTSD. The authors included studies (randomized controlled trials, retrospective studies, non-randomized trials) of patients with PTSD who were prescribed or using a cannabinoid to reduce PTSD symptoms. Ten trials published through December 2018 were included. Results showed that the studies were small and of low quality. The authors concluded that making clinical recommendations about using cannabinoids in routine clinical practice is not yet possible but that future well-controlled, randomized, double-blind clinical trials are highly warranted.

Kulka, R. A., Schlenger, W. E., Fairbanks, J. A., Hough, R. L., Jordan, B. K., Marmar, C. R., & Weiss, D. S. (1990). **The National Vietnam veterans readjustment study: Tables of findings and technical appendices.** New York: Brunner/Mazel.

Manhapa, A., Stefanovics, E., & Rosenheck, R. (2015). **Treatment outcomes for veterans with PTSD and substance use: Impact of specific substances and achievement of abstinence.** *Drug and Alcohol Dependence*, *156*, 70–77. doi:10.1016/j.drugalcdep.2015.08.036 As part of a national program evaluation, Veterans admitted to specialized intensive PTSD programs were assessed at intake and 4 months after discharge. Seven mutually exclusive groups were identified from admission self-report data ($N = 22,948$): no substance use, exclusive use of alcohol, opiates, sedatives, cocaine, marijuana, and use of three or more substances. All outcome (PTSD symptoms, violent behavior, suicidality, and medical problems) measures except for employment showed significant improvement, with few differences between the groups. Specific type of substance used prior to entry into treatment had limited effect on treatment outcomes.

McDevitt-Murphy, M. E., Williams, J. L., Bracken, K. L., Fields, J. A., Monahan, C. J., & Murphy, J. G. (2010). **PTSD symptoms, hazardous drinking, and health functioning among U.S.OEF/OIF veterans presenting to primary care.** *Journal of Traumatic Stress*, *23*, 108–111. doi:10.1002/jts.20482 This study tested whether alcohol misuse mediated the relationship between PTSD symptoms and functional health outcomes in 151 U.S. Iraq and Afghanistan Veterans (136 men and 15 women). PTSD symptoms, hazardous drinking, and health functioning were correlated with each other. Hazardous drinking partially mediated the relationship between PTSD and functional mental health, but not physical health.

McGovern, M. P., Lambert-Harris, C., Xie, H., Meier, A., McLeman, B., & Saunders, E. (2015). **A randomized controlled trial of treatments for co-occurring substance use disorders and post-traumatic stress disorder.** *Addiction*, *110*, 1194–1204. doi:10.1111/add.12943 This study compared ICBT plus standard care, individual addiction counseling plus standard care, and standard care alone on substance use and PTSD symptoms in 221 community patients with PTSD+SUD. Results showed PTSD symptoms reduced in all conditions with no difference between them. In secondary analyses, ICBT had better toxicology results than the other two conditions, had a greater reduction in reported drug

use than standard care, and had higher attendance than individual counseling. ICBT may improve drug related outcomes, but not PTSD outcomes, more than SUD-only treatment.

Najavits, L. M. (2006). **Seeking safety: Therapy for posttraumatic stress disorder and substance use disorder.** In Follette VM, Ruzek JI, eds. *Cognitive-Behavioral Therapies for Trauma. 2nd ed.*, pp. 228-257. Guilford Press. This chapter provides an overview of an integrated treatment model developed to address comorbid PTSD and substance use disorder. Details of the treatment model and underlying theories of behavior change, session topics, format and key principles are presented, as are practical elements such as client and clinician selection, assessment. Some early empirical findings are also provided.

Norman, S. B., Haller, M., Hamblen, J. L., Southwick, S. M., & Pietrzak, R. H. (2018). **The burden of co-occurring alcohol use disorder and PTSD in U.S. Military veterans: Comorbidities, functioning, and suicidality.** *Psychology of Addictive Behaviors, 32*, 224–229. doi:10.1037/adb0000348 This study evaluated the prevalence of psychiatric comorbidities, functioning, and quality of life in a nationally representative sample of U.S. Veterans using data from the National Health and Resilience in Veterans Study. The authors compared AUD alone, PTSD alone, and comorbid AUD/PTSD. Among those with probable AUD, 20.3% met criteria for probable PTSD. Among those, with probable PTSD, 16.8% met criteria for probable AUD. Compared to Veterans with AUD only, Veterans with AUD+PTSD were more likely to screen positive for major depression (36.8% vs. 2.3%), generalized anxiety disorder (43.5% vs. 2.9%), suicidal ideation (39.1% vs. 7.0%); to have attempted suicide (46.0% vs. 4.1%); and to be receiving mental health treatment (44.8% vs. 7.5%). They also scored lower on cognitive, mental and physical functioning, and quality of life. Veterans with comorbid AUD+PTSD were more than three times as likely as Veterans with PTSD only to have attempted suicide in their lifetimes. Results underscore the burden of co-occurring PTSD+AUD in Veterans, and the importance of engaging these Veterans in treatment.

Perez-Dandieu, B., & Tapia, G. (2014). **Treating trauma in addiction with EMDR: A pilot study.** *Journal of Psychoactive Drugs, 46*, 303–309. doi:10.1080/02791072.2014.921744 This study piloted EMDR for PTSD+SUD. Twelve patients were randomized to TAU or TAU plus eight sessions of EMDR (TAU+EMDR). Results showed that TAU+EMDR showed a significant reduction in PTSD symptoms but not in SUD outcomes. EMDR was associated with a significant decrease in depressive symptoms and significant improvement in self-esteem and alexithymia while TAU was not. This study suggests further study of EMDR for PTSD+SUD is warranted.

Petrakis, I. L., & Simpson, T. L. (2017). **Posttraumatic stress disorder and alcohol use disorder: A critical review of pharmacologic treatments.** *Alcoholism, Clinical and Experimental Research, 41*, 226–237. doi:10.1111/acer.13297 This study reviewed pharmacotherapy treatments of PTSD+AUD. Studies were grouped in 3 categories: (i) those that evaluated first-line treatments for PTSD, (ii) those that evaluated medications to target AUD, and (iii) those that evaluated medications hypothesized to be effective in targeting alcohol consumption as well as PTSD symptoms. Nine

RCTs were identified; 3 focused on medications to treat PTSD, 4 focused on AUD, and 3 to target both. All but 1 of the studies found that PTSD symptoms and drinking outcomes improved significantly over time. There was not one agent with clear evidence of efficacy in this comorbid group. Most studies provided a combination of interventions to treat both disorders. Despite contradictory results, this review suggests that individuals with PTSD+AUD can safely be prescribed medications used in noncomorbid populations and patients improve with treatment.

Pietrzak, R. H., Goldstein, R. B., Southwick, S. M., & Grant, B. F. (2011). **Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: Results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions.** *Journal of Anxiety Disorders, 25*, 456–465. doi:10.1016/j.janxdis.2010.11.010 This study is the first to examine the prevalence and Axis I comorbidity of DSM-IV diagnosis of PTSD. The lifetime prevalence of PTSD among U.S. adults was 6.4%. An additional 6.6% of U.S. adults had subthreshold, partial PTSD in their lifetimes. Lifetime full and partial PTSD are associated with elevated rates of Axis I disorders and suicide attempt. Lifetime full and partial PTSD are related to poorer past-month psychosocial functioning.

Pitman, R. K., Altman, B., Greenwald, E., Longpre, R. E., Macklin, M. L., Poiré, R. E., & Steketee, G. S. (1991). **Psychiatric complications during flooding therapy for posttraumatic stress disorder.** *The Journal of Clinical Psychiatry, 52*(1), 17–20. This case study presented data on 6 men with PTSD who received “flooding therapy” (which shares some elements with exposure therapy). The authors suggest that many patients may not be ready for flooding therapy. This study is often cited as an example of early literature that discourages using exposure therapy and trauma focused therapy.

Roberts, N. P., Roberts, P. A., Jones, N., & Bisson, J. I. (2015). **Psychological interventions for post-traumatic stress disorder and comorbid substance use disorder: A systematic review and meta-analysis.** *Clinical Psychology Review, 38*, 25–38. doi:10.1016/j.cpr.2015.02.007 This meta-analysis examined the efficacy of individual and group psychological interventions aimed at treating comorbid PTSD+ SUD, based on randomized controlled trials. Fourteen studies were included. Individual trauma-focused cognitive-behavioral intervention, delivered alongside SUD intervention, was more effective than TAU for PTSD severity post-treatment, and at subsequent follow-up. There was no evidence of an effect for level of drug/alcohol use post-treatment but there was an effect at 5–7 months. Fewer participants completed trauma-focused intervention than TAU. There was little evidence to support the use of individual or group-based non-trauma-focused interventions. The study shows that individual trauma-focused psychological intervention delivered alongside SUD intervention can reduce PTSD severity, and drug/alcohol use.

Schäfer, I., Lotzin, A., Hiller, P., Sehner, S., Driessen, M., Hillemecher, T., Schäfer, M., Scherbaum, N., Schneider, B., & Grundmann, J. (2019). **A multisite randomized controlled trial of Seeking Safety vs. Relapse Prevention Training for women with**

co-occurring posttraumatic stress disorder and substance use disorders. *European Journal of Psychotraumatology*, 10, 1577092. doi:10.1080/20008198.2019.1577092 This randomized controlled trial compared *Seeking Safety*+TAU to relapse prevention+TAU and TAU-only in female outpatients in community mental health in Germany. *Seeking Safety* plus TAU, RPT plus TAU and TAU alone showed comparable decreases in PTSD severity over the course of the study. Consistent with other studies, *Seeking Safety* and relapse prevention did not differ significantly.

Seal, K. H., Cohen, G., Waldrop, A., Cohen, B. E., Maguen, S., & Ren, L. (2011). **Substance use disorders in Iraq and Afghanistan veterans in VA healthcare, 2001-2010: Implications for screening, diagnosis and treatment.** *Drug and Alcohol Dependence*, 116, 93–101. doi:10.1016/j.drugalcdep.2010.11.027 Using administrative data, this study examined the prevalence and correlates of AUD and drug use disorder (DUD) diagnoses in Iraq and Afghanistan Veterans who were new VA users ($n = 456,502$). Of those with AUD, DUD or both, 55–75% also received PTSD or depression diagnoses. AUD, DUD or both diagnoses were 3–4.5 times more likely in Veterans with PTSD and depression. This study suggests there is a great need for integrated treatments that simultaneously address AUD and DUD in the context of PTSD and other deployment-related mental health disorders.

Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. (2016). *Treatment Episode Data Set (TEDS): 2004-2014. National Admissions to Substance Abuse Treatment Services. BHSIS Series S-84, HHS Publication No. (SMA) 16-4986.* Retrieved from <https://www.samhsa.gov/data/report/treatment-episode-data-set-teds-2004-2014-national-admissions-substance-abuse-treatment> This report presents national-level data from the Treatment Episode Data Set (TEDS) for admissions in 2014 and trend data from 2004 to 2014. It is a companion to the report Treatment Episode Data Set (TEDS): 2004-2014 State Admissions to Substance Abuse Treatment. These reports provide information on the demographic and substance abuse characteristics of admissions aged 12 and older to treatment for abuse of alcohol and/or drugs in facilities that report to individual state administrative data systems. Data include records for admissions during calendar years 2004 through 2014 that were received and processed through February 1, 2016.

Tate, S. R., Norman, S. B., McQuaid, J. R., & Brown, S. A. (2007). **Health problems of substance-dependent veterans with and those without trauma history.** *Journal of Substance Abuse Treatment*, 33, 25–32. doi:10.1016/j.jsat.2006.11.006 This study examined whether trauma history and PTSD were related to physical health in patients with SUD. The authors compared (1) no trauma exposure (SUD-only group), $n = 55$; (2) with PTSD (SUD+PTSD group), $n = 32$; and (3) trauma exposure without PTSD (SUD+trauma group), $n = 34$ on health stressors, health service utilization, and self-reported health status. The veterans were assessed quarterly for 1 year. The SUD-only group had the lowest rates of chronic health stressors, the SUD–PTSD group had the highest rates, and the SUD–trauma group fell in between. The study suggests that chronic health stressors are associated with trauma exposure and PTSD symptoms.

Tripp, J. C., Haller, M., Trim, R. S., Straus, E., Bryan, C. J., Davis, B. C., Lyons, R., Hamblen, J., & Norman, S. B. (in press). **Does exposure exacerbate symptoms for veterans with PTSD and alcohol use disorder?** *Psychological Trauma: Theory, Research, Practice, and Policy*. Clinicians may have concerns that offering exposure therapy to patients with comorbid PTSD and alcohol use disorder will lead to clinical exacerbation, COPE did not lead to more symptom (PTSD, alcohol use, depression, suicidal ideation) exacerbation than *Seeking Safety* when exposure was first introduced into therapy (between sessions 3 and 5). Results suggest clinicians should not refrain from offering exposure treatment for patients with PTSD/AUD due to concerns of symptom exacerbation.

Tripp, J. C., Worley, M. J., Straus, E., Angkaw, A. C., Trim, R. S., & Norman, S. B. (2020). **Bidirectional relationship of posttraumatic stress disorder (PTSD) symptom severity and alcohol use over the course of integrated treatment.** *Psychology of Addictive Behaviors*. Advance online publication. doi:10.1037/adb0000564 This study included 107 Veterans who were randomized to receive either COPE or *Seeking Safety* and completed measures of PTSD and alcohol use at every other session. Multilevel models estimated the prospective associations between PTSD and alcohol use during treatment. Results indicated that greater PTSD symptom severity was associated with greater future alcohol use and greater alcohol use was associated with greater future PTSD symptom severity. The effect size for PTSD symptoms to future alcohol use was larger than the reciprocal relationship. Treatment condition did not moderate these effects. Results suggest that integrated treatments that treat both PTSD and alcohol use may be preferential to sequential model of care where individuals are expected to achieve abstinence or reduced use prior to receiving trauma-focused treatment.

Tull, M. T., Gratz, K. L., Coffey, S. F., Weiss, N. H., & McDermott, M. J. (2013). **Examining the interactive effect of posttraumatic stress disorder, distress tolerance, and gender on residential substance use disorder treatment retention.** *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors*, 27, 763–773. doi:10.1037/a0029911 This study examined the effect of a PTSD+SUD diagnosis on residential SUD treatment completion. Participants were 214 substance-dependent patients consecutively admitted to a residential SUD treatment facility. Results showed a significant PTSD \times gender \times distress tolerance interaction (although no main effects were found). Among men, those with current PTSD and low distress tolerance completed less SUD treatment than others.

Van Woudenberg, C., Voorendonk, E. M., Bongaerts, H., Zoet, H. A., Verhagen, M., Lee, C. W., van Minnen, A., & De Jongh, A. (2018). **Effectiveness of an intensive treatment programme combining prolonged exposure and eye movement desensitization and reprocessing for severe post-traumatic stress disorder.** *European Journal of Psychotraumatology*, 9 1487225. doi:10.1080/20008198.2018.1487225 This study evaluated an intensive 8-day trauma-focused treatment program for PTSD. 347 PTSD patients (70% women; mean age = 38.32 years) received daily PE and EMDR. At post-treatment, 82.9% showed clinically meaningful PTSD symptom reduction and 54.9% had lost their diagnosis. Dropout was very low (2.3%). The study suggests that intensive trauma-focused treatment programs can be effective to treat PTSD with low dropout rates.

Watts, B. V., Schnurr, P. P., Mayo, L., Young-Xu, Y., Weeks, W. B., & Friedman, M. J. (2013). **Meta-analysis of the efficacy of treatments for posttraumatic stress disorder.** *The Journal of Clinical Psychiatry, 74*, e541–e550. [doi:10.4088/JCP.12r08225](https://doi.org/10.4088/JCP.12r08225)

This meta-analysis examined the efficacy of treatments for PTSD. PubMed, MEDLINE, PILOTS, and PsycINFO databases were searched for randomized controlled clinical trials of any treatment for PTSD in adults published between January 1, 1980, and April 1, 2012, and written in the English language. The sample consisted of 137 treatment comparisons drawn from 112 studies. Results showed that effective psychotherapies included cognitive therapy, exposure therapy, and EMDR. Effective pharmacotherapies included paroxetine, sertraline, fluoxetine, risperidone, topiramate, and venlafaxine. The study showed that while there are several effective options, not all medications or psychotherapies are effective.

Yasinski, C. W., Rauch, S. A. M., Post, L., Sherrill, A. M., Maples-Keller, J. L., Breazeale, K., Zwiebach, L., Dunlop, B., Louks, L., & Rothbaum, B. O. (2018). *Biological, demographic, and psychological predictors of change in and intensive outpatient program for PTSD.* Presented at the Military Health System Research Symposium, Orlando, FL. This study presented pre and post-treatment data from an intensive outpatient PTSD treatment program that offered massed PE for Veterans who served in Iraq and Afghanistan. Results show high effect size for PTSD symptom reduction and low dropout.