

Expanding the Boundaries of PTSD Treatment

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HOW BEST TO TREAT POSTTRAUMATIC STRESS DISORDER (PTSD) is a long-standing question. Treatments for PTSD, which began in the late 19th century, have varied greatly.¹ In the current era, numerous PTSD treatments are available, some with a strong evidence base.² In this issue of *JAMA*, the findings of 2 randomized controlled trials of interventions for PTSD expand the boundaries of treatment to relatively underserved populations: the trial by Mills et al³ assesses interventions in persons with PTSD and substance dependence, and the trial by Monson et al⁴ assesses interventions in couples in which 1 partner has PTSD.⁴

The trial by Mills et al³ evaluated Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure (COPE) plus usual treatment for substance dependence (n=55) vs usual treatment for substance dependence alone (n=48). COPE involved an individual modality treatment totaling 19.5 hours, whereas usual treatment was any type of substance use treatment available in the patient's community, including counseling, detoxification, residential rehabilitation, and pharmacotherapy. Prolonged exposure therapy is a type of cognitive-behavioral therapy that exposes patients to memories and reminders of traumatic events associated with intense negative emotions such as anxiety, anger, and sadness. Although this is the first published randomized controlled trial using prolonged exposure in patients with PTSD and substance use disorder, trials of other models for concurrent treatment of PTSD and substance use disorders have shown positive findings.⁵ Prolonged exposure therapy is an evidence-based treatment for PTSD currently being implemented on a large scale within the US Veterans Affairs Healthcare System⁶; thus, results of this trial of prolonged exposure for co-occurring PTSD and substance dependence are of immediate interest.

Patients with PTSD have been treated with prolonged exposure therapy since the 1990s, and several variants of this therapy have been developed.² Although the evidence base for prolonged exposure therapy is strong, previous clinical trials have consistently excluded many of the complex PTSD cases that clinicians routinely encounter, such as patients

with suicidal ideation; histories of self-harm, homelessness, and intimate partner violence; and comorbid conditions such as psychosis and substance use disorder. In fact, patients with substance use disorders have been excluded from most PTSD treatment trials.⁷ For exposure-based models in particular, PTSD experts indicated that the treatment was not appropriate for patients with comorbid PTSD and substance use disorders until patients attained substantial recovery from substances. In recent years, pilot studies have evaluated exposure-based treatments for patients with PTSD and substance use disorders, with no finding of exacerbation of symptoms⁷ and with improvements in various domains,^{8,9} but the study by Mills et al³ is the first randomized controlled trial to assess the efficacy of prolonged exposure for co-occurring PTSD and substance use disorder, specifically substance dependence, the more severe form of the disorder. It is thus a welcome addition to the PTSD literature.

However, the results of the study by Mills et al³ showed no differences between patients in the COPE plus usual treatment condition and those in the usual treatment alone condition in outcomes for any substance use variable, depression, or anxiety at any point. For the outcome of PTSD symptoms, there were no differences between conditions at 3 months, which was the point with the greatest number of patients still participating and would be the typical end-of-treatment point for a 13-session treatment such as COPE. However, the investigators allowed a time frame of 9 months so that study participants had more time to attend treatment sessions. At 9 months, compared with baseline, PTSD had significantly improved in both study conditions, but there was a greater reduction in PTSD symptoms in the COPE group.

The strengths of this trial comprise inclusion of well-trained clinicians, monitoring of treatment quality, measurement of the amount of therapies provided as usual treatment, validated measures of patient outcomes, and appropriate statistical analyses. The investigators conducted the study in a substance abuse treatment setting, and the trial included a broad range of patients typically excluded in studies of prolonged exposure therapy, such as

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patients with substance dependence, injection drug use, and recent substance use. In addition, study participants included patients who were unemployed, had prior criminal justice involvement, abused multiple drugs, had histories of childhood or repeated trauma, had made prior suicide attempts, or had co-occurring borderline personality disorder. Notably too, patients were not paid for treatment attendance, which has occurred in some prior trials of prolonged exposure therapy, including the precursor to this trial,⁹ and which may have artificially inflated results in those trials.

By the end of the trial by Mills et al, as is common with complex populations, both study conditions still had notable impairment in all domains assessed, despite the improvements from baseline. The majority of patients still had PTSD and moderate depression, and nearly half of the patients still had evidence of substance dependence, despite receiving treatment and close monitoring in this trial and, for 65% of the patients, other treatments for PTSD prior to this trial. Such findings highlight the difficulty of working with patients with PTSD and complex comorbidities. Allowing up to 9 months for study participants assigned to the intervention group to complete their treatment sessions resulted in a lack of consistent timing for end-of-treatment outcome assessment, which was a methodological weakness of this trial. Even with the time extension, the COPE dropout rate was considered high by the investigators, with patients attending a median of only 5 of 13 sessions.

In sum, the trial by Mills et al addresses important scientific and clinical questions, but its limited results indicate the need for continued work. Professionals consistently report that the comorbidity of PTSD and substance use disorder is more difficult to treat than PTSD alone.¹⁰ Although prolonged exposure therapy may be considered by many clinicians to be optimal therapy for PTSD in the absence of comorbidity, the results of this trial indicate that the benefit on PTSD of prolonged exposure therapy for patients with PTSD and substance dependence was only modestly better than usual treatment at 9 months and not better on substance use variables, depression, or anxiety at any point. Moreover, prolonged exposure therapy requires intensive training,⁶ which is not typically feasible in substance abuse settings, where group therapy modalities and a less skilled workforce predominate. Thus, exposure-based therapy for co-occurring PTSD and substance dependence cannot be widely recommended based on the results of this trial alone. Which patients can most benefit from prolonged exposure therapy and how to assess readiness for it are areas for future work.

In another trial in this issue of *JAMA*, Monson et al⁴ address Cognitive-Behavioral Conjoint Therapy (CBCT) for couples in which one partner had PTSD. This intervention comprised 18.75 hours of treatment sessions that include a blend of cognitive-behavioral approaches relevant to couple treatment and PTSD. Patients assigned to receive couple

therapy (n=20) had clinically meaningful reductions in PTSD symptom severity and a modest improvement in relationship satisfaction, as compared with patients (n=20) assigned to a wait list (who were scheduled to receive couple therapy after the conclusion of the trial). Strengths of this trial include the inclusion of same-sex as well as heterosexual couples, the detailed description of the treatment model, validated assessments, fidelity monitoring, and blinded evaluation.

In this study, the primary weaknesses were not what occurred but what was left out. There were no data on how concurrent psychotherapies may have affected outcomes or whether the couples were compensated financially for their participation in the trial, and neither the patients assigned to the wait-list condition nor patients who dropped out of treatment were included in the follow-up assessment. From a clinical perspective, the study sample also appeared generally "easier to treat" than is typical in community settings (including the study by Mills et al³), as indicated by baseline measurements of relationship satisfaction, a general lack of severe comorbidities, and the support of an intimate partner who was willing to participate in treatment. In the report by Monson et al,⁴ the sample was predominantly white and employed, with virtually no substance use disorder at baseline.

Although the results of this trial were positive, study participants were carefully selected, and thus the applicability of this intervention to a wide range of clinical settings and patient characteristics remains unclear. For example, the authors describe their CBCT intervention as being designed to treat PTSD and its comorbid symptoms but address very few psychiatric comorbidities. Treatment strategies may be quite different, for example, for patients with PTSD and substance use disorder than for patients with PTSD and obsessive-compulsive disorder. The study by Monson et al also did not assess for Axis II disorders, which are known to influence outcomes.

Because of the selection of study participants in this trial, it is difficult to generalize the results to couples who may have more strained relationships. In this trial, the couples had high relationship satisfaction and stability at baseline (those randomized to receive CBCT had been together for 8 years on average). In addition, couples were excluded if one or both had recent substance dependence, if there was evidence of severe intimate partner aggression in the past year, or if both partners had PTSD. Thus, the trial by Monson et al⁴ cannot be interpreted as being applicable to couples with these additional challenges, which may be the couples in greatest need of help. Hopefully, future trials will evaluate couples therapy for PTSD among a broader range of patients.

The results of the trials by Mills et al³ and Monson et al⁴ are important scientific attempts to study new options for treatment of PTSD. Overall, comparative studies of PTSD therapies find that they rarely outperform each other in efficacy.^{11,12} Thus, the cost and appeal of treatments to clini-

cians and patients, their intensity of intervention, and clinical setting and training issues may ultimately be as or more relevant than comparative efficacy in choosing a course of treatment for PTSD. In the current era, there is a focus on short-term treatments (in part an antidote to the overly long psychotherapies of much of the 20th century). However, it is not clear how long treatment needs to be maintained to produce enduring positive outcomes, especially for patients with PTSD and comorbidities and difficult social circumstances. The field of PTSD therapy is still young, and the pursuit of clinically meaningful treatments for all types of patients, like the process of recovery for patients with PTSD, is an ongoing challenge.

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Evolving Research on the Treatment of Health Effects of Violence and Human Rights Abuses

From Observational Studies to Randomized Trials

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THE 1999 JAMA THEME ISSUE ON VIOLENCE AND HUMAN RIGHTS included a number of studies that reported on violence in schools,¹ the increasing incidence of child abuse,² rates of screening for intimate partner violence,³ and the mental health of refugees and non-combatants in war.⁴ In an Editorial in that issue,⁵ we commented that although the prevention and treatment of violence and human rights abuses was a maturing discipline, nearly all of the published reports on these topics as of 1999 described problems rather than evaluations of the efficacy of interventions.

Since then many randomized trials of interventions that address the causes and consequences of violence and human rights violations have been published, including a number in JAMA.⁶⁻¹¹ This issue of JAMA includes reports of 3 new randomized trials of interventions: a trial of screening for intimate partner violence¹² and 2 trials of interventions for

posttraumatic stress disorder for survivors of violence.^{13,14} The implications of these trial reports for clinical practice and public health are discussed in accompanying Editorials,^{15,16} as are the methodologic strengths and limitations of these studies. In this context, it is worth reflecting on what researchers, public health and international aid workers, and clinicians have been able to accomplish in the past several years of intensive work in the fields of violence and human rights.

The evolution of the quality of the science of violence and human rights is represented by recent trends in the published literature. As of July 2012, PubMed¹⁷ cites 66 907 articles indexed with the term *violence*, including 789 articles indexed as randomized controlled trials (RCTs). Nearly half of these articles reporting RCTs about violence (47%; 367) were published just within the last 5 years. PubMed also has indexed 111 653 articles with the term *human rights*,

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