CLINICIAN'S TRAUMA UPDATE

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TREATMENT

Head-to-head comparison of PE and CPT

Results of a new RCT led by the National Center for PTSD that compared PE and CPT in Veterans found a statistical advantage for PE, but the difference was not clinically significant. The trial was the first to compare the treatments in Veterans, and is the largest study of psychotherapy for PTSD ever conducted.

The investigators randomized 916 male and female Veterans at 17 sites to receive PE or CPT, both delivered in 10-14 sessions. Veterans assigned to PE improved an average of 2.42 more points on the CAPS-5, the primary outcome, relative to Veterans assigned to CPT (d = .17, below the pre-specified threshold of .25 for clinical significance). Participants assigned to PE also were more likely to achieve response, loss of diagnosis, and remission. There were no differences between PE and CPT on secondary outcomes of depression, substance use, and quality of life. Because Veterans improved meaningfully from before to after treatment in both PE (d = .99) and CPT (d = .71), and the difference in between treatments in CAPS-5 severity was so small, the investigators did not recommend PE over CPT. Instead, they recommend shared decision-making to help Veterans select their preferred treatment. Future analyses will support shared decision-making by examining moderators of treatment response.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1586155.pdf

Schnurr, P. P., Chard, K. M., Ruzek, J. I., Chow, B. K., Resick, P. A., Foa, E. B., . . . Shih, M. C. (2022). Comparison of prolonged exposure vs cognitive processing therapy for treatment of posttraumatic stress disorder among US veterans: a randomized clinical trial. *JAMA Network Open, 5,* Article e2136921. PTSDpubs ID: 1586155

Brief intervention targets trauma-related guilt

Feelings of guilt and beliefs that one violated an important value are common and potentially debilitating reaction after a traumatic event. National Center for PTSD investigators led a multi-site randomized controlled trial of a new intervention targeting maladaptive guilt. Trauma-Informed Guilt Reduction (TRiGR) is a six-session protocol consisting of psychoeducation, cognitive restructuring, and identifying adaptive ways to express the values that underlie trauma-related guilt.

Participants included 145 post-9/11 Veterans (92.4% male) who reported clinically significant guilt following deployment. Most (84.8%) also met criteria for PTSD, although that was not a requirement for participation. Veterans were randomized to either TRiGR or Supportive Care Therapy, an active control condition that included psychoeducation and nondirective, supportive counseling. Self-reported guilt decreased for Veterans in both conditions, but reductions from baseline to 6-month follow-up were greater for those assigned to TRiGR (d = .99). PTSD and depressive symptoms also showed greater reductions for those in TRiGR versus SCT. Although guilt symptoms improve with other EBPs, TriGR provides a brief protocol that may be useful for trauma survivors who have prominent guilt. Ongoing efforts are examining the effectiveness of TRiGR for other types of trauma- or stressor-related guilt, such as that experienced in the context of the COVID-19 pandemic.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1586433.pdf

Norman, S. B., Capone, C., Panza, K. E., Haller, M., Davis, B. C., Schnurr, P. P., . . . Angkaw, A. (2022). A clinical trial comparing trauma-informed guilt reduction therapy (TrIGR), a brief intervention for trauma-related guilt, to supportive care therapy. *Depression and Anxiety.* Advance online publication. PTSDpubs ID: 1586433

Alternative treatment modalities improve outcomes in CPT

Delivering mental health treatment outside an office may reduce barriers to care and improve outcomes. For example, in-home delivery of PE was shown to be as effective as telehealth with less dropout (see the February 2020 *CTU-Online*), but in-home CPT had not been studied. Investigators from University of Texas Health Science Center compared the efficacy and acceptability of in home, office, or telehealth CPT using an equipoise-stratified randomized design.

Service members and Veterans ($N = 120$) were randomized to receive CPT in-home, in-office, or via telehealth. Participants could opt out of one treatment modality prior to randomization. Telehealth was most acceptable, with 17% refusing this modality, compared to 29% and 54% refusing in-office and in-home, respectively. However, dropout was lowest for in-home (25%), followed by telehealth (34%) and in-office (43%) modalities. PTSD symptoms improved in all modalities, but pre-post improvements were larger for in-home ($d = 2.1$) and telehealth ($d = 2.0$) compared to in-office ($d = 1.3$), although these differences did not persist at 6-month follow-up or for clinician-rated symptoms. These results support the use of alternative delivery modalities for PTSD treatment. In-home care is highly effective but may be limited by reduced patient acceptability and travel burden for clinicians, whereas telehealth appears both acceptable and efficient while improving treatment outcomes.

Read the article: https://doi.org/10.1186/s12888-022-03699-4

Peterson, A. L., Mintz, J., Moring, J. C., Straud, C. L., Young-McCaughan, S., McGeary, C. A., . . . Resick, P. A. (2022). In-office, in-home, and telehealth cognitive processing therapy for posttraumatic stress disorder in veterans: A randomized clinical trial. *BMC Psychiatry, 22*, Article 41. PTSDpubs ID: 1586330

Disappointing results from RCT of ketamine for PTSD

Open-label studies have shown promising but inconsistent effects of ketamine on PTSD symptoms (see February 2021 *CTU -Online*). Single infusions often result in short-lived improvements. Extending the duration of ketamine's effects is of interest. However, a recent study conducted by the Consortium to Alleviate PTSD reported disappointing results from a double-blind placebo-controlled RCT of repeated administration of ketamine in patients with PTSD.

Veterans and service members ($N = 158$) with PTSD were assigned to one of three arms: 8 infusions over four weeks of standard dose (0.5 mg/kg) or low dose (0.2 mg/kg) ketamine or placebo. While all three groups showed improvements on the PCL-5 (the primary outcome), the ketamine groups did not improve more than placebo (pre-posttreatment *d*s: standard dose = 1.61, low dose = 1.53, placebo = 1.13). In line with previous trials of ketamine for depression, the Montgomery-Asberg Depression Rating Scale (a secondary outcome) did show dose-related effects at post-treatment that did not endure to the 4-week follow-up. The ketamine groups reported more dissociative and psychotic symptoms compared to placebo, but these resolved 1-2 hours post-infusion. While this study provided additional support for ketamine's short- but not long-term efficacy for depression, it did not support ketamine as a PTSD treatment. Ongoing and future research can explore ketamine as an adjunct to psychotherapy (see December 2020 *CTU-Online*).

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1586306.pdf

Abdallah, C. G., Roache, J. D., Gueorguieva, R., Averill, L. A., Young-McCaughan, S., Shiroma, P. R., . . . Krystal, J. H. (2022). Dose-related effects of ketamine for antidepressant-resistant symptoms of posttraumatic stress disorder in veterans and active duty military: a double-blind, randomized, placebo-controlled multi-center clinical trial. *Neuropsychopharmacology.* Advance online publication. PTSDpubs ID: 1586306

Written Exposure Therapy shown to be noninferior to CPT in active-duty military

Brief treatments such as Written Exposure Therapy (WET) may appeal to those who anticipate difficulties completing longer courses of treatment. WET was found to be noninferior to CPT for treating PTSD in a primarily civilian population (see the February 2018 *CTU-Online*) but had not been tested with active-duty military. A study led by investigators from the National Center for PTSD compared WET to CPT in a military population.

Participants were 169 U.S. active-duty service members with PTSD (81% male, mean age = 34) randomized to receive WET or CPT. WET consisted of 5 45-minute weekly sessions in which participants wrote about their trauma for 30 minutes, followed by a therapist check-in. CPT was delivered twice weekly in one-hour sessions for 6 weeks. Participants were assessed with the CAPS-5 at baseline and at 10, 20, and 30 weeks after the first treatment session. PTSD symptoms improved in both WET ($d = .48$-$.54$) and CPT ($d = .54$-$.78$). WET was statistically noninferior to CPT, but improvement was modest in both groups. Fewer participants dropped out of WET (24%) than CPT (45%). The low dropout rate suggests WET may increase access to a full course of treatment, although effect sizes were lower than other studies of trauma-focused treatments. Additional research with service members and Veterans will provide further information about the efficacy of WET with these populations.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1586434.pdf

Sloan, D. M., Marx, B. P., Resick, P. A., Young-McCaughan, S., Dondanville, K. A., Straud, C. L., . . . Peterson, A. L. (2022). Effect of written exposure therapy vs cognitive processing therapy on increasing treatment efficiency among military service members with posttraumatic stress disorder: A randomized noninferiority trial. *JAMA Network Open, 5*, Article e2140911. PTSDpubs ID: 1586434

Cognitive-Behavioral Conjoint Therapy for PTSD in a VA clinic

A previous RCT with a mixed community and Veteran sample provided promising evidence for Cognitive-Behavioral Conjoint Therapy for PTSD (CBCT), a 15-session trauma-focused treatment delivered to dyads to improve PTSD and relationship satisfaction (see the August 2012 *CTU-Online*). However, that study included few Veterans, who often show poorer response to psychotherapy for PTSD than non-Veterans. Investigators at the Cincinnati VA Medical Center published findings on CBCT delivered to couples in their PTSD outpatient program.

This study included Veterans with PTSD ($N = 102$) or subthreshold PTSD ($N = 11$) and their intimate partners. Most couples included a male Veteran (91.2%) with a female partner (93.8%), but 3 couples (2.7%) were in same-sex partnerships. Participants received

10.5 sessions on average and 58 couples (51.3%) completed treatment. Veteran-rated PTSD symptom severity (d = .70) and relationship happiness (d = .40) improved over the course of treatment, as did scores on secondary measures of relationship satisfaction, depression, and partner accommodation of PTSD symptoms. Although these findings show that PTSD and other outcomes improved, effects were modest and smaller than those observed in the 2012 RCT. Future controlled studies can test CBCT against individual PTSD treatments to determine for whom CBCT might be indicated and most effective.

Read the article: https://doi.org/10.1002/jts.22781

Pukay-Martin, N. D., Fredman, S. J., Martin, C. E., Le, Y., Haney, A., Sullivan, C., . . . Chard, K. M. (2021). Effectiveness of cognitive behavioral conjoint therapy for posttraumatic stress disorder (PTSD) in a U.S. Veterans Affairs PTSD clinic. *Journal of Traumatic Stress.* Advance online publication. PTSDpubs ID: 1585442

Demographic and clinical factors are unreliable predictors of trauma-focused psychotherapy utilization

Many patients with PTSD do not receive a trauma-focused psychotherapy (TFP), which are the most effective psychotherapies for PTSD. Investigators at the Syracuse VA Medical Center conducted a naturalistic program evaluation of psychotherapy utilization in 242 Veterans enrolled in a VA PTSD clinic to understand why these treatments are underutilized.

The investigators explored demographics, referral source, trauma experiences and symptoms, suicidal ideation, and emotional nonacceptance as potential predictors of referral, treatment initiation and completing an adequate dose. Just over half (55.9%) of Veterans referred to the PTSD clinic were then referred to TFP. Just over a quarter (27%) initiated TFP and 14% received an adequate dose. Veterans referred to TFP were more likely to begin treatment and to receive an adequate dose than those referred to non-TFP. Of 15 demographic and clinical variables examined, few were associated with utilization: only current suicidal ideation and reporting startle symptoms predicted initiating TFP if referred, while being married/partnered predicted completing an adequate dose of TFP. These findings provide some insight into factors that may influence treatment utilization; however, replication is necessary (see this issue's Take Note for two systematic reviews on predictors of treatment engagement). A shared limitation of this and previous research is that reasons underlying providers' referral decisions and patients' dropout are unknown. This information is necessary to maximize TFP utilization.

Read the article: https://doi.org/10.1037/ser0000583

Possemato, K., Steiger, S., Sindoni, M., Moe, R., Higham, J., & Tubbs, C. (2021). A clinician/researcher partnership to understand patterns and predictors of trauma-focused psychotherapy and nontrauma-focused psychotherapy use among veterans with PTSD. *Psychological Services.* Advance online publication. PTSDpubs ID: 1584124

ASSESSMENT

Reliable and clinically significant change in the CAPS-5 and PCL-5

Researchers at the National Center for PTSD aggregated data from three previously published RCTs to calculate the reliable change index (RCI) and clinically significant change (CSC) for the CAPS-5 and PCL-5, instruments that are commonly used in measurement-based care and research. Understanding the clinical significance of an individual patient's symptom change is crucial to understanding treatment response.

Investigators calculated the RCI and CSC using pre- and post-treatment data in 312 Veterans with PTSD, along with cross-sectional data from 228 trauma-exposed Veterans without PTSD. The RCI (change greater than measurement error) was 12-13 points for the CAPS-5, and 15-18 points for the PCL-5. A score of 8 on the CAPS-5 and 28 on the PCL-5 was indicative of CSC (a posttreatment score that is more representative of a person without PTSD than with PTSD). Both the RCI and CSC were associated with significantly better post-treatment psychosocial functioning. Although this study provides valuable information about meaningful metrics of change on the CAPS-5 and PCL-5, the data do not provide a final answer on what constitutes "improvement." Findings were calculated using convenience samples of male Veterans. Because the RCI and CSCs are influenced by estimates of variability and test-retest reliability, it will be helpful to have data from more, and more heterogeneous, samples to maximize reliability and generalizability.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1585445.pdf

Marx, B. P., Lee, D. J., Norman, S. B., Bovin, M. J., Sloan, D. M., Weathers, F. W., . . . Schnurr, P. P. (2022). Reliable and clinically significant change in the Clinician-Administered PTSD Scale for DSM-5 and PTSD Checklist for DSM-5 among male veterans. *Psychological Assessment, 34,* 197-203. PTSDpubs ID: 1585445

Shortened PTSD assessment via machine learning

Structured clinical interviews are the gold-standard assessment for PTSD, but the time required can present a challenge for routine clinical use. A team led by investigators at Boston University used machine learning to determine if a clinical interview could be shortened without losing diagnostic accuracy.

The investigators examined data from 1,265 Veterans (51% female) who participated in Project VALOR, a longitudinal study of post-9/11 Veterans. The participants completed the PTSD module of the Structured Clinical Interview for *DSM-5* (SCID-5); 65.7% of the sample were diagnosed with PTSD. The investigators used random forest models, a type of machine learning that employs an iterative process of combining predictors to classify an outcome, i.e., PTSD diagnosis. All 20 PTSD symptoms were initially included in sex-stratified models and characterized according to how much they contributed to the diagnostic classification). The investigators then removed symptoms from the model in reverse-order of importance to identify the smallest set of symptoms that still resulted in high classification accuracy (e.g., AUC > .90). The final model for men contained 16 items; the model for women contained 14 items. Both gender-specific and common symptoms emerged. Although a relatively modest reduction in items, the findings support this method as a potential strategy to streamline diagnostic assessments for PTSD.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1557058.pdf

Jiang, T., Dutra, S., Lee, D. J., Rosellini, A. J., Gauthier, G. M., Keane, T. M., . . . Marx, B. P. (2021). Toward reduced burden in evidence-based assessment of PTSD: A machine learning study. *Assessment, 28,* 1971-1982. PTSDpubs ID: 1557058

Take NOTE

Exposure therapy for PTSD

Investigators from the National Center for PTSD and Yale University School of Medicine reviewed the literature on exposure therapy for PTSD.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1585394.pdf

McLean, C. P., Levy, H. C., Miller, M. L., & Tolin, D. F. (2022). Exposure therapy for PTSD: A meta-analysis. *Clinical Psychology Review, 91,* Article 102115. PTSDpubs ID: 1585394

Treating co-occurring suicidal thoughts and PTSD

A systematic review led by investigators at the University of Central Florida reviews evidence-based treatment of co-occurring suicidal thoughts and PTSD.

Read the article: https://www.ptsd.va.gov/professional/articles/article-pdf/id1585592.pdf

Rozek, D. C., Baker, S. N., Rugo, K. F., Steigerwald, V. L., Sippel, L. M., Holliday, R., . . . Smith, N. B. (2021). Addressing co-occurring suicidal thoughts and behaviors and posttraumatic stress disorder in evidence-based psychotherapies for adults: A systematic review. *Journal of Traumatic Stress.* Advance online publication. PTSDpubs ID: 1585592

Predicting PTSD treatment response and retention

Two systematic reviews led by the RAND Corporation explore patient predictors of PTSD treatment response and retention.

Read the articles:

https://doi.org/10.1002/jts.22757

Maglione, M. A., Chen, C., Franco, M., Gizaw, M., Shahidinia, N., Baxi, S., & Hempel, S. (2021). Effect of patient characteristics on posttraumatic stress disorder treatment retention among veterans: A systematic review. *Journal of Traumatic Stress.* Advance online publication. PTSDpubs ID: 1583821

https://doi.org/10.7249/RR4191

Maglione, M. A., Chen, C., Franco, M., Gizaw, M., Shahidinia, N., Baxi, S. M., & Hempel, S. (2022). Predictors of PTSD treatment retention and response: A systematic review. Santa Monica, CA: RAND Corporation. PTSDpubs ID: 1586435

Veterans Health Administration

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