Author/s:
O'Donnell, ML;Lau, W;Chisholm, K;Agathos, J;Little, J;Terhaag, S;Brand, R;Putica, A;Holmes, ACN;Katona, L;Felmingham, KL;Murray, K;Hosseiny, F;Gallagher, MW

Title:
A Pilot Study of the Efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Treating Posttraumatic Psychopathology: A Randomized Controlled Trial

Date:
2021-06-01

Citation:
O'Donnell, M. L., Lau, W., Chisholm, K., Agathos, J., Little, J., Terhaag, S., Brand, R., Putica, A., Holmes, A. C. N., Katona, L., Felmingham, K. L., Murray, K., Hosseiny, F. & Gallagher, M. W. (2021). A Pilot Study of the Efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Treating Posttraumatic Psychopathology: A Randomized Controlled Trial. Journal of Traumatic Stress, 34 (3), pp.563-574. https://doi.org/10.1002/jts.22650.

A Pilot Study of the Efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders in Treating Posttraumatic Psychopathology: A Randomized Controlled Trial

Meaghan L. O'Donnell[1, 2], Winnie Lau[1, 2], Katherine Chisholm[1, 2], James Agathos[1, 2], Jonathon Little[1, 2], Sonia Terhaag[1, 2], Rachel Brand[1], Andrea Putica[1, 2], Alexander C. N. Holmes[3], Lynda Katona[4], Kim L. Felmingham[5], Kim Murray[1], Fardous Hosseiny[6], & Matthew W. Gallagher[7]

[1]Phoenix Australia Centre for Posttraumatic Mental Health, Melbourne, Australia

[2]Department of Psychiatry, University of Melbourne, Melbourne, Australia

[3]Royal Melbourne Hospital, Melbourne, Australia

[4]Alfred Hospital, Melbourne, Australia

[5]School of Psychological Sciences, University of Melbourne, Melbourne, Australia

[6]Centre of Excellence on Post-Traumatic Stress Disorder, Ottawa, Canada

[7]Department of Psychology, University of Houston, Houston, Texas, USA

Author Note

This work was supported by a National Health and Medical Research Council grant (APP1073041). The funding body had no involvement in the study design, data collection, analysis, or interpretation or writing of the manuscript.

Correspondence concerning this article should be addressed to Meaghan O'Donnell

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/jts.22650.

Level 3, Alan Gilbert Building, 161 Barry Street, Carlton, VIC 3053, Australia. E-mail: mod@unimelb.edu.au

Abstract

The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) is an intervention that targets common mechanisms that maintain symptoms across multiple disorders. The UP has been shown to be effective across many disorders, including generalized anxiety disorder, major depressive episodes (MDEs), and panic disorder, that commonly codevelop following trauma exposure. The present study represented the first randomized controlled trial of the UP in the treatment of trauma-related psychopathology, including posttraumatic stress disorder (PTSD), depression, and anxiety symptoms. Adults (N = 43) who developed posttraumatic psychopathology that included PTSD, MDE, or an anxiety disorder after sustaining a severe injury were randomly assigned to receive 10–14 weekly, 60-min sessions of UP (n = 22) or usual care (n = 21). The primary treatment outcome was PTSD symptom severity, with secondary outcomes of depression and anxiety symptom severity and loss of diagnosis. Assessments were conducted at intake, posttreatment, and 6-month posttreatment follow-up. Posttreatment, participants who received UP showed significantly larger reductions in PTSD, Hedges' g = 1.27; anxiety, Hedges' g = 1.20; and depression, Hedges' g = 1.40, symptom severity compared to those in the usual care group. These treatment effects were maintained at 6-month follow-up for PTSD, anxiety, and depressive symptom severity. Statistically significant posttreatment loss of PTSD, MDE, and agoraphobia diagnoses was observed for participants in the UP group but not those in the usual care condition. This study

provides preliminary evidence that the UP may be an effective non–trauma-focused treatment for PTSD and other trauma-related psychopathology.

A Pilot Study of the Efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders for Treating Posttraumatic Psychopathology: A Randomized Controlled Trial

The psychiatric impacts of trauma exposure can be profound and highly complex (O'Donnell et al., 2016). Although posttraumatic stress disorder (PTSD) is characterized as the signature trauma-related disorder, other disorders commonly emerge in the aftermath of traumatic events, including major depressive episode (MDEs), anxiety disorders (e.g. generalized anxiety disorder [GAD], panic disorder, specific phobias, and social anxiety disorder [SAD]), and substance use disorders (Bryant et al., 2010). It is important to note that there are high rates of comorbidity among these disorders in the aftermath of trauma exposure, which are associated with high levels of long-term disability and increased burden on health services (O'Donnell et al., 2016); comorbidity is particularly common in treatment-seeking patients with PTSD (O'Donnell et al., 2012).

Comorbidity increases the difficulty of clinical decision-making. Current indicated "best-practice" treatments differ between disorders, and this may necessitate complex treatment planning and longer therapy duration to sequentially treat each single disorder (Farchione et al., 2012). The efficacy of single-disorder treatment protocols may also be compromised by comorbidities. Furthermore, evidence suggests that in individuals with a primary diagnosis of PTSD, comorbidities such as major depressive disorder (Stein et al., 2012), GAD (Tarrier et al., 2000), or other emotional

states, such as guilt and depression (Phelps et al., 2018), may hinder PTSD treatment response. As such, there is a clear mandate for treatment options that adequately and simultaneously address comorbidity across the full spectrum of posttraumatic mental health.

Transdiagnostic interventions broadly refer to treatments that can be used across diagnostic categories (Gutner & Presseau, 2019). A subset of these, termed "mechanistically transdiagnostic interventions," act across disorder categories by explicitly targeting common psychological processes, or "mechanisms," that causally underlie a range of disorders (Gutner et al., 2016; Gutner & Presseau, 2019). As such, by targeting mechanisms that are common to multiple disorders, a single protocol can be effective in treating a range of disorders that are caused or maintained by the same mechanisms.

One such intervention is the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP; Barlow, Farchione, Sauer-Zavala, et al., 2017), which targets common mechanisms associated with emotional disorders. Core psychological vulnerabilities such as emotion avoidance and deficits in emotion regulation are proposed to underlie symptomatology across a number of emotional disorders (Sheppes et al., 2015; Suárez et al., 2009). Indeed, there is evidence that the experience and avoidance of negative affect accounts for much of the shared variance of common psychiatric disorders (T. Brown et al., 1998). The UP explicitly targets these core mechanisms, providing a more parsimonious approach to treatment while adequately addressing comorbidity. There is a burgeoning literature base that attests to the efficacy of the UP in a range of disorders,

including GAD, major depressive disorder, panic disorder, SAD, obsessive–compulsive disorder, alcohol use disorders, and borderline personality disorder (Sakiris & Berle, 2019).

There is a strong theoretical basis for why the UP may also be an effective intervention for trauma-exposed individuals, particularly those with PTSD. Meta-analytic reviews have demonstrated the robust influence that deficits in emotion regulation can have on both vulnerability to and maintenance of PTSD and related disorders (Aldao et al., 2010). Similarly, emotional avoidance, and anxiety sensitivity—each of which is targeted by the UP (Barlow, Farchione, Sauer-Zavala, et al., 2017)—are implicated in maintaining symptomatology in PTSD (Gallagher, 2017; Kotov et al., 2010; Paulus et al., 2018). Of note, although these emotion regulation deficits are found in PTSD, they are also common to other anxiety and depressive disorders (Aldao et al., 2010; Sloan et al., 2017), which may explain the high levels of comorbidity associated with PTSD.

To date, only one study of which we are aware has investigated the use of the UP as an intervention for trauma-exposed individuals. A pilot study conducted by Varkovitzky et al. (2017) found significant posttreatment improvements in PTSD and depressive symptomatology in a sample of veterans. Unfortunately, methodological limitations of this study, including a lack of control group, no follow-up data, a lack of an intent-to-treat analysis, and group format, prevent firm conclusions from being drawn. Nonetheless, the study provides promising early signs for the use of the UP for posttraumatic psychopathology.

Intrusive memories of a traumatic event are central to PTSD phenomenology (Iyadurai et al., 2019), with cognitive models of PTSD suggesting they play a role in driving the other three symptom clusters (i.e., avoidance, negative alterations in cognitions and mood, and hyperarousal; Ehlers & Clark, 2000). Current first-line PTSD treatments recognize this by explicitly targeting these intrusive trauma memories and, as such, are described as being trauma-focused (i.e., focusing directly on the memory of the traumatic event). Prolonged exposure therapy, for example, involves exposing an individual to trauma reminders and uses fear extinction learning to promote a gradual extinction of the conditioned fear response (Rothbaum & Davis, 2003). Trauma-focused treatments have been associated with reductions in intrusive memory symptoms that suggest the trauma memory is being processed (Horesh et al., 2017). Studies are required to identify whether the UP, a non–trauma-focused intervention, impacts intrusive memory symptoms.

The primary aim of this pilot study was to test the efficacy of the UP for the treatment of PTSD symptom severity in a methodologically rigorous trial. Secondary aims were to test the UP's impact on comorbidity, including comorbid depression and anxiety symptom severity, as well as loss of diagnosis (i.e., PTSD, MDE, agoraphobia, panic disorder, GAD, and social phobia). To identify whether the UP impacted intrusive memory symptoms, we also examined changes in scores on the Intrusion subscale of the PTSD Checklist (PCL) for the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-5*; i.e., the PCL-5). We hypothesized that participants who took part in the UP would show larger reductions in PTSD symptom severity relative to those in a usual care condition. Secondary hypotheses included that the UP would be superior to usual care in

reducing depressive, severity, anxiety, and intrusive memory symptom severity as well as in regard to loss of diagnoses, as previously described.

Method

Participants and Procedure

Study Design

This parallel-group, assessor-blinded, randomized controlled trial compared posttraumatic mental health outcomes of participants who received either the UP or usual care. All participants were assessed at baseline, posttreatment, and 6 months following treatment completion. Participants in the usual care condition were offered the UP intervention following the 6-month assessment. The study was approved by Melbourne Health (2014.097) and the Alfred Hospital's (27/17) human ethics committees. Informed consent was obtained from all participants prior to their participation. The trial was registered prospectively with the Australian New Zealand Clinical Trials Registry (ACTRN12614000823673).

Participant Recruitment, Screening, and Characteristics

Participants were recruited through two tertiary hospitals following admission for serious physical injury in Melbourne, Australia. Recruitment took place between September 2014 and August 2019 and ceased due to time restrictions. This study utilized a two-step screening process to determine individuals' eligibility regarding treatment participation. Inclusion criteria for the

screening phase of the trial included (a) having sustained an injury that resulted in a hospital admission of longer than 24 hr, (b) that the injury event met PTSD Criterion A as defined in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM-IV*), (c) being between 18 and 70 years of age, and (d) good English comprehension. Exclusion criteria were (a) having sustained a moderate-to-severe traumatic brain injury, (b) being actively suicidal or having sustained an injury caused by deliberate self-harm, and (c) active mania or psychosis. Eligible patients were assessed using the Posttraumatic Adjustment Screen (PAS; O'Donnell et al., 2008) before hospital discharge. The PAS was used to identify individuals who were at risk for developing PTSD or MDE. Patients who crossed a screening threshold were contacted 4 weeks later, at which time a clinical research assistant conducted a telephone interview. During this interview, the Mini International Neuropsychiatric Interview–6.0 (M.I.N.I.-6; Sheehan et al., 1998) was used to screen potential participants for PTSD, MDE, and several anxiety disorders. Eligibility for inclusion in the treatment phase of the trial required a posttraumatic psychiatric diagnosis, as assessed via the M.I.N.I.-6, including (a) a psychiatric disorder that had developed postinjury and, in the case of PTSD, was directly linked to the injury event), or (b) a preexisting disorder that was exacerbated postinjury. Individuals were excluded from the UP condition if they were currently undergoing psychological treatment; participants in the usual care condition could receive concurrent psychological treatment during the study. In addition, individuals were deemed ineligible for treatment if they had current alcohol or substance dependence.

The flow of participants who enrolled in the treatment study is depicted in Figure 1. A total of 43 participants met the criteria for a postinjury psychiatric disorder and enrolled in the study. These participants had experienced a range of injury events, including motor vehicle accidents, workplace accidents, and assaults. A total of 28 participants reported a primary diagnosis of PTSD, 12 reported a primary diagnosis of MDE, and three reported a primary diagnosis of agoraphobia. Participants were randomized to either the UP (n = 22) or usual care (n = 21) treatment groups using a covariate adaptive randomization process that controlled for gender, number of comorbid disorders, and PTSD severity. Randomization was conducted by an independent researcher external to the study team. Allocation concealment was ensured by using a coded number system. The clinical research assistant who administered the clinical diagnostic interviews via telephone and the statistician who conducted all analyses were blinded to intervention condition. Both treatment groups completed self-report measures of PTSD, depression, and anxiety symptom severity at pretreatment, 2 weeks posttreatment, and at a 6-month posttreatment follow-up.

Treatment Conditions

Unified Protocol. Participants in the UP condition who completed therapy received between 10 and 14 weekly, face-to-face, 60-min UP therapy sessions. Sessions took place at the Phoenix Australia Traumatic Stress Clinic in Melbourne, Australia. Treatment sessions sequentially covered the eight manualized treatment modules outlined by Barlow, Farchione, Sauer-Zavala, et al. (2017), namely: motivational enhancement for treatment engagement, psychoeducation and tracking of emotional experiences, emotion awareness training, cognitive appraisal and reappraisal, emotion

avoidance and emotion-driven behaviors, awareness and tolerance of physical sensations, interoceptive and situation-based emotion exposures, and relapse prevention. A senior clinician (Matthew Gallagher) who is an expert in the UP trained the therapists and provided monthly supervision sessions to the trial clinicians to ensure adherence to the UP program.

Usual Care. To give an indication of how patient outcomes improve under standard practice, participants in the usual care condition were free to engage in psychological or pharmacological treatment as they wished. Data on the kinds of services and interventions participants accessed were collected. Participants in the usual care condition who still met the criteria for an emotional disorder at the 6-month posttreatment follow-up were offered the opportunity to receive UP treatment after the study.

Measures

Demographic and Injury Characteristics

Information regarding age, gender, and educational attainment was collected. Injury severity was measured using the Injury Severity Score (ISS; Baker et al., 1974). The ISS is an established medical score of injury severity that is based on an anatomical injury severity classification and is correlated with mortality and morbidity. Scores range from 1 to 75, with scores higher than 15 classified as a major injury.

Predictive Screening

The PAS (O'Donnell et al., 2008), a 10-item screening tool, was used to identify participants who were at a high risk of subsequently developing PTSD or MDE. Each item is scored on a scale of 0 (*not at all*) to 4 (*totally*). The PAS-P subscale, which identifies the risk for developing PTSD, is calculated by summing the scores of all 10 items, with possible scores ranging from 0 to 40. The PAS-D subscale is used to identify the risk for MDE and is calculated by summing five of the 10 items, for a possible score range of 0 to 20. The PAS-P has demonstrated a sensitivity of .82 and a specificity of .84, and the PAS-D has shown a sensitivity of .72 and a specificity of .75 (O'Donnell et al., 2008). Participants who score 16 or higher on the PAS-P or 4 and higher on the PAS-D are considered to be at high risk for developing PTSD or MDE, respectively (O'Donnell et al., 2008). In the current study, Bentler's (2005) dimension-free greatest lower-bound reliability was .88 for the PAS-P scores and .79 for the PAS-D scores.

Psychological Disorders

The M.I.N.I.-6 (Sheehan et al., 1998), a short, structured diagnostic interview based on *DSM-IV* diagnostic criteria, was administered via telephone by a clinical research assistant and used to assess postinjury psychiatric disorders in individuals who were deemed to be at high risk for developing PTSD and/or MDE. The following modules were administered: PTSD, MDE, panic, agoraphobia, social phobia, GAD, alcohol use disorder, and travel phobia. Each module provides a dichotomous outcome (i.e., "yes" or "no") with regard to the presence of a particular disorder. The M.I.N.I.-6 has demonstrated strong psychometric properties, with sensitivity and specificity above .70 for all of the modules used in the present study, as well as high interrater and test–retest

reliability (Sheehan et al., 1998). In addition to the pretreatment delivery, the MINI-6 (Sheehan et al., 1998) was also delivered posttreatment and at 6-month follow-up.

PTSD Symptom Severity

The severity of PTSD symptoms was identified as the primary outcome and measured using the PCL-5 (Blevins et al., 2015). The PCL-5 is a 20-item, self-report scale that is used to measure the severity of *DSM-5* PTSD symptomatology. Participants rate the degree to which they are bothered by each symptom, scoring responses on a 5-point scale ranging from 0 (*not at all*) to 4 (*extremely*). Scores are summed to provide an overall symptom severity score (range: 0–80), with higher scores denoting more severe symptoms. The PCL-5 has four subscales relating to the PTSD symptom clusters (i.e., Intrusion, Avoidance, Negative Alterations in Cognitions and Mood, and Alterations in Arousal and Reactivity). In the present study, we used the overall PCL-5 scores as a continuous measure of PTSD symptom severity. All administrations of the PCL-5 were anchored to past-month symptoms except for the posttreatment assessment, which asked participants to rate symptoms they had experienced over the past 2 weeks, given that posttreatment assessments were conducted at 2 weeks posttreatment. The PCL-5 has demonstrated high levels of internal consistency, convergent and discriminant validity, and strong structural validity (Blevins et al., 2015). Bentler's (2005) dimension-free lower-bound reliability for the PCL-5 pretest scores was .99 in the current study. Post hoc analyses were also conducted to measure changes in the Intrusion subscale, which consists of five items that are scored described previously, with overall scores ranging from 0–20. In

the present study, the internal consistency of the PCL-5 Intrusion subscale scores very good at intake, Cronbach's α = .85.

Secondary Outcome Measures

Depressive Symptoms. Depressive symptom severity was measured using the Quick Inventory of Depressive Symptomatology (QIDS-SR16; Rush et al., 2003), a 16-item self-report scale that is used to measure depressive symptoms experienced over the past week. Participants are asked to select, from four potential options scored from 0 to 3, the response with which they relate most closely, with higher scores signifying more severe symptoms. A total QIDS-SR16 score was calculated in accordance with Rush et al. (2003; score range: 0–27) as a continuous measure of depressive symptom severity. The QIDS-SR16 has demonstrated high levels of internal reliability and concurrent validity (Trivedi et al., 2004). In the present study, Cronbach's alpha was .78 at intake.

Anxiety Symptoms. Anxiety symptom severity was measured using the State Anxiety subscale of the State–Trait Anxiety Inventory–Form Y (STAI-Y; Spielberger, 1983), a 20-item self-report subscale that is used to evaluate current feelings of apprehension, tension, nervousness, and worry. Items are rated on a scale from 1 (*not at all*) to 4 (*very much so*) and summed to obtain a total subtest score with a possible range of 20 to 80, where higher scores indicate a higher level of anxiety. The STAI-Y has demonstrated high levels of internal consistency, test–retest reliability, and construct and concurrent validity (Spielberger, 1983, 1989). In the present study, Cronbach's alpha was .91 at intake.

Data Analysis

We used an intent-to-treat analysis to ensure that all patients enrolled and randomly allocated to the UP treatment group or the usual care group were included in the analysis and analyzed according to the originally assigned groups. Comparisons across groups were made using between-group *t* tests and chi-square tests for independent samples to ensure there were no pretreatment differences on key demographic variables at intake. We used *Mplus* (Version 8.4; Muthén & Muthén, 1998–2019) to estimate the proportion of individuals with a M.I.N.I.-6 diagnosis of PTSD, MDE, and agoraphobia at intake, posttreatment, and 6-month follow-up. The Wald test was used to test the null hypothesis that change in these proportions over time differed significantly from zero.

Mplus (Version 8.4; Muthén & Muthén, 1998–2019) was then used to estimate eight one-way analyses of covariance (ANCOVAs) using the methods described by Green and Thompson (2012). This approach has the advantage of being extremely flexible. Assumptions required by ordinary least squares (OLS) regression can be circumvented via model specification and the use of alternative estimation methods, including those suitable for use with missing and nonnormally distributed data. Each ANCOVA compared the total scores on the dependent variable between the UP treatment and usual care groups at posttreatment and then again between these groups at 6-month follow-up, each time controlling for pretreatment total scores on the relevant dependent variable (i.e., the PCL-5, QIDS, STAI, or PCL-5 Intrusion subscale). For each ANCOVA, the grand-mean

centered covariate (i.e., subtracting the grand mean of the pretest outcome variable from all scores on that measure) was included as a predictor in the models in addition to a constant (i.e., intercept).

To be consistent with the standard assumption of homogeneity of slopes, the coefficients for the covariate were constrained to be equal across groups in each of the eight ANCOVAs; in addition, error variances were constrained to be equal across groups, consistent with the homogeneity of variance assumption. These two assumptions were checked by estimating three model types (see Supplementary Table S1). The first model type (Model A) constrained error variances to be equal across groups while allowing the slopes and intercepts to be free across groups. The second model type (Model B) constrained the slopes for the covariate to be equal across groups while allowing the error variances and intercepts to be free across groups. The third model type (Model C) constrained the error variances and slopes to be equal across groups while allowing the intercepts to be free across groups. The robust maximum likelihood (MLR) chi-square estimates for Model Cs were compared to Model As and Model Bs using Satorra and Bentler's (2001) scaled chi-square difference test. A statistically nonsignificant chi-square difference test confirms the assumption of homogeneity of slopes or error variances.

To assess the main ANCOVA models for the PCL-5, STAI, QIDS, and PCL-5 Intrusion subscale at posttreatment and 6-month follow-up, the intercepts in each group were first constrained to be equal across groups. The MLR chi-square estimates from these constrained models (i.e., Model Ds) were compared to Model Cs where the intercepts were free to differ across groups. A statistically significant chi-square difference test indicates that the intercepts are different. A sequentially

Bonferroni adjusted *p* value of .05 is used to maintain the family-wise Type I error rate for each of the eight chi-square difference tests used in the test for the equality of intercepts.

The magnitude of the difference between intercepts was indexed using four effect size estimates that included Hedges' *g,* Glass' delta*,* Cohen's f^2, and partial R^2. Cohen's f^2 uses equation 3.7.2 from Cohen et al. (2013, p. 94). The proportion of variance in the dependent variable (i.e., partial R^2) accounted for by the treatment method, controlling for the pretreatment covariate, was estimated using equation 24.9 in Green and Thompson (2012, p. 401). Model constraints are used within each Model C to test the statistical significance of Hedges' *g* and Glass' delta using a *z* test.

Based on each of the Model Cs, supplementary constraints also used a Wald test to test the null hypothesis that the difference between the treatment and usual care groups differ significantly from zero for each of the uncentered intake scores PCL-5, STAI, QIDS, and PCL-5 Intrusion subscale intake scores. A statistically nonsignificant Wald test shows that there are no differences between groups on each of the dependent variables at intake.

In the ANCOVA models, we managed missing data by using MLR estimation, which uses full information maximum likelihood to estimate model parameters, adjusting for the uncertainty due to missingness (Asparouhov & Muthén, 2008, 2010) under Rubin (1987)'s missing-at-random (MAR) assumption. The *Mplus* approach used throughout this manuscript is preferable when data are missing and nonnormal. Small-scale Monte Carlo simulations (e.g., Green & Thompson, 2012) have

shown that for simple ANOVA models of the type used here, robust results can still be obtained at small sample sizes.

Each dependent variable and covariate were summed to create a total score—if any one item was missing, the total score was also missing. For each analysis, item parcels were used as auxiliary missing data correlates, consistent with Graham's (2003) saturated correlates approach and the method described by Eekhout et al (2015). These auxiliary variables used item parcels taken from the PCL-5, QIDS, STAI, and PCL-5 Intrusion subscale at pretreatment, posttreatment, and 6-month follow-up. To reduce the risks of multicollinearity, two-thirds of the available items were used in the calculation of the mean scores for each auxiliary variable. Any case that had a missing value on all of the variables contained within an item parcel being averaged was given a missing value for the mean. The configurations of auxiliary variables used in each ANCOVA are shown in Supplementary Table S2.

For the analyses examining the loss of diagnosis over time, we used *Mplus* (Muthén & Muthén, 1998–2019) to generate 100 multiple imputed datasets using a Markov chain Monte Carlo (MCMC) algorithm and a multigroup model with Bayesian estimation under the MAR assumption. There were 100 between-imputation (i.e., thinning) iterations used together with a median Bayesian point estimate. Convergence was judged to have occurred around the 20,000th iteration, where the proportional scale reduction (PSR) factor was close to 1.02. An ample number of iterations (i.e., 100,000) were used to ensure the PSR did not prematurely approach 1.02 merely by chance. To model the dependence in the longitudinal scores, all variables for the same individual were recorded

on one row; that is, there was only one row for each participant. Participant age and the item parcels, as described previously, for the PCL-5, QIDS, and STAI scores at intake, posttreatment, and follow-up were modeled as continuous variables and included to improve the estimation of parameters associated with the M.I.N.I. diagnoses. A categorical model was used to impute the binary variables, including gender, and the M.I.N.I. diagnoses for PTSD, MDE, and agoraphobia. The multiple imputation yielded a sample size of 43 cases for the analyses, reported in Table 2. McNemar's asymptotic tests for significance of change and chi-square tests for independent samples were applied to each imputed data set, and results were pooled using the "miceadds" *R* package (Robitzsch & Grund, 2020) to estimate the D_2 statistic described by Enders (2010). Insufficient within-group variation for M.I.N.I. diagnoses of GAD, SAD, panic disorder, alcohol abuse, and travel phobia prevented these variables from being used within the multiple imputation or in McNemar's statistical tests for loss of diagnosis. Only pairwise case counts are reported herein for these diagnoses.

Results

Sample Characteristics

Descriptive statistics for demographic variables, diagnoses, and the dependent variables are shown in Table 1. Most participants recruited for the treatment component of the study were male (65.1%) and had sustained a moderately severe injury. Chi-square tests and independent samples *t* tests revealed the UP and usual care groups were similar prior to receiving treatment—that is, there

were no differences between treatment groups on any demographic or clinical variables except MDE, which was more prevalent in the usual care group than the UP group. There was also no difference between the two groups regarding PCL-5, STAI, QIDS, or PCL-5 Intrusion subscale scores (Table 1). These results confirm that the covariate adaptive randomization process was largely successful.

Usual Care

Participants in the usual care condition completed a postintervention interview regarding the types of services and interventions they accessed during the treatment period. Fifteen participants completed this interview, 14 of whom (93.3%) reported having received some form of medication for stress, sleep problems, depression, or pain; nine participants (i.e., 64.2% of those who received any medication) reported still using medication at the posttreatment assessment. In total, 60.0% of participants received psychotherapy (*M* = 3.89 sessions, *M* session duration = 53.33 min), and all nine individuals who received psychotherapy also received medication.

Loss of Diagnosis

We compared the proportions of participants in the UP and usual care groups who had a M.I.N.I diagnosis at intake, posttest, and follow-up. Only diagnoses of PTSD, MDE, and agoraphobia were found frequently enough to allow us to conduct loss-of-diagnosis analyses. In the treatment group, there was a statistically significant reduction in the proportion of participants with PTSD, MDE, and agoraphobia at posttreatment compared to intake as well as in the proportion of

participants with PTSD and MDE at follow-up compared to intake (Table 2). Consistent with our expectations, in the usual care group, there was not any statistically significant change with regard to the proportions of participants with a diagnosis of PTSD, MDE, or agoraphobia at posttreatment compared to intake. When comparing intake to follow-up in the usual care group, there was a statistically significant reduction in the number of participants with MDE, although no changes were observed from intake to follow-up for either PTSD or agoraphobia.

Between-Group Differences

We first tested the assumption of equality of slopes and error variances for each of the four dependent variables. The chi-square difference tests showed that apart from Model 7A (discussed later), these assumptions were satisfied for all models. The more constrained models (i.e., Models A and B) did not demonstrate a statistically significantly better fit to the data compared to Model C (see Supplementary Table S1). The results for the evaluation of assumptions of normality of sampling distributions, linearity, and the reliability of covariates were also satisfactory for each of the four ANCOVAs.

Results from the first ANCOVA, shown in Table 3, in which the PCL-5 scores at posttreatment were compared across groups, showed that the less-constrained model (i.e., Model 1C) was a better fit to the data, $\Delta\chi^2(1, N = 43) = 19.40$, $p < .001$, than the constrained model (i.e., Model 1D). This finding demonstrates that the intercepts were statistically significantly different between the two groups, with those in the UP group reporting lower symptom severity than those in the usual care

group. The magnitude of this difference (see Table 3) was large, Hedges' g = 1.27, 95% CI [0.72, 1.83], partial R^2 = .40. Cohen's f^2 and the adjusted PCL-5 and QIDS total mean scores at posttreatment and 6-month follow-up are shown in Table 3 for all four ANCOVAs. Results from the second ANCOVA, in which the PCL-5 scores at follow-up were compared across groups, showed that participants in the UP group also reported lower PTSD symptom severity than those in the usual care group, $\Delta\chi^2(1, N = 43) = 16.23$, $p < .001$, Hedges' g = 1.07, 95% CI [0.39, 1.75], partial R^2 = .22.

Participants in the UP group reported lower anxiety symptom severity at posttreatment and 6-month follow-up relative to those in the usual care group. Specifically, results for the ANCOVA that compared the STAI at posttreatment across groups showed that the less-constrained model (i.e., Model 1C) was a better fit to the data, $\Delta\chi^2(1, N = 43) = 6.88$, $p = .009$, than the constrained model (i.e., Model 1D), Hedges' g = 1.20, 95% CI [0.72, 1.68], partial R^2 = .43. The STAI intercepts were also significantly different between groups at follow-up, $\Delta\chi^2(1, N = 43) = 16.51$, $p < .001$, Hedges' g = 1.40, 95% CI [0.84, 1.96], partial R^2 = .35.

The results for depressive symptom severity were similar, with participants in the UP group reporting significantly lower depression scores at posttreatment and follow-up relative to those in the usual care group. Specifically, results for the ANCOVA that compared the QIDS at posttreatment across groups showed that the less-constrained model (i.e., Model 1C) was a better fit to the data, $\Delta\chi^2(1, N = 43) = 13.28$, $p < .001$, than the constrained model (i.e., Model 1D), Hedges' g = 1.40, 95% CI [0.83, 1.97], partial R^2 = .48. The QIDS intercepts were also significantly different between groups at follow-up, $\Delta\chi^2(1, N = 43) = 20.71$, $p < .001$, Hedges' g = 1.86, 95% CI [1.33, 2.39], partial R^2 = .54.

Finally, participants in the UP group reported significantly lower intrusion scores across time points relative to those in the usual care group. Specifically, the ANCOVAs comparing the PCL-5 Intrusion subscale at posttreatment across groups showed that the homogeneity of variance assumption was violated. One benefit of using *Mplus* (Muthén & Muthén, 1998–2019) is that this assumption can be accommodated by allowing the variances of the groups to differ (Fan & Hancock, 2012; Green & Thompson, 2012). When freeing this equality constraint, the model remains just-identified, and Model 7B can be used to directly assess the ANCOVA hypothesis. The less-constrained model (i.e., Model 7B) was a better fit to the data, $\Delta\chi^2(1, N = 43) = 5.36$, $p = .021$, than the constrained model (i.e., Model 1D), Hedges' $g = 0.74$, 95% CI [0.13, 1.35], partial $R^2 = .27$. The last ANCOVA, which compared the PCL-5 Intrusion subscale at follow-up across groups, showed that the less constrained model (i.e., Model 1C) was not a better fit to the data, $\Delta\chi^2(1, N = 43) = 2.28$, $p = .131$, than the constrained model (i.e., Model 1D), Hedges' $g = 0.43$, 95% CI [-0.14, 1.01], partial $R^2 = .09$. Overall, the results show that the treatment produced statistically significant improvements in PCL-5, STAI, and QIDS total scores when compared to usual treatment and, with the exception of the PCL-5 Intrusion subscale, these differences were large and remained relatively stable between posttreatment and follow-up.

Discussion

To our knowledge, this was the first randomized controlled trial to test the UP in a sample of injury survivors with trauma-related psychopathology. The study showed that UP significantly reduced PTSD symptom severity across time relative to usual care. This was also the case for loss of

diagnosis, with 82.3% of participants in the UP group losing their PTSD diagnosis posttreatment, which is consistent with or better than other studies of PTSD treatments, including trauma-focused treatments, such as prolonged exposure (PE) and cognitive processing therapy (CPT; Steenkamp et al., 2015). We reported that 52.9% of the overall sample maintained the loss of diagnosis across the 6 months following treatment completion, suggesting that for some participants, symptom reduction was not maintained. Although many PTSD treatment studies do not report loss of diagnosis in the medium-term follow-up period, often referred to as "remission," the rate we found is similar to those reported in large PTSD trials (Resick et al., 2017). This is notable, as loss of diagnosis is the best marker of good end-state functioning after PTSD treatment (Schnurr & Lunney, 2016).

These findings are important, as current best practice recommendations for PTSD treatment include trauma-focused interventions such as PE, CPT, and eye movement desensitization and reprocessing (Phoenix Australia–Centre for Posttraumatic Mental Health, 2020). Trauma-focused treatments are underpinned by informational processing theories that emphasize the role of a traumatic memory network in maintaining PTSD symptoms (Rothbaum & Davis, 2003). Trauma-focused interventions purport to process the trauma memory, leading to a decline in symptomatology (Brown et al., 2019). The UP does not take a trauma-processing approach and, as such, could be considered a non–trauma-focused intervention. The finding that the UP was associated with a significant reduction in PTSD symptoms provides preliminary evidence that targeting emotion avoidance and emotion dysregulation is an alternative to direct trauma

processing. Our findings are consistent with findings that non–trauma-focused therapies, such as present-centered therapy or cognitive behavioral therapy, have some support for their efficacy as PTSD treatments (Lewis et al., 2020), although there is not enough evidence to support them as first-line treatments for PTSD.

The finding that intrusive phenomena responded to the UP suggests that the UP was associated with reducing the key phenomena associated with PTSD even though it did not target the trauma memory. Specifically, the decrease in PTSD symptoms among participants in the UP group was not limited to arousal, negative cognitions, and avoidance symptoms, all symptom groups the UP has been shown to effectively target. Although the present findings broadly support the UP's emotion-focused approach, we are not able to comment on what specific mechanisms were associated with the reduction of intrusive phenomena, and this would be an important area of future research. The UP also successfully targeted comorbidity in the present study. Most participants in the trial had PTSD with comorbid MDE or an anxiety disorder. Both depression and anxiety symptoms were significantly reduced over time, with large effect sizes comparable or slightly superior to those seen for self-report measures of anxiety and depression in other main efficacy trials of the UP relative waitlist control conditions (Barlow, Farchione, Bullis, et al., 2017). Further, 15 of 22 participants in the UP condition had no reported diagnosis after treatment, compared to only three of 21 participants in the usual care group. This collectively suggests that the UP is useful for the clinical complexity often seen in trauma-exposed patients.

In addition to changes in PTSD, we found significant between-group differences regarding depression and anxiety, with UP demonstrating large effect sizes in both anxiety and depression symptom severity reduction. This was also the case for diagnosis, with 58.3% of participants in the UP group with MDE and 75.0% of those with agoraphobia losing their diagnosis by 6 months posttreatment. Although there is evidence that most trauma-focused treatments will lead to some reduction in depression and anxiety symptoms (Cusack et al., 2016), most PTSD studies do not report changes in diagnosis; thus, the impact of trauma-focused therapies on MDE and anxiety disorders is unknown.

The findings from this study should be interpreted in the context of several limitations. First, our study was limited by its small sample size and the dropout rate over time, which impacted the external validity of our findings. Our dropout rate was relatively high, which was mostly associated with participants not commencing treatment (i.e., 86% of dropouts did not begin treatment). It is possible that our proactive "screen and treat" model was associated with a high noncommencement rate because when a patient seeks out treatment themselves as opposed to being invited into treatment, they may be more motivated to engage in the treatment. Second, we acknowledge that the QIDS-SR16 had relatively low internal consistency (i.e., Cronbach's $\alpha = .78$), which may have impacted our findings. Third, although we did ask participants to rate PTSD symptoms related to the injury event, we did not evaluate prior trauma exposure, so it is not clear whether participants had preexisting trauma symptoms. Fourth, we recognize that individuals in the usual care group received fewer treatment sessions than those in the UP condition, and the degree to which this dose

difference impacted our findings is unknown. Fifth, we acknowledge that the mean PCL-5 scores in the UP group were still relatively high following treatment (Adjusted *M* = 42) even though they dropped significantly over time. This needs to be investigated further in a larger study. Finally, participants in the present study were survivors of injury, and the degree to which the findings generalize to other trauma survivors is unknown. In conclusion, the present findings study showed that the UP, a transdiagnostic, emotion-focused intervention, shows promise in treating posttraumatic psychopathology including PTSD, depression, and anxiety. Further studies are required to investigate its equivalence to current first-line treatments for PTSD, such as PE.

Open Practices Statement

This study was preregistered with the Australian New Zealand Clinical Trials Registry (ACTRN12614000823673) and can be accessed at https://www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=366627. The data and materials used in this study have not been made available on a permanent third-party archive. Consent was not obtained from participants to make their individual data publicly available; however, requests for other materials should be sent via email to the lead author at mod@unimelb.edu.au.

References

Aldao, A., Nolen-Hoeksema, S., & Schweizer, S. (2010). Emotion-regulation strategies across psychopathology: A meta-analytic review. *Clinical Psychology Review*, *30*(2), 217–237. https://doi.org/10.1016/j.cpr.2009.11.004

Asparouhov, T., & Muthén, B. (2008). *Auxiliary variables predicting missing data. Technical appendix*. Muthén & Muthén.

Asparouhov, T., & Muthén, B. (2010). *Chi-square statistics with multiple imputation (Version 2). Technical appendix*. Muthén & Muthén.

Baker, S. P., O'Neil, B., Haddon, W., & Long, W. B. (1974). The injury severity score: A method for describing patients with multiple injuries and evaluating emergency care. *Journal of Trauma and Acute Care Surgery*, *14*(2), 187–196.

Barlow, D. H., Farchione, T. J., Bullis, J. R., Gallagher, M. W., Murray-Latin, H., Sauer-Zavala, S., Bentley, K. H., Thompson-Hollands, J., Conklin, L. R., & Boswell, J. F. (2017). The unified protocol for transdiagnostic treatment of emotional disorders compared with diagnosis-specific protocols for anxiety disorders: A randomized clinical trial. *JAMA Psychiatry*, *74*(9), 875–884. https://doi.org/10.1001/jamapsychiatry.2017.2164

Barlow, D. H., Farchione, T. J., Sauer-Zavala, S., Latin, H. M., Ellard, K. K., Bullis, J. R., Bentley, K. H., Boettcher, H. T., & Cassiello-Robbins, C. (2017). *Unified protocol for transdiagnostic treatment of emotional disorders: Therapist guide* (2nd ed.). Oxford University Press.

Bentler, P. M. (2005). *EQS structural equations program manual* [Multivariate software]. http://www.econ.upf.edu/~satorra/CourseSEMVienna2010/EQSManual.pdf

Blevins, C. A., Weathers, F. W., Davis, M. T., Witte, T. K., & Domino, J. L. (2015). The Posttraumatic Stress Disorder Checklist for *DSM- 5* (PCL- 5): Development and initial psychometric evaluation. *Journal of Traumatic Stress*, *28*(6), 489–498. https://doi.org/10.1002/jts.22059

Brown, L. A., Zandberg, L. J., & Foa, E. B. (2019). Mechanisms of change in prolonged exposure therapy for PTSD: Implications for clinical practice. *Journal of Psychotherapy Integration*, *29*(1), 6–14. https://doi.org/10.1037/int0000109

Brown, T. A., Chorpita, B. F., & Barlow, D. H. (1998). Structural relationships among dimensions of the *DSM-IV* anxiety and mood disorders and dimensions of negative affect, positive affect, and autonomic arousal. *Journal of Abnormal Psychology*, *107*(2), 179–192. https://doi.org/10.1037/0021-843X.107.2.179

Bryant, R. A., O'Donnell, M. L., Creamer, M., McFarlane, A. C., Clark, C. R., & Silove, D. (2010). The psychiatric sequelae of traumatic injury. *American Journal of Psychiatry*, *167*(3), 312–320. https://doi.org/10.1176/appi.ajp.2009.09050617

Cohen, J., Cohen, P., West, S. G., & Aiken, L. S. (2013). *Applied multiple regression/correlation analysis for the behavioral sciences* (3rd ed.). Lawrence Erlbaum & Associates.

Cusack, K., Jonas, D. E., Forneris, C. A., Wines, C., Sonis, J., Middleton, J. C., Feltner, C., Brownley, K. A., Olmsted, K. R., & Greenblatt, A. (2016). Psychological treatments for adults with posttraumatic stress disorder: A systematic review and meta-analysis. *Clinical Psychology Review*, *43*, 128–141. http://doi.org/10.1016/j.cpr.2015.10.003

Eekhout, I., Enders, C. K., Twisk, J. W., De Boer, M. R., De Vet, H. C., & Heymans, M. W. (2015). Including auxiliary item information in longitudinal data analyses improved handling missing questionnaire outcome data. *Journal of Clinical Epidemiology*, *68*(6), 637–645. https://doi.org/10.1016/j.jclinepi.2015.01.012

Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy*, *38*(4), 319–345.

Enders, C. K. (2010). *Applied missing data analysis*. Guilford Press.

Fan, W., & Hancock, G. R. (2012). Robust means modeling: An alternative for hypothesis testing of independent means under variance heterogeneity and nonnormality. *Journal of Educational and Behavioral Statistics*, *37*(1), 137–156. https://doi.org/10.3102/1076998610396897

Farchione, T. J., Fairholme, C. P., Ellard, K. K., Boisseau, C. L., Thompson-Hollands, J., Carl, J. R., Gallagher, M. W., & Barlow, D. H. (2012). Unified protocol for transdiagnostic treatment of emotional disorders: A randomized controlled trial. *Behavior therapy*, *43*(3), 666–678. https://doi.org/10.1016/j.beth.2012.01.001

Gallagher, M. W. (2017). Transdiagnostic mechanisms of change and cognitive–behavioral treatments for PTSD. *Current Opinion in Psychology*, *14*, 90–95. https://doi.org/10.1016/j.copsyc.2016.12.002

Graham, J. W. (2003). Adding missing-data-relevant variables to FIML-based structural equation models. *Structural Equation Modeling*, *10*(1), 80–100. https://doi.org/10.1207/S15328007SEM1001_4

Green, S. B., & Thompson, M. S. (2012). A flexible structural equation modeling approach for analyzing means. In R. H. Hoyle (Ed.), *Handbook of structural equation modeling* (pp. 393–416). Guilford Press.

Gutner, C. A., Galovski, T., Bovin, M. J., & Schnurr, P. P. (2016). Emergence of transdiagnostic treatments for PTSD and posttraumatic distress. *Current Psychiatry Reports*, *18*(10), 95. https://doi.org/10.1007/s11920-016-0734-x

Gutner, C. A., & Presseau, C. (2019). Dealing with complexity and comorbidity: Opportunity for transdiagnostic treatment for PTSD. *Current Treatment Options in Psychiatry*, *6*(2), 119–131. https://doi.org/10.1007/s40501-019-00170-2

Horesh, D., Qian, M., Freedman, S., & Shalev, A. (2017). Differential effect of exposure- based therapy and cognitive therapy on post- traumatic stress disorder symptom clusters: A randomized controlled trial. *Psychology and Psychotherapy: Theory, Research, and Practice*, *90*(2), 235–243. https://doi.org/10.1111/papt.12103

Iyadurai, L., Visser, R. M., Lau-Zhu, A., Porcheret, K., Horsch, A., Holmes, E. A., & James, E. L. (2019). Intrusive memories of trauma: A target for research bridging cognitive science and its clinical application. *Clinical Psychology Review*, *69*, 67–82. https://doi.org/10.1016/j.cpr.2018.08.005

Kotov, R., Gamez, W., Schmidt, F., & Watson, D. (2010). Linking "big" personality traits to anxiety, depressive, and substance use disorders: A meta-analysis. *Psychological Bulletin*, *136*(5), 768–821. https://doi.org/10.1037/a0020327

Lewis, C., Roberts, N. P., Andrew, M., Starling, E., & Bisson, J. I. (2020). Psychological therapies for post-traumatic stress disorder in adults: Systematic review and meta-analysis. *European Journal of Psychotraumatology*, *11*(1), 1729633. https://doi.org/10.1080/20008198.2020.1729633

Muthén, L. K., & Muthén, B. O. (1998-2019). *Mplus* (Version 8.4) [Computer software]. Muthén & Muthén.

O'Donnell, M. L., Alkemade, N., Creamer, M. C., McFarlane, A. C., Silove, D., Bryant, R. A., & Forbes, D. (2016). The long-term psychiatric sequelae of severe injury: A 6-year follow-up study. *The Journal of Clinical Psychiatry*, *77*(4), 473–479. https://doi.org/10.4088/JCP.14m09721

O'Donnell, M. L., Creamer, M. C., Parslow, R., Elliott, P., Holmes, A. C., Ellen, S., Judson, R., McFarlane, A. C., Silove, D., & Bryant, R. A. (2008). A predictive screening index for

posttraumatic stress disorder and depression following traumatic injury. *Journal of Consulting and Clinical Psychology*, *76*(6), 923–932. https://doi.org/10.1037/a0012918

O'Donnell, M. L., Lau, W., Tipping, S., Holmes, A. C., Ellen, S., Judson, R., Varker, T., Elliot, P., Bryant, R. A., & Creamer, M. C. (2012). Stepped early psychological intervention for posttraumatic stress disorder, other anxiety disorders, and depression following serious injury. *Journal of Traumatic Stress*, *25*(2), 125–133. https://doi.org/10.1002/jts.21677

Paulus, D. J., Gallagher, M. W., Bartlett, B. A., Tran, J., & Vujanovic, A. A. (2018). The unique and interactive effects of anxiety sensitivity and emotion dysregulation in relation to posttraumatic stress, depressive, and anxiety symptoms among trauma-exposed firefighters. *Comprehensive Psychiatry*, *84*, 54–61. https://doi.org/10.1016/j.comppsych.2018.03.012

Phelps, A., Steel, Z., Metcalf, O., Alkemade, N., Kerr, K., O'Donnell, M., Nursey, J., Cooper, J., Howard, A., & Armstrong, R. (2018). Key patterns and predictors of response to treatment for military veterans with post-traumatic stress disorder: A growth mixture modelling approach. *Psychological Medicine*, *48*(1), 95–103. https://doi.org/10.1017/S0033291717001404

Phoenix Australia–Centre for Posttraumatic Mental Health. (2020). *Australian guidelines for the prevention and treatment of acute stress disorder, posttraumatic stress disorder, and complex PTSD*. https://www.phoenixaustralia.org/australian-guidelines-for-ptsd/

Resick, P. A., Wachen, J. S., Dondanville, K. A., Pruiksma, K. E., Yarvis, J. S., Peterson, A. L., Mintz, J., & and the STRONG STAR Consortium. (2017). Effect of group vs. individual cognitive processing therapy in active-duty military seeking treatment for posttraumatic stress

disorder: A randomized clinical trial. *JAMA Psychiatry*, *74*(1), 28–36. https://doi.org/10.1001/jamapsychiatry.2016.2729

Robitzsch, A., & Grund, S. (2020). *miceadds: Some additional multiple imputation functions, especially for 'mice'. R package (Version 3.9–2).* https://CRAN.Rproject.org/package=miceadds

Rothbaum, B. O., & Davis, M. (2003). Applying learning principles to the treatment of post- trauma reactions. *Annals of the New York Academy of Sciences*, *1008*(1), 112–121. https://doi.org/10.1196/annals.1301.012

Rubin, D. B. (1987). *Multiple imputation for nonresponse in surveys*. Wiley.

Rush, A. J., Trivedi, M. H., Ibrahim, H. M., Carmody, T. J., Arnow, B., Klein, D. N., Markowitz, J. C., Ninan, P. T., Kornstein, S., & Manber, R. (2003). The 16-item Quick Inventory of Depressive Symptomatology (QIDS), Clinician Rating (QIDS-C), and Self-Report (QIDS-SR): A psychometric evaluation in patients with chronic major depression. *Biological Psychiatry*, *54*(5), 573–583. https://doi.org/10.1016/s0006-3223(02)01866-8

Sakiris, N., & Berle, D. (2019). A systematic review and meta-analysis of the unified protocol as a transdiagnostic emotion regulation based intervention. *Clinical Psychology Review*, *72*, 101751. https://doi.org/10.1016/j.cpr.2019.101751

Satorra, A., & Bentler, P. M. (2001). A scaled difference chi-square test statistic for moment structure analysis. *Psychometrika*, *66*(4), 507–514.

Schnurr, P., & Lunney, C. (2016). Symptom benchmarks of improved quality of life in PTSD. *Depression and Anxiety*, *33*(3), 247–255. https://doi.org/10.1002/da.22477

Sheehan, D. V., Lecrubier, Y., Sheehan, K. H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., & Dunbar, G. C. (1998). The Mini-International Neuropsychiatric Interview (MINI): The development and validation of a structured diagnostic psychiatric interview for *DSM-IV* and *ICD-10*. *Journal of Clinical Psychiatry*, *59*(Suppl20), 22–33.

Sheppes, G., Suri, G., & Gross, J. J. (2015). Emotion regulation and psychopathology. *Annual Review of Clinical Psychology*, *11*(1), 379–405. https://doi.org/10.1146/annurev-clinpsy-032814-112739

Sloan, E., Hall, K., Moulding, R., Bryce, S., Mildred, H., & Staiger, P. K. (2017). Emotion regulation as a transdiagnostic treatment construct across anxiety, depression, substance, eating, and borderline personality disorders: A systematic review. *Clinical Psychology Review*, *57*, 141–163. https://doi.org/10.1016/j.cpr.2017.09.002

Spielberger, C. D. (1983). *State–Trait Anxiety Inventory for adults.* https://doi.org/10.1037/t06496-000

Spielberger, C. D. (1989). *State–Trait Anxiety Inventory: Bibliography* (2nd ed.). Consulting Psychologists Press.

Steenkamp, M. M., Litz, B. T., Hoge, C. W., & Marmar, C. R. (2015). Psychotherapy for military-related PTSD: A review of randomized clinical trials. *JAMA*, *314*(5), 489–500. https://doi.org/10.1001/jama.2015.8370

Stein, N. R., Dickstein, B. D., Schuster, J., Litz, B. T., & Resick, P. A. (2012). Trajectories of response to treatment for posttraumatic stress disorder. *Behavior Therapy*, *43*(4), 790–800. https://doi.org/10.1016/j.beth.2012.04.003

Suárez, L. M., Bennett, S. M., Goldstein, C. R., & Barlow, D. H. (2009). Understanding anxiety disorders from a" triple vulnerability" framework. In M. M. Antony & M. B. Stein (Eds.), *Oxford handbook of anxiety and related Disorders* (pp. 152–172). https://doi.org/10.1093/oxfordhb/9780195307030.013.0013

Tarrier, N., Sommerfield, C., Pilgrim, H., & Faragher, B. (2000). Factors associated with the outcome of cognitive–behavioural treatment of chronic post-traumatic stress disorder. *Behaviour Research and Therapy*, *38*(2), 191–202. https://doi.org/10.1016/S0005-7967(99)00030-3

Trivedi, M. H., Rush, A., Ibrahim, H., Carmody, T., Biggs, M., Suppes, T., Crismon, M. L., Shores-Wilson, K., Toprac, M., & Dennehy, E. (2004). The Inventory of Depressive Symptomatology, Clinician Rating (IDS-C) and Self-Report (IDS-SR), and the Quick Inventory of Depressive Symptomatology, Clinician Rating (QIDS-C) and Self-Report (QIDS-SR) in public sector patients with mood disorders: A psychometric evaluation. *Psychological Medicine*, *34*(1), 73–82. https://doi.org/10.1017/S0033291703001107

Varkovitzky, R. L., Sherrill, A. M., & Reger, G. M. (2017). Effectiveness of the unified protocol for transdiagnostic treatment of emotional disorders among veterans with posttraumatic stress disorder: A pilot study. *Behavior Modification*, *42*(2), 210–230. https://doi.org/10.1177/0145445517724539

Table 1

Baseline Demographic and Diagnostic Characteristics

Characteristic	Unified Protocol (*n* = 22)			Usual care (*n* = 21)			Statistical test	*p*
	M	*SD*	*n*	*M*	*SD*	*n*		
Age (years)	37.36	13.89		41.05	13.59		$t(41) = -0.88$	.385
Female sex			8			7	$\chi^2(1, N = 43) = 0.043$	.835
Completed high school			13			11	$\chi^2(1, N = 43) = 0.389$	.533
Injury severity	11.20	9.64		10.74	6.56		$t(32) = 1.66$	.869

score

PCL-5 score	62.81	14.08		61.33	13.13	$W(1, N = 43) = 0.12$	.724
STAI score	55.67	12.33		57.13	8.88	$W(1, N = 43) = 0.20$	.654
QIDS score	14.94	4.83		16.02	3.55	$W(1, N = 43) = 0.68$	.409
PCL-5 Intrusion score	14.65	4.60		13.14	4.50	$W(1, N = 43) = 3.22$	.072
PTSD diagnosis			17			11	$\chi^2(1, N = 43) = 2.93$	.087
Subclinical PTSD			1			1	-	
Agoraphobia			9			10	$\chi^2(1, N = 43) = 1.96$	.658
Major depressive			12			18	$\chi^2(1, N = 43) = 4.95$	.026

disorder				
Panic disorder	4	6	$\chi^2(1, N = 43) =$ .650	.420
Social anxiety disorder	5	5	-	
Generalized anxiety disorder	3	5	$\chi^2(1, N = 43) =$ .734	.391
Travel phobia	4	1	$\chi^2(1, N = 43) =$ 1.883	.170
Alcohol use disorder	0	0	-	
Any diagnosis	22	21	-	
Comorbid	10	14	$\chi^2(1, N = 43) =$	.161

Notes. PTSD = posttraumatic stress disorder; PCL-5 = Posttraumatic Stress Disorder checklist for *DSM-5*; STAI = State Trait Anxiety Inventory; QIDS = Quick Inventory of Depressive Symptomatology; *W* = Wald test.

[a]Includes participants with a primary diagnosis of PTSD who also has one or more additional diagnoses.

Table 2

Diagnosis Frequencies at Intake, Posttreatment, and Follow-Up, with McNemar's Tests for Loss of Diagnosis

	Diagnosis count			Intake vs. posttreatment				Intake vs. follow-up			
Variable	Intake	Posttreatment	Follow-up	*F*	df_n	df_d	*p*	*F*	df_n	df_d	*p*
				Unified Protocol (*n* = 22)							
PTSD	17	3	8	11.88	1	114,157.92	< .001	6.53	1	20,223.78	.011
Depression	12	5	5	5.44	1	9,683.20	.020	5.62	1	8,720.00	.018
Agoraphobia	9	1	3	5.31	1	29,422.71	.021	1.61	1	5,872.57	.205
GAD	3[a]	1[a]	1[a]								

SAD	5[a]	1[a]	2[a]								
Panic disorder	4[a]	0[a]	0[a]								
Travel phobia	4[a]	1[a]	2[a]								
No diagnosis	0	15	12	9.62	1	14,970.05	.002	5.41	1	28,380.31	.020
Usual care (n = 21)											
PTSD	11	12	10	0.60	1	2,044.97	.438	0.30	1	2,142.20	.584
Depression	18	14	8	1.62	1	7,612.05	.203	5.07	1	6,280.35	.024
Agoraphobia	10	5	13	1.29	1	1,607.20	.256	0.67	1	1,472.55	.412
GAD	5[a]	2[a]	2[a]								
SAD	5[a]	4[a]	6[a]								

Panic disorder	6[a]	4[a]	5[a]									
Travel phobia	1[a]	0[a]	3[a]									
No diagnosis	0	3	3	0.13	1	2,665,068.14	.71	0.5	1	39,151.09	.45	

Notes. Diagnoses were assessed using the Mini International Neuropsychiatric Interview–6. McNemar's test results were pooled over the 100 imputed data sets to generate the D_2 statistic, which is evaluated against an *F* distribution (Enders, 2010). PTSD = posttraumatic stress disorder; GAD = generalized anxiety disorder; SAD = social anxiety disorder; df_n = numerator degrees of freedom; df_d = denominator degrees of freedom.

[a]Raw pairwise counts. McNemar's tests were not conducted due to small sample sizes.

Table 3

Effect Sizes and Group Means for Comparisons Among Group Intercepts for Symptom Scale Analyses of Covariance

Model	UP adjusted mean[a]	UC adjusted	Hedges' *g*	95% CI[b]	*p*[c]	Partial R^{2d}	Cohen's f^{2e}

		mean					
PCL-5							
1C: Posttreatment	42.47	60.17	1.27	[0.72, 1.83]	< .001	.40	0.66
2C: Follow-up	41.69	56.97	1.07	[0.39, 1.75]	.009	.22	0.28
STAI							
3C: Posttreatment	43.75	56.79	1.20	[0.72, 1.68]	< .001	.43	0.75
4C: Follow-up	42.90	59.55	1.40	[0.84, 1.96]	< .001	.35	0.54
QIDS							
5C: Posttreatment	9.37	15.63	1.40	[0.83, 1.97]	< .001	.48	0.92
6C: Follow-up	8.20	16.27	1.86	[1.33, 2.38]	< .001	.54	1.17

PCL-5(I)

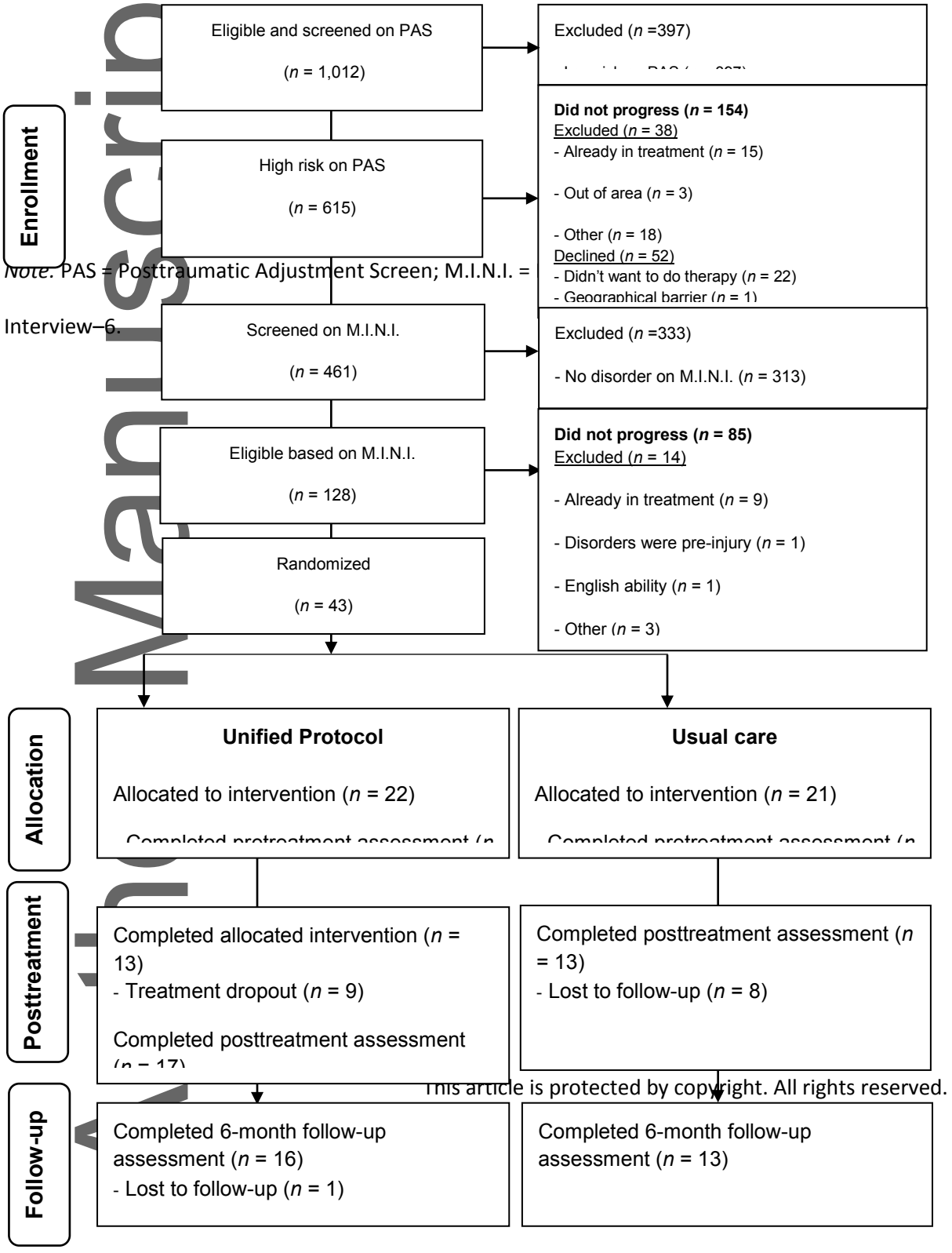
7C: Posttreatment	10.26	13.56	0.74[f]	[0.13, 1.35][f]	.046	.27	.37
8C: Follow-up	10.90	12.92	0.43	[-0.14, 1.01]	.215	.09	.10

Note. PCL-5 = Posttraumatic Stress Disorder Checklist for *DSM*-5; STAI = State Trait Anxiety Inventory; QIDS = Quick Inventory of Depressive Symptomatology; PCL-5(I) = PCL-5 Intrusion subscale.

[a]Represents the adjusted mean on the postintervention and follow-up measure (i.e., PCL-5, STAI, QIDS, or PCL-5(I)) for participants who scored at the mean on the pretest measure. [b]Symmetric bootstrapped confidence interval. [c]Two-tailed probability of the *z* test for Hedges' *g* or Glass' delta. [d]Estimated using Equation 24.9 in Green and Thompson (2012, p. 401). [e]Calculated using Equation 3.7.2 from Cohen et al. (2013, p. 94). [f]Effect size calculated as Glass' delta.

Figure 1

CONSORT Diagram of Participant Flow Through the Trial



Note. PAS = Posttraumatic Adjustment Screen; M.I.N.I. = Interview–6.