Enhanced Skills Training in Affective and Interpersonal Regulation versus Treatment as Usual for ICD-11 Complex PTSD: A Pilot Randomised Controlled Trial (The RESTORE Trial)

Thanos Karatzias[a, b]   Mark Shevlin[c]   Marylène Cloitre[d, e]   Walter Busuttil[f]
Katherine Graham[f]   Laura Hendrikx[f]   Philip Hyland[g]   Natasha Biscoe[f]
Dominic Murphy[d, h]

[a]School of Health and Social Care, Edinburgh Napier University, Edinburgh, UK; [b]NHS Lothian Rivers Centre for Traumatic Stress, Edinburgh, UK; [c]School of Psychology, Ulster University, Northern Ireland, UK; [d]National Center for PTSD Dissemination and Training Division, VA Palo Alto Health Care System, Palo Alto, CA, USA; [e]Department of Psychiatry and Behavioural Sciences, Stanford University, Stanford, CA, USA; [f]Research Department, Combat Stress, Surrey, UK; [g]Department of Psychology, Maynooth University, Kildare, Ireland; [h]King's Centre for Military Research, Kings College London, London, UK

Abstract

Introduction: Complex PTSD (CPTSD) is a relatively new condition in ICD-11. This pilot randomised controlled trial aimed to compare a four-module intervention developed to target all symptoms of ICD-11 CPTSD, namely Enhanced Skills in Affective and Interpersonal Regulation (ESTAIR) with treatment as usual (TAU). The purpose of the study was to assess feasibility, safety, acceptability, and preliminary outcomes at the end of treatment and 3-month follow-up. ***Methods:*** A total of $N = 56$ eligible veterans with CPTSD were randomised to either ESTAIR ($n = 28$) or TAU ($n = 28$). Linear mixed models were conducted to assess CPTSD severity, the primary outcome, as measured by the International Trauma Questionnaire (ITQ). ***Results:*** Treatment dropout in ESTAIR and TAU was low and equivalent (18% vs. 11%; χ^2 (1) = 1.19, $p = 0.275$), and study retention was high, supporting the feasibility of the study. No

serious adverse effects and very few adverse effects occurred, none of which were deemed related to the study. ESTAIR provided significantly greater reduction in CPTSD severity across time for ITQ PTSD ($p < 0.001$) and DSO ($p < 0.001$) symptoms. CPTSD pre-to-post effect sizes for ESTAIR were large (PTSD $d = 1.78$; DSO $d = 2.00$). Remission of probable CPTSD diagnosis at post-treatment was substantially greater in ESTAIR compared to TAU with only 13.6% versus 84% ($p < 0.001$) retaining the diagnosis. ***Conclusion:*** A trial of ESTAIR versus TAU for the treatment of ICD-11 CPTSD indicates the potential efficacy of ESTAIR as well as its feasibility, safety, and acceptability.

© 2024 The Author(s).
Published by S. Karger AG, Basel

Introduction

The 11th version of the *International Classification of Diseases* (ICD-11) [1] has included two trauma-based disorders; PTSD and Complex PTSD. The description of

Correspondence to:
Thanos Karatzias, t.karatzias@napier.ac.uk

Karger
⊕ OPEN ACCESS

PTSD in ICD-11 is simpler than that provided within the DSM-5. In contrast to the 20 symptoms spread across four symptom clusters in DSM-5, ICD-11 PTSD includes six "core" symptoms across three clusters, each of which is directly related to one's traumatic exposure. These include re-experiencing in the here and now, avoidance, and a sense of current threat. Diagnosis of ICD-11 PTSD requires the presence of one symptom per cluster, plus evidence of functional impairment. Complex PTSD (CPTSD) is a broader diagnosis that includes the core PTSD symptoms plus an additional set of three symptom clusters – collectively referred to as "disturbances in self-organisation" (DSO) – intended to capture pervasive psychological disturbances associated most typically with chronic and multiple types of traumatic exposures. The symptoms clusters are affective (hyper-activation and hypo-activation) dysregulation (AD), negative self-concept (NSC), and disturbances in relationships (DR). A CPTSD diagnosis requires that the PTSD criteria be met in addition to endorsement of DSO symptoms plus impairments in functioning associated with these symptoms.

Evidence from clinical samples [2] as well as population-based samples [3, 4] suggests that CPTSD is a more common condition than PTSD. Although comparisons between general populations and military populations are lacking, a recently completed cohort study (n = 178) of a veteran help-seeking population found that 56% met diagnostic criteria for CPTSD versus 14% who met criteria for PTSD [5]. A larger study with 599 veterans in Denmark found that 13.0% met ICD-11 criteria for PTSD and 31.4% for CPTSD [6]. Considering how common CPTSD is in military and general population samples, it is now imperative to identify effective treatments to aid recovery from this debilitating condition.

One recent meta-analytic review [7] suggested that existing interventions commonly used for PTSD, such as cognitive-behavioural therapy (CBT) or eye movement desensitisation and reprocessing (EMDR), can provide less benefit for CPTSD symptoms if there is history of childhood trauma. However, more recent evidence, e.g., [8] suggests that exposure therapies can be useful for both PTSD and CPTSD. Emerging evidence suggests that other interventions might also be effective for some CPTSD symptoms. In a pilot study exploring the effectiveness of on-line delivered mindfulness approaches in young adults with CPTSD, Dumarkaite and colleagues [9] found that mindfulness therapy can reduce symptoms of NSC and disturbed relationships but not PTSD and affect dysregulation symptoms. These studies have some limitations including that they have included people without the full CPTSD diagnosis and people who did not have functional impairment. Hence, there is need for further work on the effectiveness of existing therapies for CPTSD.

Another recent meta-analysis reviewed studies specific to populations that had experienced complex trauma (e.g., military, childhood abuse, refugees) [10]. This work indicated that interventions with a multi-modular (i.e., separate modules that are flexible in order targeting specific symptom clusters) format which included both skills-based and trauma-focused strategies were the most promising interventions for the affect dysregulation and disturbed relationships symptom clusters of CPTSD. Although a flexibly applied multi-modular treatment approach has been applied to other mental health conditions [11], it is new to the trauma field signalling a treatment innovation which has been suggested as a promising area of enquiry for CPTSD [4]. Enhanced Skills Training in Affective and Interpersonal Regulation (ESTAIR) has been designed as a flexibly sequenced modular intervention, guided by measurement-based assessment of symptoms and patient identified needs and preferences [12]. ESTAIR involves 25 sessions; a formulation session plus four modules of 6 sessions on average, each addressing the different symptom clusters of CPTSD.

A briefer multi-modular version of ESTAIR with a fixed sequence, Skills Training in Affective and Interpersonal Regulation coupled with Narrative Therapy (STAIR-NT) has been evaluated in three randomised control trials (RCTs) with good evidence of effect. When compared with minimal attention wait-list, significant improvement in affect regulation problems, interpersonal skills deficits, and DSM-PTSD symptoms were maintained at 3 and 9 months [13]. In a component analysis trial, full DSM-PTSD remission and greater improvement in interpersonal problems and lower attrition rates were more likely to be achieved in STAIR-NT compared to both narrative therapy without skills training and a skills focused intervention without narrative therapy in individuals with DSM-PTSD related to childhood abuse [14]. STAIR-NT was equivalent to an extended (16 sessions) form of prolonged exposure (PE) for DSM-PTSD related to childhood abuse [15]; however, a follow-up moderator analysis found that higher severity of childhood sexual abuse was a predictor of worse treatment outcome in both PE and intensified PE conditions, but not for STAIR-NT [16]. STAIR-NT has shown preliminary positive findings in non-western cultural contexts for ICD-11 CPTSD. In a recent open pilot investigation of STAIR-NT in Japan (n = 10), it was found that among the seven completers, six at post-treatment and all at follow-up, none met

requirements for a CPTSD diagnosis [17]. While promising, STAIR-NT does not address the self-concept cluster of DSO, which is a core component of CPTSD and highly relevant in the context of polytraumatisation [18]. As opposed to STAIR-NT, ESTAIR addresses all symptom clusters of CPTSD.

No previous study has explored the feasibility of offering a modular therapy that targets all symptom clusters of CPTSD in veterans. The RESTORE trial aimed to address this gap in the literature. RESTORE was designed to assess the feasibility, safety, and acceptability of a new treatment for CPTSD (i.e., ESTAIR) as well as preliminary outcomes for ESTAIR as compared to treatment as usual (TAU). Feasibility was assessed in terms of (1) satisfactory participant enrolment, (2) treatment dropout, and (3) study retention (data collection) through all phases of the study. Safety was assessed in terms of the occurrence of serious adverse events (SAEs) and adverse events (AEs). Acceptability was characterised as participant interest in the ESTAIR protocol and treatment targets (PTSD and DSO) as assessed by post-treatment interviews. The primary treatment outcome was CPTSD severity defined by its primary components of PTSD and DSO symptoms. Secondary outcomes included depression, anxiety, somatic symptoms, and alcohol misuse.

Method

Study Design

This pilot RCT of the ESTAIR intervention with a 3-month follow-up was completed in collaboration with a national United Kingdom charity which offers clinical services to military personnel with mental health problems including PTSD and CPTSD. The study received ethical approval from Edinburgh Napier University (Project 1723177) and was preregistered with ClinicalTrials.Gov (NCT04752072). The study was planned and implemented in accordance with the Consolidated Standards of Reporting Trials (CONSORT) cluster trial extension [19].

This study was designed to provide information that would serve as the foundation for implementing a larger trial characterised by similar design parameters (e.g., allocation ratio, blind assessment, multiple sites). The planned randomised pilot study was a 28-month feasibility/pilot of a single site, single (rater) blind trial of ESTAIR (psychological intervention) versus TAU alone for the treatment of CPTSD using the International Trauma Questionnaire (ITQ) [20] as the primary outcome. At present, there are no recommended treatments for CPTSD, and thus TAU was chosen as a control condition as this provided a fair comparison with routine clinical practice.

Participants

Potential participants were drawn from those referred to the charity's treatment centres who had completed a mental health assessment as part of this referral and had registered for treatment.

The ITQ [20] was used to identify those with a probable diagnosis of ICD-11 CPTSD. All new referrals were discussed at a weekly case management meeting. The following procedure was implemented to recruit participants for the study. Firstly, the research assistant attended the case management meeting to screen veterans for eligibility for the study. If eligible, potential participants were then approached to take part by the research assistant by letter and were sent a participant information sheet and consent form. This invitation was followed up by a telephone call by the research assistant to discuss any questions about the study and participants' willingness to participate. Those willing to participate were then asked to attend a one-to-one or online meeting with the research assistant. At this meeting, they were asked again if they had any questions about the study, signed the consent form, and completed pre-treatment measures. All forms could also be returned via mail. Following this, participants were randomised to one of the two treatment conditions. The ITQ was administered at the end of every module for those in the ESTAIR condition; if the person was CPTSD diagnosis free in the ESTAIR condition then they were offered a full post-treatment assessment. Those in the ESTAIR condition who were not diagnosis free were offered the following module. Those randomised to the TAU group were offered the standard treatment and they completed the ITQ at pre-, post-treatment, and 3-month follow-up. Subsequent input from the service following completion of the trial was offered, as required, and as per normal service standards.

Participants in both groups were asked to complete all outcome measures at baseline (week 0), at post-treatment (week 25) and then again after a 12-week follow-up (week 37). The International Trauma Questionnaire (ITQ: [20]) was also completed by the ESTAIR group at the end of every module. In addition, data were recorded on retention and rates of non-attendance. The research assistant was masked to group allocation to demonstrate to future funders this is achievable in a future trial.

Inclusion criteria were adults (18 years or older) in the caseload of a national UK charity, armed forces veteran, help-seeking for trauma-related psychological distress, meeting diagnostic criteria for CPTSD as measured by the ITQ, proficiency in English language and signed informed consent provided. Exclusion criteria were presence of severe psychotic disorder (defined by previous clinical diagnosis), current alcohol or drug use disorder (assessed at clinical interview), serious cognitive impairment (assessed at clinical interview) or planned concurrent additional treatment.

Participants were free to withdraw from the study at any point, without giving any reason and without their legal rights or usual care being affected. Investigators were also able to withdraw participants if they deemed their continuation to be harmful. The trial management group reviewed all instances of adverse events, whether or not they were judged to be attributable to the trial or interventions, and, based on this information, determine whether the participant should have been withdrawn. Non-identifiable data from participants who have been withdrawn were used to assess the feasibility of the study.

Randomisation and Masking

Block randomisation was used to ensure balanced assignment to the intervention and comparison group. Randomly permuted blocks (based on 12 blocks with 4 subjects per block) were used to reduce the risk of predicting group assignment and ensure equal groups sizes. Randomised lists were generated using an online,

closed-source, web service (http://www.randomization.com/). Randomisation was completed by an author (M.S.) who was not otherwise involved in the implementation of the treatment.

Treatment Conditions
Enhanced Skills Training in Affective and Interpersonal Regulation

ESTAIR [12] consisted of up to 25 sessions which included an initial formulation session and then 4 modules addressing the symptoms of CPTSD. The four modules, in order of delivery, focused on AD (6 sessions), DR (6 sessions), NSC (5 sessions), and PTSD (7 sessions). The AD module focuses on identifying and labelling feelings, emotion management, distress tolerance, acceptance of feelings, and experiencing positive emotions. The DR module focuses on exploration and revision of maladaptive schemas; effective assertiveness; awareness of social context; and flexibility in interpersonal expectations and behaviours that are displayed in social interactions. The NSC module focuses on how to stay in the present moment and combat dissociation; self-compassion and mindfulness skills; and challenging thinking patterns and developing a balanced view of self. The PTSD module focuses on emotional processing of trauma memories through verbal narration and cognitive reappraisal and targets re-experiencing, avoidance, and hyperarousal symptoms.

Therapist Training and Adherence. ESTAIR was delivered by a CBT therapist (Masters' level). The therapist received a 2-day workshop on ESTAIR followed by biweekly supervision by one of two experts in the treatment (MC, TK) depending on the module. A selection of treatment sessions was video-taped and assessed for treatment integrity and fidelity. A total of 12 randomly selected sessions (three per module) were scored for fidelity by an assessor independent to this trial who was an experienced CBT therapist and trained in adherence rating of ESTAIR using a fidelity scale that was developed alongside the ESTAIR protocol. Session goals were assessed using four categories (implemented, partially implemented, not implemented, or not applicable). Overall, it was concluded that ESTAIR was delivered to the protocol with all sessions being successfully delivered and all components fully implemented. Defined completers were those who attended at least 80% of treatment (20 sessions) and received at least one session per module.

Treatment as Usual

TAU typically consisted of receiving a mental health assessment by a trained mental health professional (e.g., psychologist, psychiatrist) followed by offering a treatment package that includes psycho-education, symptom-management, and/or active monitoring. TAU interventions were provided by trained mental health professionals. Of the $n = 28$ randomised to TAU, $n = 23$ received individual or group intervention and $n = 5$ received no active intervention, but they received active monitoring. Of the 23 who received individual or group therapy, one person received three EMDR sessions. No other participant received trauma-focussed therapy. TAU interventions were recorded for all participants.

Measures

Feasibility related to satisfactory participant enrolment was defined as achieving the target goal of randomising $n = 60$ veterans over a 2-year period. Treatment dropout for ESTAIR was defined as leaving treatment before all four modules were completed (80% of treatment) and for TAU leaving before 24 weeks of treatment had been completed. Study retention (data collection) was defined as the percent of randomised participants that completed posttreatment and follow-up assessments. Safety was defined as presence of serious adverse events (SAEs) and adverse events (AEs) as measured by the Adverse Events Questionnaire (AEQ: [21]). Acceptability was characterised via post-treatment interviews using qualitative data analytic strategies described below regarding participant interest in the ESTAIR protocol and treatment targets (PTSD and DSO). The primary treatment outcome was CPTSD severity as assessed by its two components, post-traumatic stress disorder (PTSD) and disturbances in self-organisation (DSO) symptoms. In addition to our primary outcome measure (ITQ [20]), we included several exploratory clinical outcomes to enable designing and planning a future definitive clinical trial. The following measures were used.

Life Events Checklist

The life events checklist (LEC) [22] is a 17-item self-report measure for potentially traumatic events in the respondent's lifetime. The LEC assesses exposure to 16 events plus one item assessing any other extraordinarily stressful event. The respondent checks whether they (1) directly experienced, (2) witnessed, (3) learned about, (4) are not sure, and (5) does not apply to them. The LEC has demonstrated adequate reliability and validity.

International Trauma Questionnaire

The International Trauma Questionnaire (ITQ) [20] includes 6 items that measure the 3 symptom clusters of PTSD. There are also 3 questions that assess functional impairment related to the PTSD and DSO symptoms, separately. The items are scored on a 5-point Likert scale ranging from 0 (not at all) to 4 (extremely), indicating how much a symptom has bothered the respondent in the past month. The PTSD and DSO item sets are summed to reflect symptom severity with a range of possible scores for both from 0 to 24. The Likert scores can also be recoded into binary variables with scores greater than or equal to 2 representing endorsement. There have been extensive psychometric evaluations of the ITQ that report evidence for the construct validity across different samples and cultures [23], and high levels of internal consistency [24] and test-retest reliability [25].

Patient Health Questionnaire-9 (PHQ-9)

Respondents indicate how often they have been bothered by each symptom over the last 2 weeks using a four-point Likert scale ranging from 0 (not at all) to 3 (nearly every day). Possible scores range from 0 to 27, with higher scores indicative of higher levels of depression. To identify participants likely to meet the criteria for depressive disorder, a cut-off score of 15 was used as it has been reported that this score produces specificity of 0.96 [26].

Generalised Anxiety Disorder 7-Item Scale

Respondents indicate how often they have been bothered by each symptom over the last 2 weeks on a four-point Likert scale (0 = not at all, to 3 = nearly every day). Possible scores range from 0 to 21, with higher scores indicative of higher levels of anxiety. The

generalised anxiety disorder 7-item scale (GAD-7) has been shown to be a reliable and valid measure in multiple studies. To identify participants likely to meet the criteria for generalised anxiety a cut-off score ore of 15 was used as it has been reported that this score produces specificity of 0.96 [27].

Alcohol Use Disorders Identification Test

Probable alcohol use disorder (AUDs) [28] was measured using the AUDIT-C, a brief self-report measure comprised of the first three questions of the alcohol use disorders identification test. The clinical utility of the AUDIT-C has been demonstrated in multiple samples including the general population, military veterans, and hospitalised patients. Scores on the AUDIT-C range from 0 to 12, and scores ≥4 effectively capture a DSM-5 diagnosis of AUD.

Patient Health Questionnaire-15 (PHQ-15)

The scale includes the most common DSM-IV somatization disorder somatic symptoms. Participants were required to rate the severity of symptoms as 0 ("not bothered at all"), 1 ("bothered a little"), or 2 ("bothered a lot"). Responses are coded as 0 ("not at all"), 1 ("several days"), or 2 ("more than half the days" or "nearly every day") to produce total scores ranging from 0 to 30 and scores of ≥5, ≥10, ≥15 represent mild, moderate, and severe levels of somatization. The reliability and validity of the PHQ-15 [29] are acceptable.

Adverse Events Questionnaire (AEQ)

SAEs were defined as (i) death by suicide; (ii) suicide attempt; (iii) suicidal crisis without attempt; (iv) severe symptom exacerbation (increase of 2 standard deviations or more on ITQ). Adverse events (AEs) were defined as a score of ≥3 (agree "quite a lot" or "a lot") on any relevant item (e.g., subjectively worsening mental state, heightened stigma, increased medication use, increased conflict). AEQ [21] was completed by clinicians during the intervention at the end of every module or upon the report of an SAE or AE by the participant in or out of session. The clinician was instructed to report all adverse events to the trial management group. The trial management group was asked to review this form and determine whether the event could reasonably be attributed to the intervention or participation in the trial. The trial management group reviewed all instances of adverse events, whether or not they were judged to be attributable to the trial or interventions, and, based on this information, determine whether the participant should be withdrawn and/or whether the trial should be suspended, stopped or continued.

Acceptability of Materials and Intervention (Qualitative Data)

Every participant who completed treatment in the ESTAIR arm (n = 22) was emailed a link to the qualitative questionnaire hosted on Survey Monkey once they had completed the end of treatment quantitative measures at 25 weeks. Non-completers were also invited to participate. Instructions included that completion of the qualitative survey was voluntary that all responses would be anonymous and that their therapist would not have access to the feedback. The survey included seven questions asking participants about their positive and negative experiences during treatment (e.g., What, if anything, have you found particularly positive about the treatment? Give examples). All responses were free-text.

Data Analysis

Recruitment, treatment completion, and study retention rates at all stages of the trial were recorded and summarised. Any comments regarding acceptability of the intervention and the outcomes were recorded and summarised.

Analyses on clinical measures were conducted in 4 linked phases. Firstly, the longitudinal changes in the summed scores across the treatment conditions were tested using linear mixed models based on the GAMLj package [30] in the jamovi software [31]. Time (baseline, post-treatment, and follow-up) and treatment (TAU or ESTAIR) were fixed effects and participants were random effects. Main effects and the interaction were estimated for each dependent variable separately based on restricted maximum likelihood estimation that uses all available data and does not require listwise deletion, which made this an intention-to-treat analysis. Maximum likelihood methods produce unbiased estimates of treatment effects in the presence of missing data, whereas complete case analysis produces biased estimates [32]. Efficacy of treatment would be indicated by a significant time by treatment interaction. Estimated marginal means were reported and plotted. Secondly, the same analyses were conducted on all secondary outcomes. The third phase involved cross tabulating probable PTSD/CPTSD diagnostic status at post-treatment to determine if there were differences in change in status. All participants screened positive for CPTSD at baseline so any differences can be interpreted in light of this. A significant χ^2 statistic would indicate differences in diagnostic status across TAU and ESTAIR, and standardised residuals greater than 2 were used to understand the overall effect. Finally, the mean PTSD and DSO scores from the ITQ were estimated and reported for each module for the ESTAIR group only. Quantitative analyses were performed by MS.

For qualitative data, all responses were collated and analysed using thematic analysis in order to provide a rich description of meaningful patterns contained in the data [33] via QDA Miner Lite [34]. Due to the pre-defined topic area of treatment experiences and preset questions in the survey, a thematic analysis approach was used. We anticipated participants would comment on the structure and content of sessions, as well as the therapeutic relationship. The data were repeatedly read, and preliminary codes were applied to sentences and paragraphs where patterns of meaning were identified. It was possible for multiple codes to be applied to segments of text. Codes which hung together were then grouped into themes. Qualitative analysis was performed by NB, although debriefing was used to establish great consistency in interpreting the data [35]. This is a reflexive, rather than a coding reliability approach. Whilst both approaches have their advantages, we felt the latter more suited to an inductive thematic analysis [36].

Results

Enrolment

As shown in the CONSORT chart (see Fig. 1), 92 people were screened for eligibility; 36 were excluded and of those 11 (12%) declined participation, with a total of 56 (61% of those initially approached) participants randomised to either the ESTAIR (n = 28) or the TAU (n = 28).
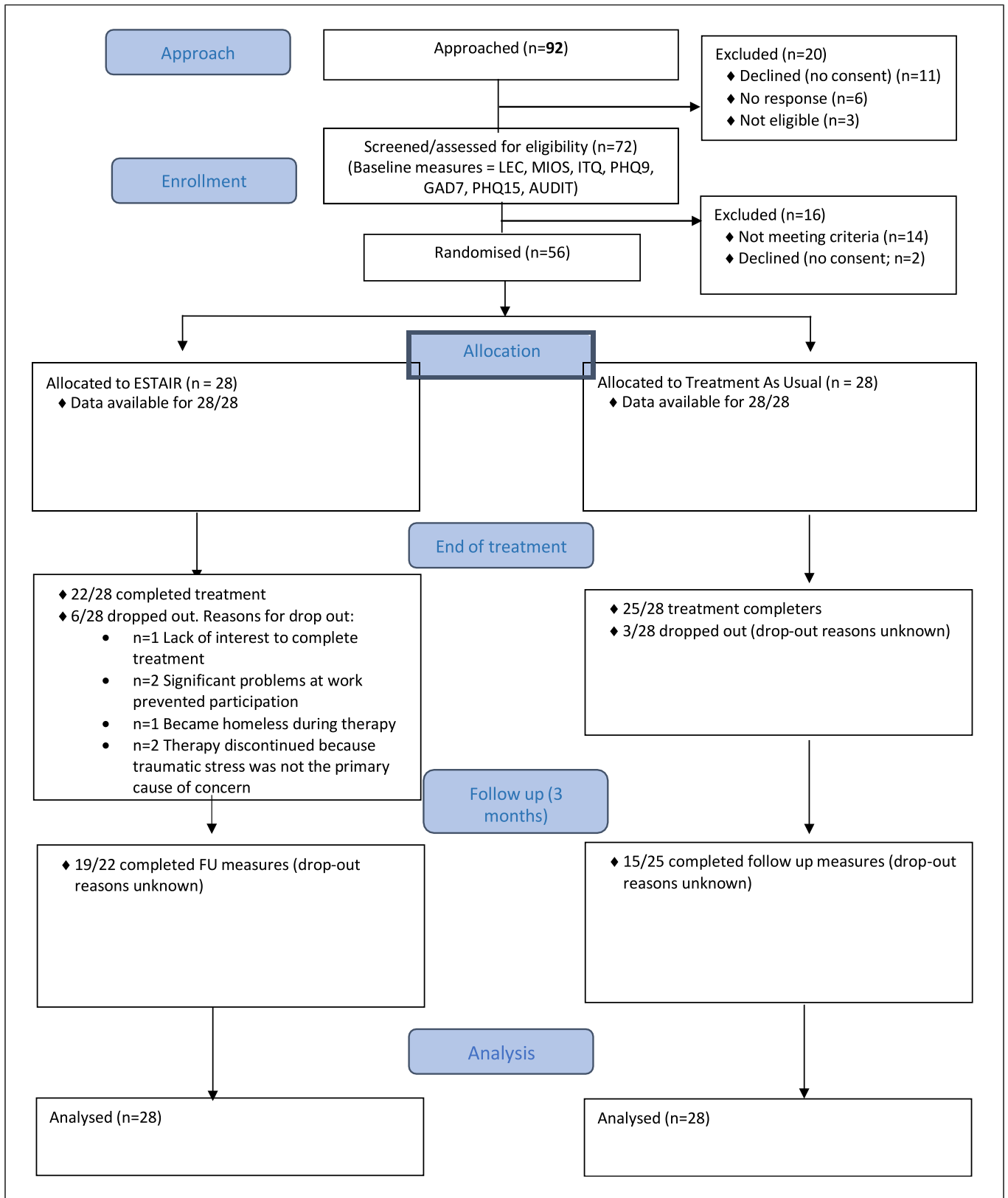
Fig. 1. Restore CONSORT.

Karatzias et al.

Treatment Completion

During the treatment phase, 18% (n = 6) dropped out of ESTAIR and 11% (n = 3) dropped out of TAU; this difference was not significant ($\chi^2(1)$ = 1.19, p = 0.275). Reasons for dropout in the ESTAIR treatment included changes in personal circumstances (n = 3), discontinuation because traumatic stress was no longer the primary cause of concern (n = 2), and lack of interest in completing treatment (n = 1). Reasons for those who dropped out of the TAU condition (n = 3) were not known. There was some additional attrition during the follow-up phase in ESTAIR and TAU, but this difference was not significant ($\chi^2(1)$ = 1.19, p = 0.274).

Study Retention

A total of 78% of ESTAIR participants and 89% of TAU participants completed post-treatment assessments. At follow-up, 68% of ESTAIR and 54% of TAU participants completed assessments. There were no significant differences in retention rates between the two conditions. Data availability was substantial and ranged between 54% and 89% across measures at post-treatment and 3-month follow-up (Fig. 1).

Sociodemographics

The responses to the LEC indicated very high levels of trauma exposure; the most frequently reported events were "Exposure to combat or exposure to a war-zone" (92.9%), "Any other very stressful event or experience" (89.3%), "Assault with a weapon" (87.5%), "Fire or explosion" (85.7%), and "Sudden violent death" (83.9%). Exposure to multiple trauma types was common, ranging from 1 to 17, with the mean of 11.48 (SD = 3.75: Mdn = 11.50).

At baseline, there were no significant differences in sex ($\chi^2(1)$ = 1.08, p = 0.299) and age between the ESTAIR (M = 47.14, SD = 12.24) and TAU groups (M = 46.32, SD = 10.48: t (54) = 0.27, p = 0.748). Mean scores on PTSD did not differ between the TAU (M = 20.21, SD = 2.69) and ESTAIR (M = 19.57, SD = 2.88) groups ($t(54)$ = 0.86, p = 0.393) nor did the DSO scores (TAU M = 20.75, SD = 2.44; ESTAIR M = 19.78, SD = 2.67; $t(54)$ = 1.41, p = 0.082).

Table 1 shows the demographic and service-related variables. There are no significant differences between the two groups across all variables.

CPTSD Symptoms

Table 2 shows that from the linear mixed models, there was a significant time by treatment interaction for both PTSD and DSO symptoms, and the means in online supplementary sTable 1 (for all online suppl. material, see https://doi.org/10.1159/000538428). Show that there were greater decreases in scores in the ESTAIR group relative to the TAU group. Post hoc comparisons showed that there were significant differences between the groups on the PTSD scores at post-treatment ($t(111.4)$ = 5.343, p < 0.001) and also at follow-up ($t(126.0)$ = 3.729, p = 0.004). There were also significant differences between the groups on the DSO scores at post-treatment ($t(113.7)$ = 6.98, p < 0.001) and at follow-up ($t(127.0)$ = 5.11, p < 0.001).

There were significant decreases in both mean PTSD and DSO scores for TAU and ESTAIR, with the decreases being larger for DSO symptoms, and the effect sizes greater for ESTAIR than TAU (online suppl. sFig. 1). Within-group t tests showed significant decreases in PTSD ($t(14)$ = 3.38, p < 0.01; d = 0.87) and DSO ($t(14)$ = 4.05, p < 0.001; d = 1.05) scores between baseline and follow-up for the TAU group. The decreases in PTSD ($t(18)$ = 7.76, p < 0.001; d = 1.78) and DSO ($t(18)$ = 8.74, p < 0.001; d = 2.00) scores between baseline and follow-up for the ESTAIR group were also significant and with larger effect sizes.

Secondary Outcomes

Table 3 shows that for anxiety and depression, both treatment conditions were associated with reductions in symptoms, and there were significant time by treatment interactions, indicating greater improvement in the ESTAIR group as compared to TAU (online suppl. sFig. 2). For somatic symptoms, there was an overall effect of time but no interaction effect, indicating the treatments did not differ in their effectiveness. For alcohol use, there was no effect of time, treatment condition, or treatment by time interaction, indicating that there was no change in alcohol use during the study. Symptom means by condition and across time are provided in online suppl. sTable 2.

Diagnostic Status

As shown in Table 4, there was a significant association between post-treatment diagnostic status and treatment group ($\chi^2(1)$ = 23.31, p < 0.001). At post-treatment, 84.0% of TAU participants met the criteria for PTSD/CPTSD compared to 13.6% of ESTAIR participants. Being in the ESTAIR group increased the likelihood of not meeting the criteria for PTSD/CPTSD compared to the TAU group (OR = 23.62: 95% CI = 5.15, 108.26). Online supplementary sTable 3 and sFigure 3 show that there was a consistent decrease in PTSD and DSO scores across all modules in the ESTAIR group.

Table 1. Demographic and medical characteristics at baseline

	TAU (N = 28)	ESTAIR (N = 28)	Total (N = 56)	[a]t/ [b]χ (df)	p value
Age, years	46.32 (10.47)	47.14 (12.24)	46.73 (11.23)	−0.270[a] (54)	0.788
Gender (male), n (%)	25 (89.3)	27 (96.4)	52 (92.9)	1.07[b] (1)	0.299
Relationship status, n (%)				4.50[b] (4)	0.342
Single	1 (3.6)	3 (10.7)	4 (7.1)		
In a relationship	3 (10.7)	4 (14.3)	7 (12.5)		
Married/cohabitating	19 (67.9)	20 (71.4)	39 (69.6)		
Separated	2 (7.1)	1 (3.6)	3 (5.4)		
Divorced	3 (10.7)	0 (0.0)	3 (5.4)		
Employment, n (%)				3.09[b] (4)	0.542
FT/PT employment	13 (46.4)	14 (50.0)	27 (48.2)		
Stay at home parent/caregiver	0 (0.0)	2 (7.1)	2 (3.6)		
Not working	3 (10.7)	1 (3.6)	4 (7.1)		
Not working due to ill health	9 (32.1)	8 (28.6)	17 (30.4)		
Retired	3 (10.7)	3 (10.7)	6 (10.7)		
Service, n (%)				2.18[b] (2)	0.337
Royal navy	1 (3.6)	0 (0.0)	1 (1.8)		
Army	24 (85.7)	27 (96.4)	51 (91.1)		
Royal air force	3 (10.7)	1 (3.6)	4 (7.1)		
Enlistment, n (%)				2.61[b] (2)	0.270
Regular	26 (92.9)	22 (78.6)	48 (85.7)		
Reservist	0 (0.0)	1 (3.6)	1 (1.8)		
Both	2 (7.1)	5 (17.9)	7 (12.5)		
Time in service, n (%)				1.24[b] (2)	0.539
<4 years or early service leaver	2 (7.1)	3 (10.7)	5 (8.9)		
4–14 years	13 (46.4)	16 (57.1)	29 (51.8)		
15+ years	13 (46.4)	9 (32.1)	22 (39.3)		
Service role, n (%)				1.02[b] (2)	0.599
Combat	21 (75.0)	20 (71.4)	41 (73.2)		
Non-combat	7 (25.0)	7 (25.0)	14 (25.0)		
Combat support	0 (0.0)	1 (3.6)	1 (1.8)		
Deployments, n (%)				2.34[b] (3)	0.503
0	1 (3.6)	3 (10.7)	4 (7.1)		
1	4 (14.3)	6 (21.4)	10 (17.9)		
2	6 (21.4)	7 (25.0)	13 (23.2)		
3 or more	17 (60.7)	12 (42.9)	29 (51.8)		
Last rank, n (%)				3.17[b] (1)	0.075
Officer	3 (10.7)	0 (0.0)	3 (5.4)		
Other	25 (89.3)	28 (100.0)	53 (94.6)		
Time to support, n (%)				0.33[b] (1)	0.567
<5 years	10 (35.7)	8 (28.6)	18 (32.1)		
>5 years	18 (64.3)	20 (71.4)	38 (67.9)		

Safety

There were no SAEs in either ESTAIR or TAU. Three AEs were recorded in ESTAIR (i.e., suicidal thoughts due to becoming homeless, excessive use of pain medication to aid sleep, hospitalisation for life threatening illness), and none in TAU; none of the AEs was associated with the study.

Qualitative Findings on Acceptability

A total of 16 veterans who had received the ESTAIR intervention completed the qualitative survey (57% response rate) to further establish acceptability of the treatment. Two overarching themes were identified in the data: structure of treatment and impact of treatment.

Karatzias et al.

Table 2. Fixed effect omnibus tests for primary outcome variables

	PTSD			DSO		
	F	df	p value	F	df	p value
Treatment	18.9	(1, 59.4)	<0.001	35.3	(1, 59.8)	<0.001
Time	54.9	(2, 89.3)	<0.001	72.3	(2, 90.1)	<0.001
Treatment × Time	11.3	(2, 89.3)	<0.001	18.3	(2, 90.1)	<0.001

Treatment = "ESTAIR" and "Treatment as usual" between-groups variable; Time = baseline (1), post-treatment (2), and follow-up (3) within-group variable; Treatment × Time is the between-within groups interaction. PTSD = summed scores on PTSD items from International Trauma Questionnaire. DSO = summed scores on disturbances in self-organisation items from International Trauma Questionnaire. See Table 3 for *n* at each time/group.

Table 3. Fixed effect omnibus tests for secondary outcome variables

	Depression			Anxiety			Somatic			Alcohol		
	F	df	p value	F	df	p value	F	df	p value	F	df	p value
Time	62.05	(2, 82.9)	<0.001	54.06	(2, 83.3)	<0.001	18.660	(2, 78.2)	<0.001	0.188	(2, 79.0)	0.829
Treatment	16.25	(1, 58.0)	<0.001	13.25	(1, 59.0)	<0.001	0.136	(1, 55.4)	0.714	2.357	(1, 56.2)	0.130
Time × Treatment	6.80	(2, 82.9)	0.002	8.93	(2, 83.3)	<0.001	2.017	(2, 78.2)	0.140	0.554	(2, 79.0)	0.577

Table 4. Post-Treatment diagnostic status stratified by treatment condition

	Post-treatment			Total
	CPTSD	PTSD	no diagnosis	
TAU				
Count	21	0	4	25
Expected count	12.8	0.5	11.7	25.0
%	84.0	0.0	16.0	100.0
Adjusted residual	4.8	−1.1	−4.5	
ESTAIR				
Count	3	1	18	22
Expected count	11.2	0.5	10.3	22.0
%	13.6	4.5	81.8	100.0
Adjusted residual	−4.8	1.1	4.5	
Total				
Count	24	1	22	47

Structure of Treatment

The first theme encompasses perceptions on the length of treatment, the order of modules and patients' feelings about the content of the intervention. Many patients commented on not feeling rushed during the (90 min) treatment sessions, for example: "*the time of each session,* *far superior to what I've experienced with any other* *service. There was time to explain things without worrying* *how long have I got left on my appointment.*"

Contributing to this perception of having adequate time during sessions was the input of the therapist, creating a dynamic, where patients perceived they had the space to repeat any aspects of the session if needed, with one veteran commenting: "*the way treatment was administered… if* *unsure about anything it wasn't too much trouble to go over it* *again … never felt pressured at any time was always on my* *terms.*" This was likely facilitated by the atypical treatment length of 25 weeks, as well as the length of individual sessions.

Relatedly, patients commented on having a sense there was a lot of content to fit into each session: "*I think there is* *more content in each session than time allows, as if it can only* *just be crammed in if the client doesn't have much to say. We* *sometimes had to skip parts due to this*", with another patient commenting: "*there wasn't enough time to be honest to* *finish.*" However, most patients felt that, by the end of treatment, most or all their difficulties had been addressed: "*I* *believe we managed to cover everything some in more detail* *than others*" and "*I still have some difficulties…however I* *now have the tools to deal with this.*" Some veterans described having additional trauma memories that they didn't work on during treatment, although these patients either were offered subsequent treatment with the service following study

completion, or felt equipped to cope with these memories with the skills practiced in treatment, e.g.,: "*I do still have things I need to work on like other memories that I need to process, however I feel confident with the skills I have learnt to continue on and work on this under my own steam.*"

In this vein, most patients implied that the structure of ESTAIR worked for them, with skills-based modules before trauma work: "*This memory affected me quite negatively during the week, but I managed to use the skills I had learnt to keep myself on track.*" Some veterans commented on the "lengthy" build up to the narrative module being something they anticipated: "*the long lead up to dealing with the events I understand why but the events haunt me on the lead up to dealing with them.*"

Impact of Treatment

The second theme incorporates veterans' perceptions about the impact of treatment on their lives, including their emotions, self-esteem and how this has positively affected their relationships and everyday functioning, all of which are DSO symptoms targeted by the ESTAIR modules. Many veterans described positive changes to their perceptions of themselves: "*I used to hate myself and think I was a bad person who deserved this life, I no longer feel that way*" and "*I feel better about myself…I'm more confident too,*" as well as "*my ability to handle emotions is much better now. I trust myself much more.*" Veterans commented on how these changes had supported positive shifts in their relationships, for example: "*my relationship with my wife is a lot better*" and "*my relationships both personal and work have improved as I can now regulate my issues and fears,*" as well as their everyday functioning: "*I am much kinder to myself [which] helps my everyday life.*"

These changes seemed to have also been noticed by patients' friends and family e.g., "*even [my wife] said I have changed, whereas before I would have flown off the handle at stuff, she says I'm totally different now*". One veteran commented "*friends and family noticed a huge difference in me [being] more alert not so miserable more approachable*", while another described how they "*see lots of changes and improvements, which has also been echoed by my loved ones and friends*". This reflects the wider impact of treatment across patients' networks.

Discussion

To our knowledge, this is the first RCT evaluating ESTAIR for veterans with ICD-11 CPTSD. Results indicate that ESTAIR is feasible, safe, and a potentially efficacious treatment. CPTSD symptoms and CPTSD diagnoses as well as comorbid symptoms of depression and anxiety were significantly reduced compared to TAU. Comorbid somatic symptoms improved in both treatments and alcohol use, which was relatively low at baseline, did not change in either treatment. There were no serious adverse events and a small number of adverse events during the study which were not related to the study. Overall, participants found the treatment acceptable and highlighted the benefits of the treatment particularly as related to social and interpersonal relationships.

Feasibility assessment yielded encouraging results. Enrolment was satisfactory with 72 individuals screened and 56 randomised over a 2-year period. While the target randomisation number was $n = 60$, the attrition rate from screening to randomisation was low (22%), compared to many veteran studies where attrition tends be about 50% in community settings (e.g., [37]). Dropout in both treatment conditions was low (19% and 11% for ESTAIR and TAU, respectively). The average dropout rate for PTSD was found 24% in a recent meta-analysis treatment among military and veteran populations [38]. Consistent with other reviews [39, 40], the authors found that dropout was higher in trauma-focused treatments as compared to non-trauma-focused treatments (27.1% vs. 16.1%, respectively). Given that ESTAIR is a trauma-focused treatment, the dropout rate of 19% is particularly encouraging. Retention rates for the sample across the entirety of the study were good, with data availability ranging between 54% and 89% across measures at post-treatment and 3-month follow-up. Taken together, these results provide support for the feasibility, recruitment, and follow-up of service user participants with CPTSD in a future trial. Engagement with ESTAIR was high and completion rate was good. Qualitative feedback for the intervention was positive overall in terms of format (i.e., modular delivery) and content for ESTAIR. A few areas for improvement have been identified including number of tasks in some sessions and sequencing of modules (i.e., narrative module was last), which should be addressed in a future trial. ESTAIR has been safe with no adverse events attributed to the intervention itself being recorded.

The trial also included findings for several exploratory clinical outcomes that should be further explored in a fully powered clinical trial. There were significant reductions in CPTSD symptoms at post-treatment and follow-up. Over 80% of the participants in the ESTAIR group did not meet the criteria for PTSD or CPTSD at post-treatment, compared to 16.0% for the TAU group. There were significant

reductions in depression and anxiety scores for the ESTAIR group in comparison to TAU, but not for somatic problems and alcohol use. Overall, preliminary results indicate that ESTAIR can produce superior results in CPTSD symptoms and other comorbidities such as depression and anxiety that are commonly present in those with CPTSD. These results require replication in an adequately powered trial. ESTAIR is a treatment of cognitive-behavioural orientation that was especially developed for CPTSD. It theorises that trauma recovery involves processing of memories of traumatic events from the past, but also covers the impact of trauma on the present as it affects current relationships, emotional distress in day-to-day life and quality of life. Thus, it includes traditional cognitive-behavioural interventions related to processing of the trauma memories (e.g., reappraisal of their meaning) as well as practical skills, training, and related interventions to improve relationships, sense of self, emotion regulation, and mood management [12]. A CPTSD specific intervention has never been tested in a population with CPTSD before, and therefore, it is not possible to compare the present findings with those of previous research. However, earlier variants of ESTAIR have been effective to treat traumatic stress symptoms in adult survivors of childhood abuse [13, 14], indicating that modular therapies [4] can adequately treat complex traumatic stress symptoms.

ESTAIR was not superior to TAU in regard to two secondary outcomes including somatic symptoms and alcohol use. Somatic symptoms improved significantly across time although greater focus and follow-through on body-based interventions in module 1, particularly as related to pain might improve outcomes. Neither treatment indicated any improvement in alcohol use. This might be the result of floor effects. A score of 5 on the AUDIT is typically the cut-off for risk of an alcohol use disorder among men and the average score at baseline for ESTAIR and TAU were 2.82 (SD = 0.50) and 3.82 (SD = 0.50), indicating relative low use in this study sample with little room for improvement. This might be because alcohol use and substance use disorders were exclusions to this study and that the program triages veterans with AUD and SUD to programming that addresses these problems as a primary concern [41].

There are a number of limitations of this work to discuss. Firstly, and although in line with aims of the study, the sample size is quite small to generalise any findings to the wider CPTSD population. Secondly, we have only recruited veterans with CPTSD and we do appreciate that there is need for further work with other trauma treatment seeking groups. Thirdly, because of limited resources we were only able to follow-up participants' 3-month post-treatment. There is clearly a need for trials with longer follow-ups to confirm that benefits maintain over a period of at least a year or more. Fourthly, the sample size prohibited from any analysis on predictors of outcome including the role of sex to identify groups that most likely benefit from an intervention such as ESTAIR. Finally, and with regard to acceptability, we were only able to recruit completers for participation and feedback. Nevertheless, evidence suggests that patients are more likely to report negative, rather than positive, feedback about psychological treatment [42]. As such, it is likely that the sample of respondents captured negative feedback about ESTAIR, although it is also important to highlight that we did not manage to collect feedback from non-completers. Another limitation regarding acceptability is that the free-text responses may have led to a smaller dataset than qualitative interviews, although a decision was made when designing the protocol that the feedback survey would allow more participants the opportunity to provide their views on treatment. Finally, careful consideration should be given as to whether people with AUD/SUD and CPTSD should be included in future ESTAIR trials although there is evidence to suggest that targeting these symptoms separately might result in better outcomes in those with traumatic stress [43].

Notwithstanding its limitations, this is the first study to report on the feasibility of delivering a new intervention specifically designed to target the symptoms of ICD-11 CPTSD. With reference to the framework for the development and testing of interventions, we anticipate further testing of ESTAIR with flexible ordering of modules versus other trauma-focused therapies or routine care to establish its effectiveness for different trauma samples as well its cost effectiveness.

Statement of Ethics

This study protocol was reviewed and approved by from Edinburgh Napier University (Project 1723177) and was pre-registered with ClinicalTrials.Gov (NCT04752072). Written consent was obtained from all participants to participate in the study.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

Author Contributions

T.K.: design, conceptualisation, and production of first draft. M.S.: methodological support, production of first draft, and statistical analysis. M.C.: data interpretation and critical reviewing. W.B., K.G., L.J.H., N.B., and PH: critical reviewing. D.M.: design, conceptualisation, and critical reviewing. All authors have approved the final version of the paper.

Data Availability Statement

The data that support the findings of this study are not publicly available due to patient privacy reasons but are available from the corresponding author upon reasonable request.

References

1 World Health Organization. International statistical classification of diseases and related health problems (11th Revision); 2018. Available from: https://icd.who.int/browse11/l-m/en#/http%3a%2f%2fid.who.int%2ficd%2fentity%2f264310751.

2 Karatzias T, Shevlin M, Fyvie C, Hyland P, Efthymiadou E, Wilson D, et al. Evidence of distinct profiles of posttraumatic stress disorder (PTSD) and complex posttraumatic stress disorder (CPTSD) based on the new ICD-11 trauma questionnaire (ICD-TQ). J Affect Disord. 2017;207:181–7. doi: 10.1016/j.jad.2016.09.032.

3 Cloitre M, Hyland P, Bisson JI, Brewin CR, Roberts NP, Karatzias T, et al. ICD-11 posttraumatic stress disorder and complex posttraumatic stress disorder in the United States: a population-based study. J Trauma Stress. 2019;32(6):833–42. doi: 10.1002/jts.22454.

4 Karatzias T, Cloitre M. Treating adults with complex posttraumatic stress disorder using a modular approach to treatment: rationale, evidence, and directions for future research. J Trauma Stress. 2019;32(6):870–6. doi: 10.1002/jts.22457.

5 Murphy D, Shevlin M, Pearson E, Greenberg N, Wessely S, Busuttil W, et al. A validation study of the International Trauma Questionnaire to assess post-traumatic stress disorder in treatment-seeking veterans. Br J Psychiatry. 2020;216(3):132–7. doi: 10.1192/bjp.2020.9.

6 Folke S, Karstoft KI, Andersen SB, Karatzias T, Nissen LR, Nielsen ABS. Risk factors, comorbidity and social impairment of ICD-11 PTSD and complex PTSD in Danish treatment-seeking military veterans. J Psychiatr Res. 2023;163:247–53. doi: 10.1016/j.jpsychires.2023.05.055.

7 Karatzias T, Murphy P, Cloitre M, Bisson J, Roberts N, Shevlin M, et al. Psychological interventions for ICD-11 complex PTSD symptoms: systematic review and meta-analysis. Psychol Med. 2019;49(11):1761–75. doi: 10.1017/S0033291719000436.

8 Voorendonk EM, De Jongh A, Rozendaal L, Van Minnen A. Trauma-focused treatment outcome for complex PTSD patients: results of an intensive treatment programme. Eur J Psychotraumatol. 2020;11(1):1783955. doi: 10.1080/20008198.2020.1783955.

9 Dumarkaite A, Truskauskaite-Kuneviciene I, Andersson G, Kazlauskas E. The effects of online mindfulness-based intervention on posttraumatic stress disorder and complex posttraumatic stress disorder symptoms: a randomized controlled trial with 3-month follow-up. Front Psychiatry. 2022;13:799259. doi: 10.3389/fpsyt.2022.799259.

10 Coventry PA, Meader N, Melton H, Temple M, Dale H, Wright K, et al. Psychological and pharmacological interventions for posttraumatic stress disorder and comorbid mental health problems following complex traumatic events: systematic review and component network meta-analysis. PLoS Med. 2020;17(8):e1003262. doi: 10.1371/journal.pmed.1003262.

11 Schnyder U. Longitudinal development of symptoms and staging in psychiatry and clinical psychology: a tribute to Giovanni Fava. Psychother Psychosom. 2023;92(1):4–8. doi: 10.1159/000527462.

12 Karatzias T, Mc Glanaghy E, Cloitre M. Enhanced skills training in affective and interpersonal regulation (ESTAIR): a new modular treatment for ICD-11 complex posttraumatic stress disorder (CPTSD). Brain Sci. 2023;13(9):1300. doi: 10.3390/brainsci13091300.

13 Cloitre M, Koenen KC, Cohen LR, Han H. Skills training in affective and interpersonal regulation followed by exposure: a phase-based treatment for PTSD related to childhood abuse. J Consult Clin Psychol. 2002;70(5):1067–74. doi: 10.1037//0022-006x.70.5.1067.

14 Cloitre M, Stovall-McClough KC, Nooner K, Zorbas P, Cherry S, Jackson CL, et al. Treatment for PTSD related to childhood abuse: a randomized controlled trial. Aust J Pharm. 2010;167(8):915–24. doi: 10.1176/appi.ajp.2010.09081247.

15 Oprel DAC, Hoeboer CM, Schoorl M, de Kleine RA, Cloitre M, Wigard IG, et al. Effect of Prolonged Exposure, intensified Prolonged Exposure and STAIR+Prolonged Exposure in patients with PTSD related to childhood abuse: a randomized controlled trial. Eur J Psychotraumatol. 2021;12(1):1851511. doi: 10.1080/20008198.2020.1851511.

16 Hoeboer CM, Oprel DAC, De Kleine RA, Schwartz B, Deisenhofer AK, Schoorl M, et al. Personalization of treatment for patients with childhood-abuse-related posttraumatic stress disorder. JCM. 2021;10(19):4522. doi: 10.3390/jcm10194522.

17 Niwa M, Kato T, Narita-Ohtaki R, Otomo R, Suga Y, Sugawara M, et al. Skills Training in Affective and Interpersonal Regulation Narrative Therapy for women with ICD-11 complex PTSD related to childhood abuse in Japan: a pilot study. Eur J Psychotraumatol. 2022;13(1):2080933. doi: 10.1080/20008198.2022.2080933.

18 Karatzias T, Shevlin M, Hyland P, Ben-Ezra M, Cloitre M, Owkzarek M, et al. The network structure of ICD-11 complex posttraumatic stress disorder across different traumatic life events. World Psychiatr. 2020;19(3):400–1. doi: 10.1002/wps.20795.

19 Campbell MK, Piaggio G, Elbourne DR, Altman DG; CONSORT Group. Consort 2010 statement: extension to cluster randomised trials. BMJ. 2012;345:e5661. doi: 10.1136/bmj.e5661.

20 Cloitre M, Shevlin M, Brewin CR, Bisson JI, Roberts NP, Maercker A, et al. The International Trauma Questionnaire: development of a self-report measure of ICD-11 PTSD and complex PTSD. Acta Psychiatr Scand. 2018;138(6):536–46. doi: 10.1111/acps.12956.

21 Hutton P, Byrne R, Morrison T. Adverse effects in psychotherapy measure Unpublished manuscript. 2017.

22 Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric properties of the life events checklist. Assessment. 2004;11(4):330–41. doi: 10.1177/1073191104269954.

23 Redican E, Nolan E, Hyland P, Cloitre M, McBride O, Karatzias T, et al. A systematic literature review of factor analytic and mixture models of ICD-11 PTSD and CPTSD using the International Trauma Questionnaire. J Anxiety Disord. 2021;79:102381. doi: 10.1016/j.janxdis.2021.102381.

24 Murphy D, Karatzias T, Busuttil W, Greenberg N, Shevlin M. ICD-11 posttraumatic stress disorder (PTSD) and complex PTSD (CPTSD) in treatment seeking veterans: risk factors and comorbidity. Soc Psychiatry Psychiatr Epidemiol. 2021;56(7):1289–98. doi: 10.1007/s00127-021-02028-6.

25 Ho GW, Karatzias T, Cloitre M, Chan AC, Bressington D, Chien WT, et al. Translation and validation of the Chinese ICD-11 international trauma questionnaire (ITQ) for the assessment of posttraumatic stress disorder (PTSD) and complex PTSD (CPTSD). Eur J Psychotraumatol. 2019;10(1):1608718. doi: 10.1080/20008198.2019.1608718.

26 Kroenke K, Spitzer RL. The PHQ-9: a new depression diagnostic and severity measure. Psychiatr Ann. 2002;32(9):509–15. doi: 10.3928/0048-5713-20020901-06.

27 Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med. 2006;166(10):1092–7. doi: 10.1001/archinte.166.10.1092.

28 Saunders JB, Aasland OG, Babor TF, De La Fuente JR, Grant M. Development of the alcohol use disorders identification test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. Addiction. 1993; 88(6):791–804. doi: 10.1111/j.1360-0443.1993.tb02093.x.

29 Kroenke K, Spitzer RL, Williams JBW, Löwe B. The patient health questionnaire somatic, anxiety, and depressive symptom scales: a systematic review. Gen Hosp Psychiatry. 2010;32(4):345–59. doi: 10.1016/j.genhosppsych.2010.03.006.

30 Gallucci M. GAMLj: General analyses for linear models. [jamovi module]. 2019. Available from: https://gamlj.github.io/.

31 Jamovi project (2022). jamovi. (Version 2.3) [Computer Software]. Available from: https://www.jamovi.org.

32 Salim A, Mackinnon A, Christensen H, Griffiths K. Comparison of data analysis strategies for intent-to-treat analysis in pretest–post-test designs with substantial dropout rates. Psychiatry Res. 2008;160(3): 335–45. doi: 10.1016/j.psychres.2007.08.005.

33 Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3(2): 77–101. doi: 10.1191/1478088706qp063oa.

34 QDA miner lite. 2016. Available from: https://provalisresearch.com/products/qualitative-data-analysis-software/freeware/.

35 Morrow SL. Quality and trustworthiness in qualitative research in counseling psychology. J Counsel Psychol. 2005;52(2):250–60. doi: 10.1037/0022-0167.52.2.250.

36 O'Connor C, Joffe H. Intercoder reliability in qualitative research: debates and practical guidelines. Int J Qual Methods. 2020;19:160940691989922. doi: 10.1177/1609406919989220.

37 Shiner B, Westgate C, Gui J, Cornelius S, Maguen S, Watts B, et al. Measurement strategies for evidence-based psychotherapy for posttraumatic stress disorder delivery: trends and associations with patient-reported outcomes. Adm Pol Ment Health. 2020;47(3): 451–67. doi: 10.1007/s10488-019-01004-2.

38 Edwards-Stewart A, Smolenski DJ, Bush NE, Cyr B, Beech EH, Skopp NA, et al. Posttraumatic stress disorder treatment dropout among military and veteran populations: a systematic review and meta-analysis. J Trauma Stress. 2021;34(4):808–18. doi: 10.1002/jts.22653.

39 Kitchiner NJ, Roberts NP, Wilcox D, Bisson JI. Systematic review and meta-analyses of psychosocial interventions for veterans of the military. Eur J Psychotraumatol. 2012;3(1): 19267. 10.3402/ejpt.v3i0.19267.

40 Lewis C, Roberts NP, Gibson S, Bisson JI. Dropout from psychological therapies for post-traumatic stress disorder (PTSD) in adults: systematic review and meta-analysis. Eur J Psychotraumatol. 2020; 11(1):1709709. doi: 10.1080/20008198.2019.1709709.

41 Bradley KA, Bush KR, Epler AJ, Dobie DJ, Davis TM, Sporleder JL, et al. Two brief alcohol-screening tests from the alcohol use disorders identification test (AUDIT): validation in a female veterans affairs patient population. Arch Intern Med. 2003; 163(7):821–9. doi: 10.1001/archinte.163.7.821.

42 Crawford MJ, Thana L, Farquharson L, Palmer L, Hancock E, Bassett P, et al. Patient experience of negative effects of psychological treatment: results of a national survey. Br J Psychiatry. 2016;208(3):260–5. doi: 10.1192/bjp.bp.114.162628.

43 Simpson TL, Goldberg SB, Louden DKN, Blakey SM, Hawn SE, Lott A, et al. Efficacy and acceptability of interventions for co-occurring PTSD and SUD: a meta-analysis. J Anxiety Disord. 2021;84:102490. doi: 10.1016/j.janxdis.2021.102490.