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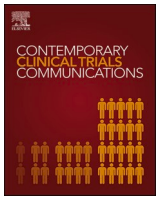

Comparing the unified protocol for transdiagnostic treatment of emotional disorders to prolonged exposure for the treatment of PTSD: Design of a non-inferiority randomized controlled trial

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ABSTRACT

Background: Prolonged Exposure (PE), a trauma-focused therapy, is one of the most efficacious treatments available for PTSD. However, many people with PTSD do not lose their diagnosis following delivery of PE. The Unified Protocol (UP) for Transdiagnostic Treatment of Emotional Disorders is a non-trauma focused treatment that may offer an alternative treatment for PTSD.

Methods: This paper describes the study protocol for IMPACT, an assessor-blinded randomized controlled trial that examines the non-inferiority of UP relative to PE for participants who meet DSM-5 criteria for current PTSD. One hundred and twenty adult participants with PTSD will be randomized to receive either 10 × 90-min sessions of UP or PE with a trained provider. The primary outcome is severity of PTSD symptoms assessed by the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) at post-treatment.

Discussion: While evidence-based treatments are available for PTSD, high levels of treatment dropout and non-response require new approaches to be tested. The UP is based on emotion regulation theory and is effective in treating anxiety and depressive disorders, however, there has been limited application to PTSD. This is the first rigorous study comparing UP to PE in a non-inferiority randomized controlled trial and may help improve clinical outcomes for those with PTSD.

Trial registration: This trial was prospectively registered with the Australian New Zealand Clinical Trials Registry, Trial ID (ACTRN12619000543189).

1. Introduction

Post-traumatic stress disorder (PTSD) is a highly disabling psychiatric disorder [1]. Recommended evidence-based treatments for PTSD [2], such as Prolonged Exposure (PE), are predominantly trauma-focused and require patients to confront the memories of their traumatic event(s) [3]. Prolonged Exposure has a strong evidence base across a number of trauma populations [2,3]. PE is underpinned by emotion and information processing theories and uses fear extinction learning to promote gradual extinction of conditioned fear responses to trauma [4]. PE necessarily involves repeated exposure to the traumatic memory/memories (imaginal exposure) and confronting related triggers (in vivo exposure) that lead to gradual reduced distress associated with the trauma memory.

Despite their strong evidence base, trauma-focused therapies have a number of limitations. First, many well controlled studies of trauma-focused treatment show less than 50% of participants lose their PTSD diagnosis and, for some higher risk populations, this percentage drops to

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about 30% [5,6]. Second, providers can be reluctant to deliver trauma-focused treatments, often due to misconceptions of potential negative effects on clients, particularly for complex presentations, including co-morbidity [7,8]. Third, dropout rates for trauma-focused treatments appear to be higher than other treatments [9,10]. These limitations of trauma-focused interventions provide a strong rationale to test alternative, non-trauma focused treatments for PTSD.

Transdiagnostic treatments have emerged recently in response to growing evidence that common mechanisms underlie psychiatric disorders, especially anxiety and mood disorders [11]. These mechanisms include but are not limited to, negative affect, emotion avoidance, anxiety sensitivity, emotion dysregulation, cognitive distortion, distress intolerance, and experiential avoidance [12]. The Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) [13] is a psychological intervention that targets these transdiagnostic mechanisms [14], and has strong theoretical origins [13]. UP synthesizes empirically supported cognitive behavioral therapy (CBT) protocols and can be viewed as a transdiagnostic, emotion-focused CBT [12]. UP is effective in the treatment of disorders of generalized anxiety, panic, obsessive compulsive disorder, social anxiety, depression, and alcohol use disorder [15]. Importantly, studies have found that UP effectively targets co-occurring disorders [16], which is particularly important given PTSD is more likely to occur as a comorbid psychiatric disorder than as a sole diagnosis [17,18].

Recently the transdiagnostic mechanisms underpinning emotional disorders have been described for PTSD [14,19]. Particularly, negative affect avoidance [20], anxiety sensitivity [21], cognitive distortions [22] and emotion regulation [23] have been implicated in the maintenance and exacerbation of PTSD symptoms. As UP actively targets emotion regulation dysfunction and emotion avoidance thought to underpin PTSD [23,24], it may support individuals to better regulate emotions and reduce tendencies to avoid distressing emotions, improving PTSD symptoms without a specific or direct focus on the trauma memory. Furthermore, by targeting transdiagnostic negative affective processes, it may address PTSD comorbidity more efficiently than trauma-focused treatments.

Two studies have explored UP in the treatment of PTSD. Varkovitzky et al. [25] found improvements in PTSD and depressive symptoms, and emotion regulation from pre-treatment to post-treatment following a 16-week UP intervention delivered in a group format to 52 veterans. While an important first study, limitations included the delivery of UP in group format, and an absence of both a control group and follow-up period. A recently published randomized controlled study provides further evidence that UP could be a useful treatment for PTSD [26]. Forty-three traumatic injury patients were randomized to receive 10–14 sessions of manualized UP or Usual Care (UC). Compared to the UC group, the UP group was associated with a significant reduction in PTSD and depressive symptoms at post-treatment which was maintained at a 6-month follow-up. While this study demonstrated preliminary evidence for UP in treating PTSD and other trauma-related psychopathology, the sample size was small and although all participants had PTSD symptoms, a PTSD diagnosis was not an inclusion criterion for the study. This early evidence shows support for UP as a viable treatment for PTSD, however the question remains as to whether UP is as effective as current first line (trauma-focused) treatments for PTSD.

The objective of this paper is to describe the design, methodology and protocol for the Intervention to Manage PTSD and Comorbidities Trial (IMPACT), a randomized controlled trial. The study has a number of aims. The primary aim is to determine if UP is non-inferior to PE in reducing symptom severity of PTSD as measured by the Clinician Administered PTSD Scale for DSM-5 (CAPS-5) at post-treatment and at 6-months following treatment completion. We hypothesize that UP will be non-inferior to PE in reducing PTSD symptom severity at the post-treatment and 6-month post-treatment assessments. Aim two is to test whether there are differences between PE and UP in their ability to address co-occurring symptoms of anxiety and depression as measured by the Patient Health Questionnaire (PHQ-9) and the Generalized Anxiety Disorder Scale (GAD-7). We hypothesize that UP will be superior to PE in treating depression and anxiety at post-treatment and at 6-month follow up. The final aim is to explore treatment drop out in both conditions. We hypothesize that UP will be superior to PE with less treatment dropout in the UP condition than the PE condition.

2. Materials and methods

2.1. Participants and setting

Participants are eligible if they meet the following inclusion criteria: (1) 18 years old and over; (2) their symptoms meet diagnostic criteria for PTSD based on the Mini International Neuropsychiatric Interview-7 (MINI-7 PTSD module)[27]; (3) provision of consent to partake in treatment; (4) English comprehension at a level to make informed consent; (5) if on psychotropic medication, on a stable dose for the last four weeks, and not intending to change during the treatment phase; (6) for *telehealth modality only:* ability to reliably participate in telehealth treatment delivery, including appropriate technology for videoconferencing and safe and private space for treatment administration. Exclusion criteria include: (1) cognitive impairment as assessed via structured clinical intake assessment; (2) active mania or psychosis, or suicidal ideation, or other active risk, as assessed via structured clinical intake assessment; (3) severe alcohol or substance use disorder, as assessed via the MINI-7 [41]; (4) currently undergoing psychological treatment as assessed against a checklist of known psychological interventions.

Recruitment into the IMPACT trial will be based on self-referral to the Phoenix Australia Traumatic Stress Clinic, Australia. The trial will be advertized through local mental health providers (e.g., psychologists, psychiatrists), social media posts, and the Phoenix Australia website.

2.2. Study design and procedures

IMPACT is a two-arm, assessor-blinded, randomized, parallel-group non-inferiority study, employing a 2 (treatment condition) x 3 (assessment point) repeated measures design in a study sample of people with a diagnosis of PTSD. Participants will be randomly allocated to one of two treatments: (a) UP or (b) PE - each consisting of 1 × 90 min clinical assessment session and 10 × 90 min sessions conducted weekly with a trained provider. Due to the potential for COVID-19 related restrictions, treatment will be delivered either face-to-face or via telehealth (videoconferencing) depending on hospital/clinic site requirements/restrictions. Participants will be assessed at: (a) pre-treatment (one week pre-treatment), (b) post-treatment (two weeks post-treatment end), and (c) 6-month post-treatment follow-up (six months post-treatment end).

Following verbal consent, prospective participants will undergo a telephone intake assessment by a trained provider to determinine trial eligibility against inclusion/exclusion criteria. If eligible, written informed consent will be obtained before participants undergo a pre-treatment assessment with a trained assessor, administered via face to face or telehealth (Zoom videoconferencing) in a 1:1 format. Participants will also be required to complete pre-treatment self-report questionnaires delivered via email link to the Research Electronic Data Capture (REDCap) survey platform [28], a secure web platform for building and managing online databases and surveys, hosted by the University of Melbourne, where this research is based. Following pre-treatment assessment, participants will be randomized to either the UP or PE treatment condition. UP and PE treatment will be delivered by trained providers including intern and registered psychologists, and mental health social workers, who hold masters or doctoral level degrees or equivalent in their respective professions. Due to the impacts of the global COVID-19 pandemic, our methodology incorporates delivery of treatment and assessments both via face to face or via telehealth (i.e., Zoom videoconferencing). Post-treatment and 6-month follow-up

assessments will be administered over the telephone.

2.3. Randomization and blinding

Randomization will occur with stratification by PTSD comorbidity (i.e., PTSD only and PTSD-plus-another psychiatric disorder/s) using randomization software in REDCap. An independent statistician will create the randomization lists. All trial assessors will be blind to treatment condition. Data analysis will be conducted by an independent statistician who is blinded to treatment condition.

2.4. Power and sample size calculation

We will test a non-inferiority hypothesis that PTSD symptom severity outcomes in the UP condition will be non-inferior to those in PE. The non-inferiority margin – or the maximum amount by which UP can be worse than PE without having a clinical meaningful difference on the CAPS-5 was identified as 10 points based on precedent [29–34]. The non-inferiority margin was originally determined to be six points on the CAPS-5 based on a single study using the CAPS-5 [35]. However, after registering the study in the Australian New Zealand Clinical Trials Registry, it became clear that there was growing evidence that recent non-inferiority PTSD studies were adopting a clinical meaningful difference on the CAPS-5 as 10 points [29–34]. In consultation with the study Data Safety and Monitoring Board (DSMB), we adopted a 10-point non-inferiority margin (hence, the clinical trial registry was updated). A power calculation was conducted based on the primary study aim of testing non-inferiority based on the CAPS-5 PTSD symptom severity scores. A sample size of 100 was determined for detecting non-inferiority of the CAPS-5 score, where non-inferiority is declared if the upper endpoint of the 95% confidence interval for the difference in mean change scores from baseline to post-treatment between UP and PE (adjusted for baseline), is less than or equal to, ten points on the CAPS-5. A total of 100 participants is required to detect non-inferiority with 80% power when UP is truly non-inferior. The false positive error rate (i.e., falsely declaring non-inferiority) with this design is at most 2.5%. Allowing for 20% loss to follow up pre/post study, the sample size increases to 120 patients. See Fig. 1 for planned flow of participants through the study.

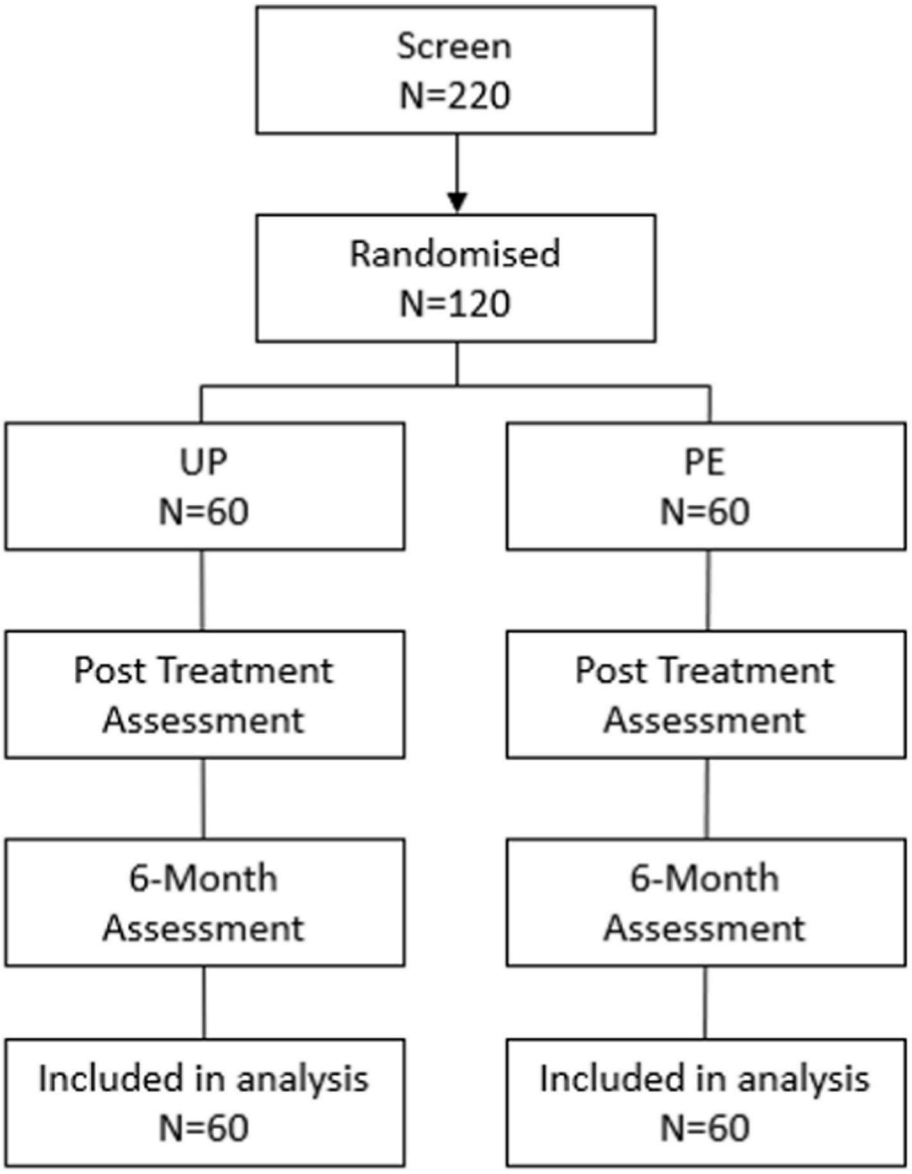

Fig. 1. Planned participant flow through the study.
UP: Unified Protocol: PE: Prolonged Exposure.

2.5. Statistical analysis

Treatment completion will be defined as completing all treatment sessions. Early treatment completion will be allowed if determined by agreement between the treatment provider and the client.

Statistical analyses: Baseline characteristics of participants in UP and PE conditions will be tabulated and analyzed descriptively (e.g., age, sex, PTSD symptom severity, presence of another psychiatric diagnosis) using t-tests, or chi-square tests depending on the type (continuous or dichotomous) distribution of the data. Data will be analyzed in accordance with intention to treat (ITT) principles. The primary analysis of the efficacy of UP relative to PE, will use imputed data using model-based Multiple Imputation (MI) that impute for missing data assessment scores (CAPS-5) at each time point. The MI models will include randomization group, and time point. Non-inferiority analyses of the primary outcome at immediate post-treatment will then be performed using linear models adjusted for baseline outcome values and the stratification variable (comorbidity), and with treatment condition as the covariate of interest. Results will be presented as adjusted differences in change scores on the CAPS-5, comparing UP and PE groups, together with 95% confidence intervals. Non-inferiority of UP to PE will be accepted if the boundaries of a two-sided 95% CI are within the non-inferiority margin (which is a 10-point difference on the CAPS-5, with a standard deviation of 20.0). In addition to the non-inferiority analyses, standard linear and mixed effects models will be used to investigate the effects of time and group on the secondary outcome measures including PHQ-9, GAD-7, and AUDIT, while standardized within-group and between-group effect sizes will also be produced.

2.6. Treatment interventions

2.6.1 Prolonged Exposure will be delivered based on the manualized treatment protocol developed by Foa and colleagues [36]. The PE protocol comprises 10 × 90-minute sessions designed for sequential delivery and is described in Table 1.

2.6.2 Unified Protocol will be delivered using the manualized treatment protocol developed by Barlow and colleagues [13]. The usual UP protocol comprises 8 modules, designed for sequential delivery over 12–18 sessions of 50 minute duration. In IMPACT, UP sessions are extended to 90 minutes over 10 weeks to align the dose of treatment with PE [38,39]. Given UP is designed to be delivered in modules that go across sessions, structuring a 90 min session is relatively simple. However, feedback from clinicians about the utility of 90 min UP sessions will be obtained. As well as a manualized protocol, the UP utilizes a participant workbook that clients work through, designed to match delivery of the modules. The UP protocol is described in Table 2.

Table 1
Treatment elements of the Prolonged Exposure Treatment Protocol in the IMPACT trial.[a]

Session	Description of session
0	Clinical assessment[b]
1	Trauma history and current difficulties are assessed; overall rationale for therapy is provided; and breathing retraining is taught to help manage anxiety. Homework involves practicing breathing retraining and reviewing the treatment rationale.
2	Common reactions to trauma are discussed; a rationale for in vivo is presented; and a hierarchical list of avoided situations developed. Homework involves in vivo exposure practice and breathing retraining, and reviewing common reactions to trauma.
3	Rationale for imaginal PE is presented; first imaginal PE activity is conducted; and discussion to help develop a realistic perspective on the event is delivered. Homework involves listening to the PE session recording, focusing on the imaginal PE, and continuing in vivo exposure.
4–9	Imaginal PE consolidated through continued revisiting and recounting, with client encouraged to describe the trauma in greater detail, focusing progressively more on the most distressing aspects of the trauma; thoughts and feelings evoked through exposure discussed; in vivo homework assignments discussed. Homework as per Session 3.
10	Shorter PE task conducted; changes in the experience of PE and trauma memory over the course of therapy reviewed; overall progress reviewed; relapse prevention strategies discussed; treatment terminated.

[a] PE protocol based on Foa et al. [37].
[b] Clinical assessment session including PE formulation conducted by providers prior to administration of the formal PE protocol.

2.7. Treatment fidelity

Providers will be trained to deliver both UP and PE to minimize provider effects. Providers will attend standard training in PE delivered by Dr Peter Tuerk which includes a two-day face-to-face training workshop, with ongoing supervision by KF. Providers will also receive UP training and supervision from MG who is a UP expert and certified UP trainer. Training will involve meeting with MG to work through the UP provider manual, and review all therapy sessions for a full client for each provider. Providers will receive monthly group supervision from experts in each treatment (fortnightly supervision in alternating treatments), to ensure adherence to the treatment protocols. Fidelity checks of a random 10% of client cases will be conducted by independent experts in PE or UP.

2.8. Measures

Table 3 lists all participant measures used in IMPACT across the trial phases.

Clinician Administered PTSD Scale for DSM-5 (CAPS-5) [40]. The CAPS-5 is the primary outcome measure for this study. It is a structured clinical interview for PTSD based on DSM-5 criteria. The 30 items reflect the presence, frequency and severity of the 20 DSM-5 PTSD criteria, along with an indication of overall severity, symptom onset and duration, associated distress and impact on functioning. The CAPS-5 is one of the most widely used and gold standard tools for diagnosing PTSD and

Table 2
Treatment elements of the Unified Protocol Treatment in the IMPACT trial.[a]

Module	Description of module
0	Clinical assessment[b]
1	Motivation enhancement for treatment engagement: Readiness for change, and therapeutic goals are established and self-efficacy fostered.
2	Psycho-education and tracking of emotional experiences (1 session) – Aims to educate patients in the nature of emotions, emotional experience and learned responses to increase awareness of emotional response patterns.
3	Emotion awareness training (1–2 sessions) – Assists patients to identify reactions and responses to emotions and practice awareness of emotional experience through development of skills to observe thoughts, emotions, physical sensations and behaviors contributing to distress.
4	Cognitive appraisal and reappraisal (1–2 sessions) – Assists patients to consider and modify maladaptive and automatic appraisals in context with emerging emotional experiences.
5	Emotion avoidance and emotion-driven behaviors (1–2 sessions) – Focuses on the behavioral parts of emotional experience and teaches patients to identify patterns of emotional avoidance and maladaptive emotion driven behaviors in order to change current patterns of emotional responding.
6	Awareness and tolerance of physical sensations (1 session) – Assists patients to increase awareness of physical sensations analogous with anxiety distress and develop increased tolerance of distressing emotions through interoceptive exposures.
7	Interoceptive and situation-based emotion exposures (2–4 sessions) – Assists patients to develop a hierarchy of emotional avoidance and assists them to increase tolerance of emotions and allow new contextual learning to occur.
8	Relapse prevention (1 session) –Treatment concepts and progress are reviewed and patients are assisted to identify ways to maintain treatment gains and anticipate future difficulties.

[a] UP protocol based on Barlow et al. [13].
[b] Clinical assessment session including UP formulation conducted by providers prior to administration of the formal UP protocol.

Table 3
SPIRIT figure of assessments at intake, pre-treatment, during treatment sessions, post-treatment, and 6-months post-treatment.

	STUDY PERIOD					
	Enrolment	Allocation	Post-allocation			
TIMEPOINT	*Intake*	*Allocation*	*Pre-treatment*	*In-treatment*	*Post-treatment*	*6-month follow-up*
ENROLMENT:						
Structured clinical intake assessment (eligibility screen)	X					
MINI-7 PTSD module	X					
Informed consent	X					
Allocation		X				
INTERVENTIONS:						
Unified Protocol				◆——		
Prolonged Exposure				◆——		
ASSESSMENTS:						
MINI-7 Alcohol + Cannabis modules	X				X	X
MINI-7 Depression, Agoraphobia, Panic, GAD, SAD modules			X		X	X
CAPS-5			X		X	X
Sociodemographic			X			
PCL-5			X	X	X	X
LEC-5			X			
GAD-7			X		X	X
PHQ-9			X		X	X
AUDIT			X		X	X
AQoL 6D			X		X	X
ITQ			X		X	X
SAPAS			X			
OASIS				X		
ODSIS				X		
Service Use Questionnaire						X
CSQ					X	

Abbreviations: MINI-7 = Mini International Neuropsychiatric Interview-7; CAPS-5 = Clinician Administered PTSD Scale for DSM-5; LEC-5 = The Life Events Checklist for DSM-5; PCL-5 = PTSD Checklist for DSM-5; PHQ-9 = The Patient Health Questionnaire 9; GAD-7 = The Generalized Anxiety Disorder Scale-7; AUDIT = The Alcohol Use Disorders Identification Test (AUDIT); AQoL-6D = Assessment of Quality of Life Scale – 6 dimension version; ITQ = The International Trauma Questionnaire; SAPAS = The Standardized Assessment of Personality – Abbreviated Scale; CSQ = Client Satisfaction Questionnaire-8; OASIS = Overall Anxiety Severity and Impairment Scale (OASIS); ODSIS = Overall Depression Severity Impairment Scale (ODSIS).

measuring PTSD severity, and has demonstrated excellent reliability and validity [40].

Mini International Neuropsychiatric Interview-7 (MINI-7) [41]. The MINI-7 is a short structured diagnostic interview based on DSM-5 and ICD-10 classifications of psychiatric disorder. Each module provides a dichotomous outcome of yes/no to detect for the presence of symptoms and diagnosis of a particular disorder. The MINI-7 will be used for two purposes: (1) to screen and assess disorders specific to inclusion/exclusion criteria to determine eligibility to the trial (PTSD, alcohol and cannibis use disorder modules); and (2) to assess for the presence of comorbid disorders (major depressive disorder, agoraphobia, panic disorder, generalized anxiety disorder, social anxiety disorder modules). The MINI has been shown to have strong psychometric properties, with sensitivity and specificity above 0.70 for modules used in the present study, as well as high inter-rater and test-retest reliability [41].

Life Events Checklist for DSM-5 (LEC-5) [42]. The LEC-5 is a 17-item self-report measure designed to screen for exposure to, or witnessing of, potentially traumatic events in a participant's lifetime [42]. It assesses exposure to 16 events known to be associated with PTSD. The LEC will be used to identify index event(s) that are linked to PTSD symptoms.

Demographics. Demographic questions pertaining to age, gender, years of education, relationship status, current study/employment, prior psychological history and current medication use for sleep or mental health difficulties, will be asked. These will be included in the pre-treatment assessment only. At 6-month follow-up only, data will be collected on any medications, psychological therapies or other mental health interventions participants have received since receiving treatment.

Structured clinical intake assessment (eligibility screen). This intake assessment is delivered over the phone by a clinical research assistant/clinician, focused on assessing inclusion and exclusion criteria. Risk and safety to self and others are assessed within the intake interview prompted by screening questions such as: "Has it been so difficult lately that you have had thoughts about hurting yourself or taking your own life?"; and "Have you had thoughts about harming someone else?". Psychosis and mania are assessed via questions such as: "Have you ever seen or heard things that others could not?"; and "Have you ever held abnormal beliefs or thought that your thoughts were being controlled by someone else?"; and "Do you ever feel abnormally and persistently high, hyper, elevated, expansive or irritable in mood?". Cognitive impairment is assessed via questions such as: "Did you ever have a head injury resulting in loss of consciousness?"

PTSD Checklist for DSM-5 (PCL-5) [43]. The PCL-5 is a 20-item scale that measures severity of DSM-5 PTSD symptoms. Participants rate items (e.g., "In the past month, how much were you bothered by: Repeated, disturbing, and unwanted memories of the stressful experience?") on a 5-point Likert scale ranging from 0 = 'Not at all' to 4 = 'Extremely'. Scores are summed to produce a total score ranging from 0 to 80, with higher scores reflecting more symptoms of PTSD. The PCL-5 is a psychometrically sound measure of PTSD symptoms, and has strong reliability and validity [44].

Patient Health Questionnaire (PHQ-9) [45]. The PHQ-9 is a nine-item scale designed to measure severity of depression symptoms. Participants rate items (e.g., "Over the last 2 weeks, how often have you been bothered by: Little interest or pleasure in doing things?") on a 4-point Likert scale ranging from 0 = 'Not at all' to 3 = 'Nearly every day'. Scores are summed to produce a total score ranging from 0 to 27, in which higher scores are indicative of higher depression symptomatology. It has good psychometric properties, with high reliability and validity [46].

Generalized Anxiety Disorder Scale (GAD-7) [47]. The GAD-7 comprises seven items measuring anxiety symptom severity. Participants rate items (e.g., "Over the last 2 weeks, how often have you been bothered by: Feeling nervous, anxious, or on edge?") on a 4-point Likert scale ranging from 0 = 'Not at all' to 3 = 'Nearly every day'. Scores are summed to produce a total score ranging from 0 to 21, in which higher scores are indicative of higher anxiety symptomatology. Using a threshold score of 10, the GAD-7 has high sensitivity at 89% and specificity at 82% for GAD [48].

Assessment of Quality of Life Scale – 6 dimension version (AQoL-6D) [49]. The AQoL-6D is a measure of quality of life and consists of 20 items where respondents indicate their level of functioning in the areas of independent living, relationships, mental health, coping, pain and senses. Participants rate items on a 5-point Likert scale ranging from 1 = 'Never' to 5 = 'Nearly all the time', and items can be summed to form a score for each of the six dimensions. The AQoL-6D has excellent psychometric properties and is a suitable basis for generating utility values for the economic evaluation of a wide range of health programmes [50].

Alcohol Use Disorders Identification Test (AUDIT) [51]. The AUDIT consists of 10 items which measure alcohol consumption, dependence symptoms, and the personal and social harm reflective of drinking. Participants rate items on a 5-point Likert scale, (e.g., "How often do you have six or more standard drinks on one occasion?", where 0 = 'Never' and 4 = 'Daily or Almost daily'). Responses to items are summed to produce a total AUDIT score (see Ref. [51] for details). The AUDIT shows good reliability and validity across a number of populations [51].

The International Trauma Questionnaire (ITQ) [52]. The ITQ is a self-report measure that assesses complex PTSD symptomatology. Participants rate 18-items (e.g., "How much have you been bothered by that problem in the last month: Feeling jumpy or easily startled?") on a 5-point Likert scale ranging from 0 = 'Not at all' to 4 = 'Extremely'. Items 1–6 are summed to create a dimensional score of PTSD symptoms, while items 10–15 are summed to provide a score of disturbances in self-organisation (DSO), and items 16–18 capture functional impairment. Research indicates the ITQ reliably captures the distinction between PTSD and DSO symptomatology characteristic of complex PTSD [52]; as well as reliably measures clinically significant treatment-related change in ICD-11 PTSD and Complex PTSD [53].

Standardized Assessment of Personality – Abbreviated Scale (SAPAS) [54]. The SAPAS is a brief and simple 8-item self-report screening instrument for personality disorder. Items correspond to a descriptive statement about the person (e.g., "In general, do you trust other people?") and scored 0 = 'No' or 1 = 'Yes'. Scores are summed to produce a total score ranging between 0 and 8. A cut-off score of 3 has been found to correctly identify the presence of DSM-IV personality disorders in 90% of cases, and the SAPAS has a sensitivity of 0.94 and specificity of 0.85 [54]. This measure will be included in the pre-treatment questionnaire only.

Client Satisfaction Questionnaire-8 (CSQ-8) [55]. The CSQ-8 is a self-reported measure of clients' satisfaction with their treatment. Participants rate items (e.g., "How would you rate the quality of service you have received?") on a 4-point Likert scale ranging from 1 to 4, where descriptors differ between items, and scores are summed to produce a total score ranging from 8 to 32, with higher scores indicating greater satisfaction. Research demonstrates that the CSQ-8 has high internal consistency and evidence shows it is useful as a brief global measure of client satisfaction [55].

2.8.1. In-treatment measures

Overall Anxiety Severity and Impairment Scale (OASIS) [56]. The OASIS is a 5-item brief self-report measure of anxiety experienced by the repsondent over the past week. Items assess frequency and intensity of anxiety symptoms, functional impairment related to anxiety symptoms, as well as behavioral avoidance. Participants rate each item (e.g., "In the past week, how much has anxiety interfered with your social life and relationships?") on a 5-point Likert scale ranging from 0 to 4, where descriptors differ between questions, and scores are summed to produce an overall score ranging from 0 to 20, with higher scores indicating greater anxiety severity and impact. Psychometric evaluations of the OASIS have indicated high internal consistency, excellent test–retest reliability, and convergent and discriminant validity in clinical and non-clinical samples [57,58].

Overall Depression Severity Impairment Scale (ODSIS) [59]. The ODSIS is a 5-item brief self-report measure of depression experienced by the respondent over the past week. Items assess frequency and intensity of depression, interference with social life and relationships, and impairment due to depression-related loss of interest and difficulty engaging in activities. Participants rate each item (e.g., "In the past week, how often have you felt depressed?") on a 5-point Likert scale ranging from 0 to 4, where descriptors differ between questions, and scores are summed to produce an overall score ranging from 0 to 20, with higher scores indicating greater depression severity and impact. The ODSIS has demonstrated excellent internal consistency, good convergent and discriminant validity in samples of outpatients with emotional disorders, undergraduate students and community-based adults [59].

Assessment fidelity of the CAPS-5 will be conducted by an independent assessor. All CAPS-5 assessments will be audio-recorded and five percent will undergo fidelity rating.

2.9. Study registration and ethics

This trial was prospectively registered with the Australian New Zealand Clinical Trials Registry, Trial ID (ACTRN12619000543189) with an anticipated date of first participant enrolment on 9 April 2019. The study has received ethical approval by the University of Melbourne Human Research Ethics Committee (2022-12463-24940-11). The most recent study protocol is Version 9, dated 15 June 2021. Alterations to the protocol were communicated to the Data and Safety Monitoring Board (DSMB) for approval, and then submitted for approval to the University of Melbourne Human Research Ethics Committee and communicated to the Australian New Zealand Clinical Trials Registry.

2.10. Data monitoring committee and clinical governance

A Data and Safety Monitoring Board (DSMB) has been established to monitor adverse events, comprising an expert trial methodologist, statistician and provider. The DSMB will review and provide direction for study protocols and a DSMB charter determines rules for reporting adverse events and for stopping the trial. The DSMB will receive six-monthly reports about the trial. The trial will also be supported by Clinical Governance procedures of the Phoenix Australia Traumatic Stress Clinic including access to a Consultant Psychiatrist and Clinical Services Director, and a weekly psychiatric oversight intake and treatment review process, to ensure the safety of participants in the trial. In any situations where providers feel that treatment continuation may not be appropriate for a participant based on their clinical judgment, they will bring this to the clinical oversight committee for discussion.

3. Discussion

PTSD is a serious psychiatric disorder associated with high levels of disability and impairment [17]. While there are evidenced-based treatments available such as PE, there are a number of limitations associated with trauma-focused treatments such as high non-response and high drop-out rates [9,10]. Furthermore, these PTSD specific treatments fail to adequately address comorbidity. Studies that test the efficacy of non-trauma focused treatments are required in order to determine their benefit as alternative evidence-based treatments for PTSD.

A transdiagnostic treatment for PTSD may provide an alternative for those clients and providers who prefer non-trauma-focused treatment that addresses the range of psychiatric disorders and symptoms presenting post-trauma, utilizing a mechanistic approach that targets underlying emotion regulation. This study proposes that a transdiagnostic treatment, UP, which demonstrates a strong evidence base for treating a range of psychiatric disorders [15] and some preliminary evidence for its efficacy in treating PTSD [26], may be an alternative to trauma-focused treatments such as PE.

To our knowledge, this is the first RCT comparing UP to the gold standard PE in a community sample with PTSD. The IMPACT trial has several strengths, including the trial design being a non-inferiority RCT comparing the active condition (UP) to the current gold standard (PE); using assessor administered PTSD assessments for the primary outcome; inclusion of a follow up to test maintenance of treatment effects; a PTSD diagnosis as an inclusion; and minimal exclusion criteria allowing participants to enter the trial who have current PTSD from a trauma/s occurring at any point in their lifetime (including childhood), and from any trauma meeting DSM-5 criteria. As the trial does not exclude a complex trauma sample, it is likely able to provide robust evidence for the utility of such evidence-based treatments, which are often criticized for lacking 'real world' effectiveness with 'real world' clients.

This study has some limitations. Due to the lack of available and relevant data, we were unable to use empirically derived non-inferiority margins, and instead using precedent as a justification for the chosen margins. Even though the IMPACT trial may determine that UP is a credible alternative to trauma-focused treatments such as PE, there might not be significant power to detect treatment differences in levels of comorbid mental health diagnoses. In addition, pending outcomes of the IMPACT trial and other similar trials, further research may be warranted to determine if the hypothesized UP mechanisms such as emotion avoidance can account for potential reductions in PTSD symptoms when receiving UP.

In conclusion, if the IMPACT trial finds UP to be as efficacious as PE, there is the potential for an alternative non-trauma-focused evidence-based intervention to provide much needed treatment for people with PTSD. There is also the potential for mental health providers to develop skills in a manualized treatment that can be used with their clients with PTSD and with other mental health disorders, thus enabling training and treatment delivery to be more time and cost effective. From this perspective, UP has the potential to support clinical decision making in presentations of PTSD comorbidity, allowing treatment to be delivered for differential and multiple diagnoses in a single transdiagnostic protocol.

Trial status

Ethics approval was received in February 2019. Recruitment is open and data will be collected till the end of 2023. The trial was registered with the Australian New Zealand Clinical Trial Registry under the ID ACTRN12619000543189.

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Author contributions

W.L. – Trial design, project leadership, writing; K.C. – Project administration; M.W.G – Trial design, clinical supervision, writing, data analysis, supervision; K.F. – Trial design, clinical supervision; K.M. – Trial provider; A.P. – Trial provider; N.D. – Project administration, clinical interviewing; S.A. – Data curation, project administration; H.O. – Trial provider; A. P. – Trial provider; J.K. – Clinical interviewing; P.B. – Clinical interviewing; F.H. – Trial support, funding acquisition; A.L. – Funding acquisition; M.N. – Trial support, funding acquisition; MOD – Project conceptualization, funding acquisition, resources, methodology, writing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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