

Statistical Analysis Plan:

Comparative Mechanisms (Moderators, Mediators) of Psychosocial
Treatments of Chronic Pain

NCT 06044649

September 18, 2023

Statistical Analysis Plan

Study Aim 1: Identify specific and shared mediators. Evidence for specific mediators would show that: (1) putative specific mediators (in CBT: for example behavioral activation and pain control beliefs; in ACT: for example, pain acceptance and self-compassion; in EAET: for example, emotional approach coping and attributions of pain to the brain rather than body) will change primarily in the relevant treatment; (2) show in lagged analyses that mediator changes precede improvements in outcomes primarily in the relevant treatment; and (3) outcome improvements will be accounted for by changes in treatment-specific mediators. Evidence for shared mediators would emerge for mediators that change with treatment and that precede and predict subsequent changes in outcomes across multiple treatments. In the event that shared mediators are identified, analyses will determine which mediators are critical and strongest across the treatments.

Analyses for Aim 1. Mixed models will initially test whether changes in mediators occur differentially across treatment groups. Linear mixed-effects models will explore putative mediators across program timepoints examining treatment condition, time, and Time x Treatment condition interactions as fixed effects. Next, we will examine whether between-session changes in mediators (e.g., behavioral activation, pain acceptance, emotional approach coping) predict subsequent changes in outcome variables, but not vice versa, as well as whether such changes occur differentially across treatment conditions. Variance in putative mediators will be decomposed into within-subject and between-subject components, which will be used as predictors of outcomes in separate linear mixed models. Additionally, cross-lagged models reversing this procedure and predicting mediator scores with person mean-centered lagged deviations in outcomes will establish temporality of the association between mediators and outcomes.

Study Aim 2: Identify moderators and moderated mediators. We will test hypotheses based on the Limit, Activate and Enhance (LA&E) model, which describes potential moderators of different treatments. We expect that people: (1) high in pain catastrophizing will respond best to CBT; (2) low in catastrophizing and/or high in experiential avoidance will respond best to ACT; (3) low in alexithymia and/or with a trauma history will respond best to EAET. Further, we expect moderators to exert effects on outcomes via hypothesized mediators (e.g., high pain catastrophizers will respond to CBT via increases in behavioral activation).

Analyses for Aim 2. Baseline characteristics hypothesized to serve as moderators of the relationship between treatment condition and outcomes (e.g., trauma history) will be examined using Treatment x Moderator x Time interactions. Significance of these interaction terms would indicate that differences in outcome time trends across treatment conditions exist based on these moderating factors. Such moderation effects would also be further tested by examining estimates via separate linear mixed models for treatment groups, exploring moderator x time simple effects to determine uniqueness of moderation to specific treatment conditions, as well as pairwise comparison linear mixed models when appropriate. In addition, we will examine whether associations between lagged mediator changes and outcome changes over the course of treatment depend on hypothesized moderators (moderated mediation effects). We will include a moderating factor as a moderator of the relationship between lagged mediator changes and outcomes via the addition of lagged Mediator x Moderator x Time interaction terms in linear mixed models. Such linear mixed models will be explored separately by treatment condition to reduce model complexity.

Study Aim 3: Comparative efficacy of psychosocial treatments. Although the examination of mediators and moderators (and moderated mediation) of CBT, ACT, and EAET is the primary aims of this trial, we also wish to test the comparative efficacy of the interventions with each other and to TAU. Based on the current comparative literature on psychosocial interventions, we hypothesize that the three treatments will all be superior to TAU control, but that the three treatments will not differ among themselves on the two primary outcomes (pain severity and pain interference) at the primary endpoint (post-treatment) as well as the secondary endpoint (6-month follow-up).

Analyses for Aim 3: Linear mixed models will compare the four treatment conditions to detect differential slopes of change from baseline to post-treatment on the two primary outcomes and again on the secondary outcomes. Significant omnibus (4-arm) tests will be followed by post-hoc comparisons of each treatment with TAU as well as each treatment with each other. Appropriate alpha correction for multiple comparisons will be used. Similar analyses will compare treatment conditions from baseline to 6-month follow-up. The magnitude of effects for between- and within-condition will be calculated for all comparisons, based on change scores corrected for test-retest reliability of the measure.