Study Title: An Integrative Technology Approach to Home-based Conjoint Therapy for PTSD

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Statistical Analysis Plan

Analytic Considerations:

a) Analysis sets. The primary analyses use the ITT sample, which consists of all participants who were randomized. Couples that terminated treatment early were invited to complete follow-up assessments and their data were included in the ITT analyses.

b) Treatment of missing data. Missing data were imputed using multiple imputation procedures in the Blimp software, which uses fully Bayesian model-based specification. In order to explore potential reasons for data missingness, dichotomous treatment status (i.e., non-completion versus completion) was modeled using logistic regression and all subject-level characteristics predicting the retention outcome were included as auxiliary variables in the imputation model.

c) Adjustment for multiple outcomes. To address possible Type I errors due to multiple dependent variables, we specified a priori the primary measures corresponding to the stated a priori hypotheses within the following specified domains: PTSD symptoms, relationship satisfaction and functional impairment. For secondary analyses using additional outcome variables within a given domain, we will report both unadjusted p-values and adjusted p-values using a Tukey-type correction for multiple outcomes. Secondary outcomes and exploratory analyses will be evaluated qualitatively in terms of consistency with primary results and conservatively in terms of statistical significance of results. Sensitivity of study results to adjustment for multiplicity of outcomes will be evaluated.

Preliminary Analyses: All statistical procedures were conducted using SPSS and R software programs. Preliminary analyses examined distributional characteristics of study variables to provide a description of the study sample and to allow for assessment of randomization. Demographic, baseline clinical characteristics of the individual Veteran and/or couple dyad, and other putative prognostic variables (e.g., relationship characteristics) were compared for imbalance across the treatment groups using analysis of variance for continuous variables and chi-square tests for categorical variables. Where, despite randomization, significant group differences at baseline were identified, those variables were included as covariates in sensitivity analyses.

Data reliability checks. Reliability and data reduction issues were addressed using descriptive and inferential statistics. Tests of scale reliability will use the Internal Consistency Method and Cronbach's alpha will be calculated. Cronbach's alpha of 0.80 or greater will be considered evidence of sufficient instrument reliability. As described in Assessment and Treatment Fidelity Monitoring, CAPS reliability will be examined via inter-rater agreement.

Analyses for Efficacy Outcomes (Aim 1):

Statistical approach. Longitudinal trajectories of outcomes from baseline to mid-treatment, post-treatment, 3-month, and 6-month follow-up time points were compared using multivariate, multilevel GLMM, which accommodates a wide range of distributional assumptions, including continuous (e.g., CAPS scores, PCL, CSI, IPF, BDI-II, STAXI), categorical/dichotomous (e.g., diagnostic status, treatment completion), ordinal, and count predictors. For outcomes including both members of dyads (e.g., relationship

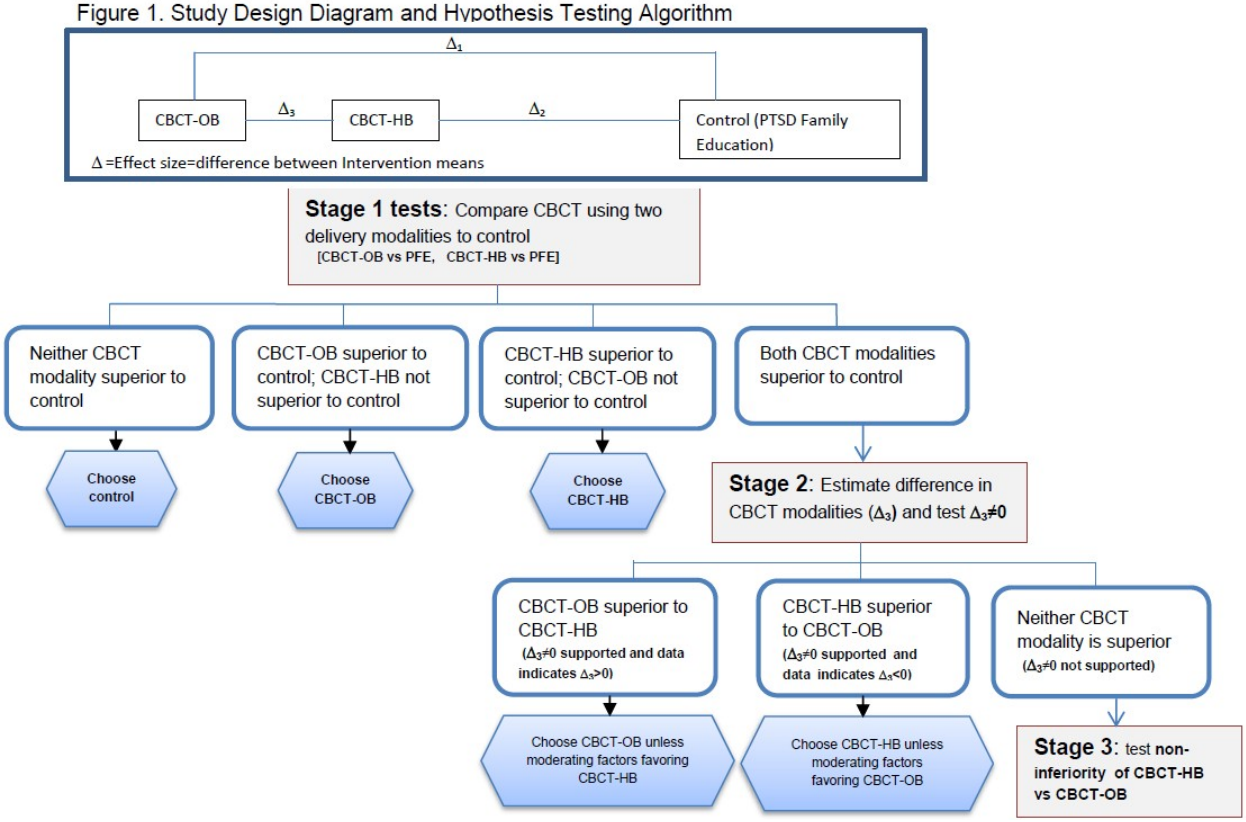
satisfaction), GLMM allowed for modeling multilevel data, as well as for testing other possible cluster effects due to correlation between participants within therapists through inclusion of random effects in the model.

Model construction. The primary efficacy outcome variables are (1) Veteran-reported PTSD symptom reduction (CAPS severity scores), (2) Veteran- and partner-reported relationship distress (CSI) and (3) Veteran-reported functional impairment (IPF). Secondary variables include PTSD diagnostic status (CAPS), self- reported PTSD symptoms (PCL), depression scores (BDI-II), anger (STAXI-2), and relationship conflict (CTS-2). Variability in scores for each of the primary and secondary outcome measures were examined individually in a series of separate multilevel models. Piecewise/spline models were used to estimate separate slopes for the treatment period and the follow-up period. Each model examined the predictive value of the primary variable of interest: (1) two time slopes (treatment and follow-up; fixed effects), (2) treatment group (fixed effects), and (3) the cross-level interactions of time*treatment group (fixed effects). Baseline scores on the dependent measure were also included as a model covariate, to control for their effect. For couple-based outcomes (e.g., CSI scores), between-dyad, within-dyad, and mixed variables were coded in the model as described by Campbell and Kashy, 2002. As preliminary analyses indicated an imbalance both relationship length and partner-reported CSI scores between treatment groups, subsequent sensitivity models were conducted to control for their effects. For Stage 1 analyses (Aim 1a), pairwise unadjusted and covariate-adjusted differences in least squares means for each outcome variable were compared at mid-treatment, post-treatment, and at the 3- and 6-month follow-up time points using appropriate model

contrasts (i.e., CBCT-OB vs. PFE and CBCT-HB vs. PFE). Next, in Stage 2 analyses (Aim 1b), unadjusted and least squares adjusted means from the GLMM contrast comparisons, along with corresponding 95% CIs, provided estimates of the magnitude (effect sizes), direction, and statistical significance of differences in outcome measures for CBCT-OB compared to CBCT-HB. Progression to a fully powered non-inferiority trial (Stage 3, Figure 1) was determined to occur only if both CBCT delivery modalities are superior to the control intervention (Aim 1a and b). This study provides necessary input information (e.g., variance-covariance and effect size estimates) for the design of the subsequent non-inferiority study.

Primary Analyses for Process Outcomes (Aim 2): Measures of treatment process outcomes include treatment satisfaction (as measured by the CSQ), therapeutic alliance (for both participants' and therapists' WAI), safety issues (tracked by clinical team) and general program management issues tracked by the coordinator. Additional measures of feasibility are recruitment (percentage who agree to participate out of number approached), compliance (percentage of session attended, percentage of homework assignments completed), and retention (dropout rate). The GLMM framework (with appropriate link functions for dichotomous, ordinal, categorical, and continuous feasibility outcomes) was used to compare the feasibility outcomes between each of the three treatment conditions at the post-treatment time point.

Figure 1. Study Design Diagram and Hypothesis Testing Algorithm



Reference

Campbell, L., & Kashy, D. A. (2002). Estimating actor, partner, and interaction effects for dyadic data using PROC MIXED and HLM: A user–friendly guide. *Personal Relationships*, *9*(3), 327-342. doi: 10.1111/1475-6811.00023