Study Protocol and Statistical Analysis Plan

Official Title: Metacognitive Therapy and Intolerance-of-Uncertainty Therapy for Generalized Anxiety Disorder in Primary Care: Randomized Controlled Pilot Study

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Study Protocol

Objective. Feasibility and preliminary efficacy of two psychological treatments based on cognitive-behavioral therapy – metacognitive therapy (MCT) and intolerance-of-uncertainty therapy (IUT) – for primary care patients with a principal diagnosis of generalized anxiety disorder in Stockholm, Sweden are investigated in a pilot study using a randomized controlled trial design. The purpose of the study is to examine the feasibility of a full-scale randomized controlled trial. Design. Randomized controlled pilot trial. Methods. Research questions primarily concern recruitment, assessment, and therapist competence and adherence. Secondary research questions concern treatment efficacy. Primary treatment outcome measure is total scores on the Penn State Worry Questionnaire (PSWQ).

Statistical Analysis Plan

Statistical analyses are performed using the SPSS (Version 27, SPSS Inc., Chicago, IL). Proportions, means, and standard deviations (SDs) are calculated for feasibility measures. Differences in session attendance between the IUT and MCT conditions are investigated using an independent t-test and differences in dropout with a Fisher's exact test. In the preliminary evaluation of treatment effects, multilevel modeling is used to estimate the effects of time and of time by condition on continuous outcome measures from the pre-treatment to the post-treatment assessment and from the post-treatment to the follow-up assessment. The maximum likelihood method is used to estimate model parameters. Different covariance structures are tested. Models are built in a stepwise fashion, starting with a basic model with a fixed intercept, then adding random parameters (intercept and slope), and finally adding a time by group interaction term to the model. Each model's fit to observed data is evaluated with the likelihood ratio test. Models with significantly better fit than previous models are retained. Standardized effect sizes for between-group effects at mid-treatment, post-treatment,

and follow-up are calculated as Cohen's *d* for multilevel models, using the SD for the pooled sample at pre-treatment and the pooled sample SD at post-treatment (for post-treatment to follow-up). For between-group effect size estimations, the beta coefficient (difference in change trajectories between treatments) is multiplied by treatment duration at mid-treatment, the average treatment duration, or the follow-up duration, and then divided by the pooled SD of observed values at pre-treatment or post-treatment. For model-based *d*, 95% confidence intervals are calculated. In keeping with the principle of intention-to-treat, data from all participants are used in the multilevel models.

Treatment response is assessed with the reliable change index (RCI), which is calculated using the internal consistency reliability of the PSWQ and the sample SD of this measure at pre-treatment. An RCI of $z \geq -1.96$ indicates reliable improvement, whereas an RCI of $z \geq 1.96$ indicates reliable deterioration. Differences in improvement and deterioration between conditions at the post-treatment and follow-up assessment are investigated with chi-square tests or Fisher's exact tests.

To assess recovery rates, two procedures are employed that combine statistically reliable change with clinically meaningful change. First, an RCI of 7 points and a cut-off of 53 points on the PSWQ as used in a previous study are applied. Second, the same RCI and a cut-off of 47 points as used in another previous study are applied. Differences in recovery rates between groups at post-treatment and follow-up assessment are investigated with chi-square tests or Fisher's exact tests.