Official Title:
Group-Based Acceptance and Commitment Therapy Versus Active Control in University Students With Emotional Symptoms

NCT:
CE2025/37

Statistical Analysis Plan

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Detailed Description for ClinicalTrials.gov

ACT-EMA-RCT (Protocol CE2025/37)

This is a randomized, parallel-group, double-masked (outcome assessors and data analysts) clinical trial comparing a manualized, group-based Acceptance and Commitment Therapy (ACT) protocol with a non-directive group therapy (NDT) active control in university students with moderate-to-high emotional symptomatology. Approximately 48 participants will be randomized 1:1. The study employs a multimethod assessment strategy comprising three tiers: (a) traditional self-report questionnaires at four time points (pre-treatment, post-treatment, 4-week follow-up, and 12-week follow-up), (b) weekly repeated measures throughout the study period, and (c) daily Ecological Momentary Assessments (EMA). This design enables both nomothetic (group-level) and ideographic (individual-level) evaluations of treatment efficacy and allows a direct comparison of sensitivity across measurement frequencies.

All participants will complete a baseline assessment period of approximately four weeks (Weeks 2–5) prior to the start of the intervention (Week 6), during which daily EMA and weekly measures will be collected in the absence of treatment. This baseline period serves as an intra-individual reference against which treatment-phase changes are evaluated. The intervention spans five weekly sessions (Weeks 6–10), followed by a post-treatment assessment (Week 10–11) and continued daily and weekly monitoring through Week 15 (4-week follow-up). A final follow-up assessment using traditional measures will be conducted at Week 23 (12-week follow-up).

Analysis of traditional pre–post–follow-up measures

Changes in PHQ-9, GAD-7 (and the composite PHQ-ADS index), and PIL-Test scores across the four assessment points will be analyzed using Bayesian linear mixed-effects models with fixed effects for condition (ACT vs. NDT), time (pre-treatment, post-treatment, 4-week follow-up, 12-week follow-up), and their interaction. Random intercepts will be specified for participants to account for individual differences in baseline levels. Within-group and between-group effects will be evaluated using Bayesian Evidence Ratios (ER), computed as the posterior probability of the effect in the expected direction divided by its complement, and interpreted following the Kass and Raftery (1995) scale (ER > 3: moderate evidence; ER > 10: strong evidence; ER > 30: very strong evidence; ER > 100: decisive evidence). Effect sizes will be reported as Cohen's *d* with 95% credible intervals. These analyses will follow the intention-to-treat (ITT) principle, with all randomized participants included regardless of treatment completion. Weakly informative priors will be used throughout to regularize estimation.

Analysis of weekly repeated measures

Weekly assessments of PHQ-4, CCFI, and RNT-3 will be analyzed using Bayesian hierarchical linear models implemented in the R package *brms* (Bürkner, 2017). A piecewise specification with two segments will model the data: the first segment captures the baseline trend, and the second captures the treatment effect through an immediate level change at treatment onset and a gradual within-treatment trend. The corresponding condition-by-phase interactions will be included to estimate differential effects between ACT and NDT. Random effects for the intercept, level change, and trend parameters will be specified at the participant level, enabling individual-level inference alongside group-level estimates. Given the relatively short length of the weekly time series, no autoregressive error structure will be included in these models, as reliable estimation of the autocorrelation parameter may be compromised with few data points per participant. Weakly informative priors will be used throughout to regularize estimation.

Analysis of daily ecological momentary assessments

Daily EMA data (PHQ-4, CCFI, RNT-3) will be analyzed using the same Bayesian hierarchical piecewise framework described above, with one key difference: a first-order autoregressive error structure, AR(1), will be included to account for the temporal dependency inherent in densely sampled daily time series. This additional component models the day-to-day carryover in residuals that is expected when measurements are taken at short intervals.

Primary inferential strategy for intensive longitudinal data

For both the weekly and daily data, the primary inferential strategy will evaluate the integrated total treatment effect at the endpoint of the treatment phase. This quantity is defined as $\Delta(T) = \beta level + \beta trend \times T$, where T corresponds to the last treatment session (Swaminathan et al., 2014). It estimates the total cumulative change from the baseline level to the end of treatment by combining the immediate level shift and the accumulated gradual trend into a single posterior quantity. This integrated approach avoids the inflated false-positive rates associated with evaluating level and trend components separately and has been shown to provide superior statistical power to detect treatment effects in comparable designs. Treatment effects will be quantified as Between-Case Standardized Mean Differences (BC-SMD; Hedges et al., 2012, 2013), which are directly comparable to Cohen's *d* in between-subjects designs.

Sensitivity analyses

Several pre-specified sensitivity analyses will be conducted: (a) a per-protocol analysis excluding participants who attended fewer than four of the five intervention sessions, (b) a comparison of results obtained from daily versus weekly data to evaluate the differential sensitivity of each measurement frequency to treatment effects, and (c) examination of the impact of EMA compliance rates on the stability of parameter estimates.

Missing data

For the Bayesian hierarchical models, missing observations in the daily and weekly time series will be handled implicitly through the likelihood-based estimation framework, which accommodates unbalanced data structures without requiring imputation. Participants with at least 50% of expected daily EMA observations will be included in the daily analyses. Weekly data compliance is expected to be higher given the lower respondent burden. For the traditional pre–post–follow-up analyses, missing data will be handled through the same Bayesian estimation framework, using all available observations.

Qualitative analysis

Semi-structured interviews conducted at post-treatment by blinded evaluators will be analyzed using thematic analysis to explore participants' subjective experiences of psychological change, perceived mechanisms of change, and intervention acceptability.

Software

All Bayesian analyses will be conducted using R (version 4.5 or later) with the *brms* package (Bürkner, 2017), which interfaces with Stan for Hamiltonian Monte Carlo sampling. Convergence will be assessed using the $\hat{R}$ diagnostic (threshold < 1.05) and visual inspection of trace plots.

References

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