Data analysis plan

”Exposure-based Cognitive Behavior Therapy vs Traditional Cognitive Behavior Therapy for Fibromyalgia” (ClinicalTrials.gov identifier: NCT05058911)

A rudimentary data analysis plan formed part of the study protocol. This more detailed plan was completed on May 24th, 2022; prior to the completion of the follow-up assessments, and prior to the extraction of efficacy data for the primary publication.

Blinding

Inferential analyses will be conducted by a person who is blind to treatment condition.

Management of missing data

Missing data will be imputed using hierarchical multiple imputation by chained equations in 20 datasets using the predictive mean matching method. The following predictors will be used: time point, the Fibromyalgia impact questionnaire (FIQ), the Brief pain inventory – short form severity scale (BPI-SF), the 2-item Generalized anxiety disorder scale (GAD-2), the 2-item Patient health questionnaire (PHQ-2), the 12-item World health organization disability assessment schedule 2.0 (WD2-12), the Godin-Shephard leisure-time physical activity questionnaire (GSLTPAQ), the Psychological inflexibility in pain scale – avoidance subscale (PIPS-avoid), the Pain catastrophizing scale (PCS), age, post-secondary education, sick leave (yes/no), the credibility/expectancy scale, the number of modules opened (1-8), and missing assessments (0-10). Imputation will be conducted separately for each treatment.

Management of dropouts

The primary analysis will adhere to the intention-to-treat principle, which means that data from all participants including dropouts will be used. For each treatment, we will report the number of dropouts understood as participants that stopped replying (for at least 3 weeks without resuming treatment) or explicitly wanted to discontinue the treatment and then did so. We will also report the primary reason for dropouts, as rated post treatment by the therapist.

Main efficacy outcome

Primary model (intention-to-treat): This model will include the fixed effects of time, treatment, and time×treatment. Random effects will be the intercept and time (slope). There will be unstructured covariance over the random effects, and we will use the residual covariance structure that results in the best model fit as indicated by the BIC (at least AR1 and unstructured will be evaluated). The primary analysis will be the significance test of the time×treatment coefficient (α=0.05).

Treatment completion

Treatment completion is operationalized as having initiated at least five modules out of eight.

Standardized effect sizes

Standardized within-group effects will be calculated as the model-implied mean change, divided by the observed standard deviation for the pooled (total) sample at the beginning of the corresponding time period. Standardized between-group effects will be calculated as the difference between within-group effects up to the endpoint of interest.

Treatment response as a dichotomous variable
Frequencies for the following dichotomous outcomes will be presented per treatment:

- Minimal clinically important improvement (FIQ at least -14% from pre-treatment) [1]
- Minimal clinically important deterioration (FIQ at least +14% from pre-treatment) [1]
- Reliable improvement [2] based on the FIQ test-retest r of 0.81 [3] and the standard deviation for the pooled (total) sample
- Reliable deterioration [2] based on the FIQ test-retest r of 0.81 [3] and the standard deviation for the pooled (total) sample

References
1. Bennett RM, Bushmakin AG, Cappelleri JC, Zlateva G, Sadosky AB. Minimal clinically important difference in the fibromyalgia impact questionnaire. J Rheumatol. 2009;36(6):1304-11.
2. Jacobson NS, Truax P. Clinical significance: a statistical approach to defining meaningful change in psychotherapy research. J Consult Clin Psychol. 1991;59(1):12-9.
3. Hedin PJ, Hamne M, Burckhardt CS, Engstrom-Laurent A. The Fibromyalgia Impact Questionnaire, a Swedish translation of a new tool for evaluation of the fibromyalgia patient. Scand J Rheumatol. 1995;24(2):69-75.