Statistical Analysis Plan

Name of Study: Memory and Fear Study (Fear of Memory Loss Study)

NCT Number: NCT04821960

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Study Information

Research questions

1. What is the efficacy of a 3-week mindfulness and behavioral activation program to reduce fear and avoidance of memory loss in community-dwelling older adults? We predict a reduction in fear and avoidance of memory loss across weeks. We also predict that participants who receive psychoeducation, mindfulness and behavioral activation training (experimental group) will exhibit a greater reduction in fear and avoidance than those who receive psychoeducation and mindfulness only (active control group).

2. What is the efficacy of a 3-week mindfulness-based program to reduce fear of dementia and improve psychosocial functioning in community-dwelling older adults? We predict that fear of dementia will decrease and psychosocial functioning will increase (mood, quality of life, social engagement and self-rated memory) across weeks.

Hypotheses

1. Fear and avoidance of memory loss will be lower at follow-up compared to baseline. Fear and avoidance scores will be lower in the experimental group than the active control group.

2. Fear of dementia, anxiety and self-reported memory failures will be lower at follow-up compared to baseline. Quality of life and social engagement will be higher at follow-up compared to baseline.

Data Description

Datasets used

Reducing Fear and Avoidance of Memory Loss (REFRAME) Study scores (PIs: Griffith, Farina and Bennett).

Data availability

Data will be fully anonymised and will be made available on clinicaltrials.gov.

Data access

The data are not public and are accessible by the study team only.

Data identifiers
No response

Access date
Data will be made available as soon as they are collected and checked.

Data collection procedures
Participants are 80 cognitively healthy adults aged 55 years and older residing anywhere in the United States with elevated fear and avoidance of memory loss (≥61 total score on the Fear and Avoidance of Memory Loss scale). Exclusion criteria were diagnosis of neurodegenerative condition (e.g., Alzheimer's disease), impaired cognitive function (< 18 score on the Montreal Cognitive Assessment), unstable medical condition, severe depression (≥ 12 score on the Geriatric Depression Scale), current participation in psychotherapy, current substance use disorder and inadequate vision or hearing to interact with study material.

Eligibility was determined by an online screening questionnaire followed by an additional phone screener. Eligible participants were randomly assigned to experimental or active control groups. Both groups completed questionnaires (pre-intervention, post-intervention and 4-week follow-up) and three weeks of self-administered program materials. The experimental group completed psychoeducation, mindfulness and behavioral activation exercises. The active control group completed psychoeducation and mindfulness only. All data was collected and stored on REDCap.

Codebook
The codebook is attached.

Variables

Manipulated variables
No response

Measured variables
Primary outcome measure:
Fear and Avoidance of Memory Loss (FAM) scale. 23-item scale with scores between 23-115. Higher scores indicate higher fear and avoidance of memory loss.

Secondary outcome measures:
Fear of Alzheimer's Disease Scale (FADS). A 30-item scale with scores between 0-120. Higher scores indicate higher fear of developing Alzheimer's disease.

Patient Reported Outcome Measures Information System-29 (PROMIS-29) quality of life, social functioning and anxiety subscales, measured in T score units. Higher scores indicate higher quality of life, social functioning and anxiety, respectively.

World Health Organisation Well-Being Index (WHO-5). 5-item scale assessing overall well-being with scores between 0-25. Higher scores indicate higher well-being.

Memory Failure Scale (MFS). 12-item scale with scores between 12-60. Higher scores indicate more frequent reported memory lapses.

Unit of analysis
No response

Missing data
No response

Statistical outliers
No outliers will be dropped from analyses, but all variables will be inspected for the shape of distributions and potential univariate outliers.

Sampling weights
No response

Knowledge of Data

Prior Publication/Dissemination
The protocol for the study was published in 2021 (O'Loughlin et al, 2021).

Prior knowledge
We looked at preliminary data from eight participants (FAM scores only) before the data analysis plan was finalised. No changes were made to the analysis plan after viewing these data. *

Analyses

Statistical models

Primary analysis:
Fear and Avoidance of Memory Loss (FAM) will be used as the dependent variable. In a mixed model, Time (T) and time-by-program group (Tx) interaction terms will be independent variables, for each time point after baseline where treatment is expected to have an effect. This is consistent with a response profile analyses (Fitzmaurice, G., Davidian, M., Verbeke, G., & Molenberghs, G. (Eds.). (2008). Longitudinal data analysis, CRC press). To test the effect of treatment, the full model will be compared to a reduced model where all effects including treatment are removed from the model.

Full model:
FAM = T1 (baseline) + T2 (week 1) + T3 (week 2) + T4 (week 3) + T5 (follow-up) + T2:Tx + T3:Tx + T4:Tx + T5:Tx

Reduced model:
FAM = T1 (baseline) + T2 (week 1) + T3 (week 2) + T4 (week 3) + T5 (follow-up)

The full and reduced models (estimated using ML) will be compared to test the significance of all terms involving treatment. Reduced models comparing post-treatment to baseline within group will test the effect of time.

Secondary analyses:
Similar models will be used with Fear of Alzheimer's disease (FADS), quality of life (QoL), social engagement (Soc), anxiety (Ax) and self-reported memory failures (MF) as the dependent variable, and Time (T) and program group (Tx) as independent variables.

Effect size
Power was estimated in G*Power with the following assumptions: medium effect size (f) = 0.25, Type I error rate = 0.05, sample size = 80, groups = 2, repeated measures = 6, correlation among repeated measures = 0.5, and nonsphericity correction epsilon = 1.0 (i.e., no correction).

Statistical power
Assumptions yielded high power (99%). We anticipated losing some participants to follow-up and investigated a nonsphericity epsilon of 0.5; power remained at 92% even with the more conservative epsilon and with n = 40. Although these power estimates are high, a goal of this study is to determine the effect sizes (within-subjects and across groups) for future randomised controlled trials.

Inference criteria
We will use a two-tailed alpha of .05 for all tests.

Reliability and Robustness testing
We will conduct regression diagnostics (e.g., inspection of residuals, multicollinearity) and conduct additional analyses as needed, such as using REML in addition to ML for model-fitting, and considering robust regression approaches.

Exploratory analysis
Exploratory analyses will include testing if (1) fear of COVID-19 (COVID-19 anxiety scale) and (2) patient beliefs about the intervention (Patient Global Impression of Change) impact its efficacy. All exploratory analyses will be labelled as such.