

DREAMER Pilot Study Protocol and Statistical Analysis Plan

Study Title: Defining REsilience And Mindfulness Effects in Rheumatoid Arthritis (DREAMER)

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Study Protocol

Background and Rationale

Rheumatoid arthritis (RA) is a chronic immune-mediated inflammatory disease associated with persistent pain, fatigue, impaired function, and reduced quality of life. Despite advances in pharmacologic therapy, many patients continue to experience substantial symptom burden and express interest in adjunctive nonpharmacologic approaches. Psychological stress is implicated as a contributor to symptom severity and disease activity in RA, yet prospective interventional data remain limited.

Mindfulness-based stress reduction (MBSR) has demonstrated benefits for stress reduction and chronic pain in multiple conditions, but evidence for its impact on RA outcomes remains mixed and limited by small samples. The DREAMER study is designed as a staged pilot program to refine and test an RA-adapted mindfulness intervention and to generate feasibility, acceptability, and preliminary mechanistic and clinical data to inform a future fully powered randomized controlled trial.

Objectives

Primary Objective

- To evaluate the **acceptability and feasibility** of Mindfulness-Based Stress Reduction augmented for Rheumatic Diseases (MBSR-RD) compared with treatment as usual (TAU) among adults with RA.

Secondary / Exploratory Objectives

- To assess intervention adherence and safety.
- To obtain preliminary estimates of change in psychological stress, stress resilience, and RA clinical outcomes to inform future trials.

Study Design

This is a **pilot, randomized, controlled, parallel-group trial** conducted over two sequential waves. Participants are randomized 1:1 to MBSR-RD or treatment as usual.

- **Design:** Randomized, assessor-blinded pilot trial. Outcome assessors conducting physician disease activity assessments will be blinded to treatment assignment.
- **Allocation ratio:** 1:1
- **Duration:** 8-week intervention with post-intervention assessment at approximately 8–9 weeks.
- **Setting:** UCSF Osher Center for Integrative Health and UCSF Parnassus campuses, with most intervention components delivered remotely via Zoom.

Participants

Inclusion Criteria

- Age ≥ 18 years
- Physician-confirmed diagnosis of rheumatoid arthritis
- Access to a web-enabled device with internet

Exclusion Criteria

- Inability to provide informed consent
- Current regular mindfulness practice (>20 minutes/week)
- Prior participation in MBSR
- RA disease activity in remission (RADAI-5 < 1.5 at screening)
- Inability to participate in an intensive 8-week online mindfulness course
- Unavailability during scheduled intervention dates

Interventions

MBSR-RD (Intervention Arm)

Participants assigned to MBSR-RD participate in an 8-week mindfulness-based stress reduction course delivered by certified MBSR instructors trained in RA-specific adaptations. The intervention retains the standard MBSR structure while incorporating modifications informed by feedback from patients with RA who previously participated in the standard MBSR course. Adaptations include modifications to yoga poses for physical limitations and flexibility in meditation duration.

Components include:

- Weekly 2.5-hour group sessions (remote)
- One day-long silent retreat (remote)
- Daily home practice (~ 45 minutes/day)
- Practice logs to track adherence

Treatment as Usual (Control Arm)

Participants assigned to TAU continue their usual medical care. They are asked to refrain from initiating new mindfulness programs during the study period. No changes to disease-modifying antirheumatic drug therapy are mandated as part of the study.

Outcome Measures

Primary Outcomes

- **Acceptability:** Patient satisfaction assessed using the Client Satisfaction Questionnaire, 8-item version (CSQ-8; score range 8–32; higher scores indicate greater satisfaction).

Secondary Outcomes

- **Study retention:** Operationalized as the proportion of randomized participants who complete the final follow-up assessments.
- **Adherence:** MBSR course attendance.

Other Pre-Specified Outcomes (Exploratory)

- Change in **RA disease activity** from baseline to 8 weeks will be assessed via three separate validated measures:
 - Clinical Disease Activity Index (CDAI)
 - Disease Activity Score in 28 joints using the erythrocyte sedimentation rate (DAS28-ESR)
 - Rheumatoid Arthritis Disease Activity Index (RADAI-5).
- Change in **patient-reported outcomes** from baseline to 8 weeks: PROMIS Pain Interference (4-item), PROMIS Fatigue (4-item), PROMIS Sleep Disturbance (8-item), PROMIS Depression (8-item), and PROMIS Global Mindfulness (13-item).
- **Psychological measures:** Perceived Stress Scale, 10-item (PSS-10); Brief Resilience Scale (BRS).

Assessments occur at baseline and at approximately 8 weeks post-randomization.

Sample Size

We aim to enroll approximately **40 adults with RA** (approximately 20 per arm). Sample size is selected to evaluate feasibility and acceptability rather than efficacy and is not based on statistical power to detect clinical effects.

Ethical Considerations

The study is approved by the UCSF Institutional Review Board. All participants provide informed consent prior to participation. The trial is conducted in accordance with ethical principles for human subjects research.

Statistical Analysis Plan

Analysis Populations

All quantitative analyses are planned for the **intent-to-treat population**, defined as all randomized participants.

General Analytic Approach

Given the pilot nature of the study, analyses will primarily be **descriptive and exploratory**. The study will not be powered to test intervention efficacy.

Primary Outcomes Analysis

The primary outcome will be **acceptability**. A modified version of the 8-item Client Satisfaction Questionnaire (CSQ-8) will be used to evaluate acceptability of the mindfulness program by patients in the treatment group. A few of the words in the original CSQ-8 were changed to make the questions relevant to the MBSR-RD program. Scores on the CSQ-8 range from 8-32, with higher scores indicating greater satisfaction and a score of at least 24 indicating adequate satisfaction. We will report the number and percentage of MBSR-RD participants with CSQ-8 scores ≥ 24 , consistent with adequate satisfaction.

Secondary Outcomes Analysis

The secondary outcomes represent **study feasibility**, which will be operationalized as a) MBSR Course Attendance and b) Study Retention. These feasibility metrics will be summarized using descriptive statistics (means, standard deviations, and proportions) as follows:

- **MBSR Course Attendance:** Adequate intervention adherence will be operationalized as the percentage of participants randomized to MBSR-RD who attend at least six of the eight group classes.
- **Study retention** will be defined as the proportion of randomized participants who complete the final follow-up assessments.

Exploratory Outcomes Analysis

Though this study will not be powered to test efficacy, we will conduct exploratory analyses using clinical outcome variables—including measures of RA disease activity (RADAI, CDAI, and DAS28-ESR) and patient-reported outcomes (via PROMIS measures)—to generate preliminary data for a future larger efficacy trial.

- Change from baseline to post-intervention will be calculated for all clinical outcomes.
- PROMIS measures will be converted to T-scores using PROMIS scoring algorithms provided by the PROMIS Assessment Center, with scores standardized to a population mean of 50 and a standard deviation of 10. PROMIS measures included in this analysis will include Pain Interference (4-item), Fatigue (4-item), Global Mindfulness (13-item), Sleep Disturbance (8-item), and Depression (8-item).
- The estimated mean net difference from baseline to the end of the intervention period between randomization arms (MBSR-RD vs. TAU) will be calculated using linear mixed models with separate models for each outcome. Models will include the following fixed effects: timepoint, study arm, and their interaction, and random effects for person nested within class group to account for the correlation of repeated measures within individuals and of participants within classes.