Analysis Plan

Development and Feasibility of Mindfulness Based Pain Reduction

NCT 04980612

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Overall Analysis Approach: Preliminary analysis will be performed to confirm that key data variables are clean and complete. As this is not an efficacy study, we do not expect statistical significance but will estimate standardized effect sizes (Cohen's *d* with 95% confidence intervals). The principal analysis will use intent-to-treat methods, in which all observations will be included for individuals, regardless of adherence to the treatment protocol. As a secondary analytic method, we will also perform-as-treated analyses with those who attend at least 5 of 8 planned group sessions. We recognize the challenge of *missing data*. We will take concerted steps to limit missing data. We have extensive experience in study retention; in a current study of a mindfulness intervention by Dr. Hecht (R61 AT009333), outcome assessment was completed in 97% of participants at 12 weeks. Finally, where appropriate, we will perform multiple imputation methods to address the effects of missing data if indicated.

Hypothesis Testing:
Hypothesis 1: **The MBPR intervention is feasible and acceptable, and** *Hypothesis 2*: **Recruitment and randomization are feasible**: We plan detailed assessments of feasibility and acceptability of the intervention, recruitment, and randomization. Domains and measures we will address are summarized in the table below.

Table : Feasibility and acceptability assessment

Feasibility Questions	**Feasibility Measures**
Can I recruit my target population?	Number screened per month; number enrolled per month; average time to enroll enough participants to form classes. Number of enrolled participants from each outreach method.
Can I randomize my target population?	Proportion of eligible screens who enroll during randomization phase. Acceptability from participant interviews.
Can I keep participants in the study?	Retention rates for study measures; reasons for dropouts.
Will participants do what they are asked to do?	Proportion of participants who attended at least 6 sessions. Average number of MBPR sessions attended; reasons for missed sessions. Average minutes of daily/weekly meditation practice (using data from the "Insight Timer" app)
Can the treatment be delivered per protocol?	Fidelity assessments using MBI:TAC and intervention content checklist, both using video recordings of teachers.
Are the assessments too burdensome?	Proportion of planned pre- and post-intervention assessments completed, duration of assessments, and quantitative and qualitative participant feedback.
Are the treatment conditions acceptable to participants?	Acceptability ratings; qualitative participant assessments; reasons for dropouts.
Are the treatment conditions credible?	Perceived benefit at end course and likelihood of recommending to a friend or family member (net promoter score) at the end of the course during randomized phase.
Is EMA assessment of pain intensity/interference feasible?	Proportion of EMA assessments responded to (we hypothesize that this will be > 80%). Qualitative data on acceptability.
Is assessment of meditation adherence with app feasible?	Correlation of meditation sessions measured with Insight Timer with self-report of practice during the same week; qualitative interviews.

Hypothesis 3: **MBPR participants will improve in key pain outcomes**. Our planned primary outcome measures in future trials will be pain interference (RTF) and pain intensity (NRS); pain acceptance and quality of life will be secondary outcomes. We will conduct exploratory hierarchical linear modeling[155] to examine the extent to which participants experience changes in pain interference at the end of the intervention and at 6-month follow-up (separate for EMA and questionnaires). For both pain outcome variables (pain interference, pain intensity) separate multilevel models will be estimated. The pain measure models will take into account that the present data set is organized within three different levels and that single observations (i.e., rating at a particular time during the day)(Level 1) are nested within days (i.e., rating on day 1-7 in week 1 or 8 of intervention)(Level 2), which are nested in variations of MBPR per

course (Level 3). As this is not an efficacy study, we will primarily report standardized effect sizes (Cohen-*d*) with 95% confidence intervals, based on standard deviation at baseline. Similar models for secondary outcomes will include pain acceptance, and quality of life as outcomes, each in a separate correlation.

Hypothesis 4: **Assessment of pain intensity/interference with a smartphone delivered EMA is feasible and correlates with standard pain outcome measures.** Feasibility/acceptability measures are noted in the table above. We will assess the correlation of our EMA measures with the Numeric Pain Rating Scale for pain intensity, and pain interference rating. We predict a correlation of >.7. We will also perform qualitative assessment to get participants assessment of where the two approaches are similar, and where they may get differing responses.

Hypothesis 5: **Assessment of meditation practice adherence is feasible using a smartphone app**. At the 8-week assessment period, we will include questions about meditation practice over the prior week and compare this with the results from use of the Meditation Insight Timer data. We will ask further questions about any sessions that were not recorded using the app, and reasons for not recording. This information will be analyzed after each group, and refinements made if needed in participant instructions and other steps to encourage use of the app as consistently as possible.

Hypothesis 6: We will conduct **exploratory analyses** to test for correlations between changes in pain outcomes and scores on the PCS, TSK, CPAQ, MAIA, and FFMQ using regression models.