A randomised controlled trial of mindfulness-based cognitive therapy: study protocol and design highlighting phase 1 and phase 2 translational research elements

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INTRODUCTION

Major Depressive Disorder (MDD) is a common condition that tends to recur. Effective interventions targeting relapse, particularly in people with a history of three or more episodes of depression, could dramatically reduce the point prevalence of the condition [1].

Mindfulness-based cognitive therapy (MBCT) is a group-based program that was developed specifically with the aim of reducing recurrence rates of MDD by increasing patients' ability to recognize and disengage from depression-related ruminative thought patterns through the cultivation of mindfulness. A recent meta-analysis [2] confirmed a highly significant reduction in relapse for MBCT compared to treatment as usual (TAU) for people with three or more episodes of depression, with effects at least equal to maintenance antidepressant medication.

The work reviewed by Piet and Hougaard [2] could be seen as meeting the core requirements of phase 1 translational research in which the safety and efficacy of treatments for selected volunteers are tested in randomized controlled trials (RCTs) [3]. As well as continuing the phase 1 agenda, there is a need now to move to phase 2 translational research – the application of MBCT within real-world settings with a view to directly informing policy and clinical practice.

Phase 1 Priorities

1. Clarifying the mechanisms of action underpinning MBCT, especially the putative mediation role of meditation practice, mindfulness and rumination.
2. Examining the effect of MBCT in the context of anxiety disorders, which are frequently comorbid with depression.
3. Preventing and assessing for resentful demoralization, a potential bias whereby the belief by participants in the control group that they are not receiving the desirable treatment has negative affects on outcome.

Phase 2 Priorities

1. Investigating the transportability of MBCT.
2. Examining the combined role of MBCT and antidepressants.
3. Extending the length of follow up.
4. Exploring the cost effectiveness of MBCT.

Aims

The aim of this effectiveness study is to examine the clinical impact and health economics of MBCT where efforts are made to assess for and prevent resentful demoralization and under real-world conditions – within a population representative of the intended target audience, that is, people with a history of 3 or more episodes of depression regardless of their antidepressant regimen. For a long-term prevention, evidence of a longer duration of effect is more desirable than the 12-18 month periods so far examined and so a 2-year follow-up is implemented in this study. The portability of MBCT professional training has not been assessed and this project will investigate outcomes from a novel training program using instructors who may not have a long-standing and deep knowledge of the intervention provided.

The secondary aim of the study is to provide for a detailed examination of the mechanisms by which this form of therapy may prevent depressive relapse, with this examination structured in a way so as also to progress the understanding of the clinical applicability of MBCT. MBCT may act to reduce relapse through a number of mechanisms outlined in the model shown in Figure 1, which was used to guide our choice of measures through the research plan that follows.

METHOD

Design and analysis

This is a prospective, single-blind RCT comparing MBCT with a supported self-monitoring condition called "DRAM (Depression Relapse Active Monitoring)". All participants receive DRAM and TAU with half the sample randomized to also receive MBCT.

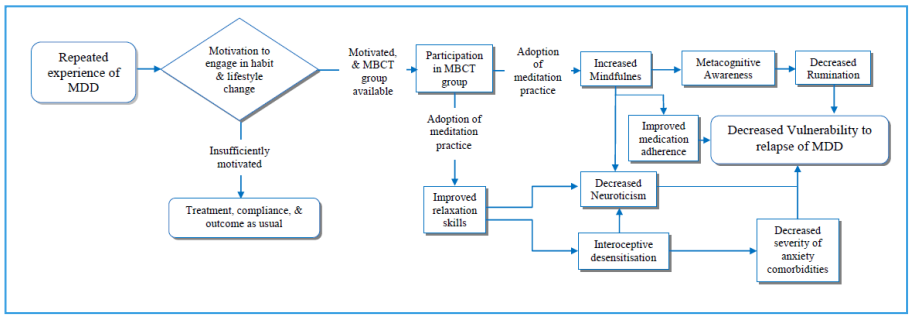

Figure 1: Proposed mechanisms for MBCT

Figure 2: DRAM card

Interventions

MBCT: MBCT is a manualized program [4] delivered by an instructor in 8 weekly 2-hour group training sessions involving up to 10 clients; optional 3-monthly 'booster sessions' are also delivered. Sessions and homework incorporate various mindfulness practices including meditation.

Instructor training: MBCT instructors were selected from a locally-developed MBCT professional training program. Trainees embarking on the program are not assumed to have a meditation practice. The program involves an initial 8-week MBCT therapy group adapted for the training situation. This is followed by a break for a minimum period of 1 month so that participants can consolidate their personal practice. The program ends with an intensive teacher development retreat over 3 full days (total of 44 hours training).

DRAM: To reduce the discrepancy between groups in treatment expectation and thus mitigate against the risk of triggering resentful demoralisation, we developed DRAM as an alternative to a TAU-only control. DRAM comprises supported self-monitoring of depressive symptoms through the monthly research assessments. To support DRAM, participants were provided with a manual and a wallet-sized card with the core self-monitoring questions and key contact numbers (Figure 2).

Participants

Participants were recruited through private and public community health and mental health services and notices in the press. Power analysis indicated a recruitment target of 102 participants per group. Inclusion criteria into the study included: three previous episodes of MDD; aged between 18-75 years; fluent in English; not currently depressed. Randomization was stratified by medication (currently taking antidepressants and/or mood stabilisers: yes/no); site of referral (primary/specialist); diagnosis (bipolar disorder: yes/no) and gender.

Measures

Diagnostic and clinical outcome: Composite International Diagnostic Interview 2.1; Patient Health Questionnaire-2/9 (PHQ 2/9) [5-6].

Economic outcomes: General-practice Users Perceived-need Inventory [7]; Service Utilisation; Days absent from work; Employment status; Assessment of Quality of Life [8]; Work and Social Adjustment Scale [9].

Secondary outcomes: State-Trait Anxiety Inventory [10]; International Personality Item Pool [11] - Neuroticism and Openness to experience subscales; Five Facet Mindfulness Questionnaire [12]; Ruminative Response Scale [13]; locally-developed measures of mindfulness practice and medication adherence.

Patient expectations: Credibility/Expectancy Questionnaire [14]; Belief about relapse.

Procedure

Following an intake assessment, eligible participants were randomized to treatment condition. A schedule of rater-blinded follow up assessments was undertaken for 26 months from the commencement of MBCT. The PHQ 2/9 was administered monthly as part of DRAM; the remaining instruments were administered 3 monthly or annually.

Statistical analysis

Intention-to-treat analyses include chi-square or Fisher's exact test for proportions, t-test or Mann-Whitney test for continuous variables, Kaplan Meier survival for time to relapse and repeated-measures ANOVAs and mediation analyses for secondary outcomes.

DISCUSSION

This study is a 'real-world' examination of MBCT as an intervention designed to prevent depressive relapse. Set within a phase 1/2 translational research framework, its findings will assist in determining the role that MBCT can play in routine clinical practice. The novel training for therapists delivering MBCT in the trial is is relatively brief and does not assume any background knowledge of meditation. It is potentially an efficient and replicable way of providing professional training in MBCT to enable more rapid dissemination in the community. Positive results from this trial not only would have implications for ease of translation into the community and its transportability to new settings but also for extending our understanding on how much training is necessary for effective delivery of MBCT.

The need to balance competing questions of interest is an important consideration in the design of RCTs. The recommended comparator for a health economic analysis is a TAU control [15], while an active alternative treatment is likely to be most informative for studies investigating mechanisms of action. As an effectiveness trial, a health economic analysis is an important aspect of the present study so favoring the selection of a TAU control in the design. We had, however, the added need to control for the potential bias of resentful demoralization and so the self-monitoring intervention DRAM was introduced as an addition to TAU. This is likely to mean that episodes of depression are picked up and treated earlier than would be the case without such monitoring and possibly lead to a relative weakening of the between-group effects for standard symptom measures. Nevertheless, we predict that the impetus to access treatment prompted by DRAM will, if anything, increase between-group differences in the health economic evaluation and so this will form a critical focus for examination.

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