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A preference-based multi-site randomized comparative effectiveness trial (CET) of Mindfulness-Based Cancer Recovery (MBCR) vs. Tai Chi/Qigong (TCQ) for cancer survivors

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ABSTRACT

Purpose: A growing number of cancer survivors suffer high levels of distress, depression and stress, as well as sleep disturbance, pain and fatigue. Two different mind-body interventions helpful for treating these problems are Mindfulness-Based Cancer Recovery (MBCR) and Tai Chi/Qigong (TCQ). However, while both interventions show efficacy compared to usual care, they have never been evaluated in the same study or directly compared. This study will be the first to incorporate innovative design features including patient choice while evaluating two interventions to treat distressed cancer survivors. It will also allow for secondary analyses of which program best targets specific symptoms in particular groups of survivors, based on preferences and baseline characteristics.

Methods and significance: The design is a preference-based multi-site randomized comparative effectiveness trial. Participants (N = 600) with a preference for either MBCR or TCQ will receive their preferred intervention; while those without a preference will be randomized into either intervention. Further, within the preference and non-preference groups, participants will be randomized into immediate intervention or wait-list control. Total mood

Abbreviations: BP, blood pressure; BPI, Brief Pain Inventory; BRS, Baroreceptor Sensitivity; CET, comparative effectiveness trial; C-SOSI, calgary symptoms of stress inventory; EQ-5D, EuroQol Five Dimensions Questionnaire; FACIT-Sp, Functional Assessment of Chronic Illness Therapy - Spirituality; FACT-F, Functional Assessment of Cancer Therapy - Fatigue; FACT-G, Functional Assessment of Cancer Therapy – General; HRV, Heart Rate Variability; MBCR, Mindfulness-Based Cancer Recovery; MBSR, Mindfulness-Based Stress Reduction; MBT, Mind-body therapy; MINDSET, Mindfulness versus supportive expressive therapy; POMS, Profile of mood states; PSQI, Pittsburgh sleep quality index; PTGI, Post-Traumatic Growth Inventory; RCT, randomized controlled trial; SET, supportive expressive therapy; STS, Sit To Stand; TCQ, Tai Chi/Qigong; TL, telomere length; TUG, Timed Up and Go; QL, quality of life

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disturbance on the Profile of mood states (POMS) post-intervention is the primary outcome. Other measures taken pre- and post-intervention and at 6-month follow-up include quality of life, psychological functioning, cancer-related symptoms and physical functioning. Exploratory analyses investigate biomarkers (cortisol, cytokines, blood pressure/Heart Rate Variability, telomere length, gene expression), which may uncover potentially important effects on key biological regulatory and antineoplastic functions. Health economic measures will determine potential savings to the health system.

1. Introduction

People diagnosed with cancer face many difficulties, including high levels of distress, anxiety, depression and symptoms such as fatigue, pain and sleep disturbance [1,2] which often persist well into survivorship [3,4]. There is also a limited but growing body of evidence supporting the efficacy of a range of mind-body therapies (MBTs) in alleviating these and other symptoms [5,6]. MBTs are therapies that harness mental practices and processes including breath work and movement to affect both psychological and physical function, often inducing the relaxation response, which is in opposition to the fight-or-flight reaction. These include mediation, yoga, imagery, relaxation, hypnosis, biofeedback, Tai Chi and Qigong, among others. While many MBTs have shown efficacy in helping cancer patients and survivors cope, most have been compared with usual care, not active controls or other viable interventions. There are also very few supportive care studies in cancer which integrate patient choice as a design feature.

One exception is the MINDSET trial in which we compared MBCR to supportive expressive group therapy (SET) and a control group (a one-day stress management seminar) for treating distressed breast cancer survivors [7]. In that large randomized clinical trial we demonstrated that while both active interventions were better than usual care, MBCR was superior to SET over a wide range of outcomes [7,8], and benefits persisted over a full year of follow-up [9]. We also found that treatment preference at baseline had an effect on outcomes, in that those women who were assigned to their chosen intervention (MBCR, SET or the control condition) improved more over time on quality of life (QL) and stress symptoms than those who did not receive their preferred treatment [8]. Similarly, a systematic review on the influence of preference on clinical outcomes in acupuncture trials reported that preference was associated with reduced program attrition, with most studies demonstrating an effect of preference on outcome, though few were clinically significant [10]. Hence, in the current study we will include patient preference in the study design and simultaneously evaluate the most efficacious MINDSET trial treatment compared with Tai Chi/Qigong (TCQ).

We chose these two therapies because both have evidence of efficacy for treating distress and improving QL in cancer care [5,6,11]. Both have also shown potential to affect important biomarkers and clinical outcomes. Both MBCR and TCQ are similarly rooted in meditative practice; however, MBCR places greater emphasis on cognitive/mental practice whereas TCQ is more explicitly a physical movement-based practice. Evidence for the efficacy of both interventions when compared to usual care is growing (see Methods), but these and other MBTs are rarely evaluated in the same study, and/or compared against one another.

We will specifically address the overarching question of which MBT works for whom, when, and for treating which symptoms? The first question is whether mental or physical mind-body practices are better than usual care, and secondly if being able to choose a practice makes a difference. Next, we ask how the primary and secondary outcomes are moderated by baseline characteristics. This requires a more sophisticated research approach that includes preference-based group allocation and has the ability to test moderation of effects by baseline characteristics, symptomatology, and treatment credibility. This pragmatic design promotes both internal and external validity.

2. Methods

2.1. Objectives and hypotheses

2.1.1. Objective 1

In the context of a preference trial, to compare the impact of either MBCR or TCQ with a waitlist control condition, on total mood disturbance (primary outcome).

Hypothesis 1. When randomly assigned, both MBCR and TCQ will be superior to wait list control pre-post intervention.

Hypothesis 2. When chosen by participants, both MCCR and TCQ will be superior to wait list control pre-post intervention.

Hypothesis 3. (exploratory): Mean between-group pre-post differences in total mood disturbance for both MBCR and TCQ will be larger in the preference vs. randomized groups.

2.1.2. Objective 2

In the context of a preference trial, to compare the impact of either MBCR or TCQ with a waitlist control condition, on secondary outcomes (psychological function, physical function, quality of life).

Hypothesis 4. When randomly assigned, both MBCR and TCQ will be superior to wait list control on secondary outcomes pre-post intervention.

Hypothesis 5. When chosen by participants, both MCCR and TCQ will be superior to wait list control on secondary outcomes pre-post intervention.

Hypothesis 6. (exploratory). Mean between-group pre-post differences in secondary outcomes for both MBCR and TCQ comparisons will be larger in the preference vs. randomized groups.

Hypothesis 7. (exploratory): MBCR groups will improve more on the psychological outcomes than TCQ; TCQ groups will improve more than MBCR on the physical outcomes.

2.1.3. Objective 3

In the context of a preference trial, to compare the impact of either MBCR or TCQ with a waitlist control condition and each other, on exploratory biomarker outcomes (cortisol, Heart-Rate Variability (HRV) and blood pressure (BP), immune function, telomere length/telomerase, gene expression) pre-post intervention. No specific hypotheses are provided for these exploratory analyses.

2.1.4. Objective 4

To investigate the health economic impact of MBCR and TCQ from pre- to post-intervention and follow-up in terms of total healthcare costs, effectiveness and cost-utility.

Hypothesis 8. There will be a greater decrease in average total costs from baseline to post-intervention in the MBCR and TCQ randomized groups compared to waitlist controls.

Hypothesis 9. The difference in changes in average effectiveness from baseline to post-intervention will not vary in the preference versus no preference groups. We speculate that all active intervention groups will