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Research paper

# Patients with a preference for medication do equally well in mindfulness-based cognitive therapy for recurrent depression as those preferring mindfulness

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ABSTRACT

*Background:* Previous studies have suggested that patients' treatment preferences may influence treatment outcome. The current study investigated whether preference for either mindfulness-based cognitive therapy (MBCT) or maintenance antidepressant medication (mADM) to prevent relapse in recurrent depression was associated with patients' characteristics, treatment adherence, or treatment outcome of MBCT.

*Methods:* The data originated from two parallel randomised controlled trials, the first comparing the combination of MBCT and mADM to MBCT in patients preferring MBCT ($n=249$), the second comparing the combination to mADM alone in patients preferring mADM ($n=68$). Patients' characteristics were compared across the trials ($n=317$). Subsequently, adherence and clinical outcomes were compared for patients who all received the combination ($n=154$).

*Results:* Patients with a preference for mADM reported more previous depressive episodes and higher levels of mindfulness at baseline. Preference did not affect adherence to either MBCT or mADM. With regard to treatment outcome of MBCT added to mADM, preference was not associated with relapse/recurrence ($\chi^2=0.07$; $p=.80$), severity of (residual) depressive symptoms during the 15-month follow-up period ($\beta=-0.08$, $p=.49$), or quality of life.

*Limitations:* The group preferring mADM was relatively small. The influence of preferences on outcome may have been limited in the current study because both preference groups received both interventions.

*Conclusions:* The fact that patients with a preference for medication did equally well as those with a preference for mindfulness supports the applicability of MBCT for recurrent depression. Future studies of MBCT should include measures of preferences to increase knowledge in this area.



## 1. Introduction

Major depressive disorder (MDD) is a common and highly debilitating mental disorder that is characterized by high rates of relapse or recurrence (Richards, 2011). To date, the most commonly used treatment to prevent future episodes of MDD is the use of maintenance antidepressant medication (mADM). Although there is evidence that mADM are more effective than placebo in reducing the risk of relapse (Borges et al., 2014; Kaymaz et al., 2008), adherence to mADM is generally low (Bockting et al., 2008) and the prophylactic effectiveness seems to decrease with the number of previous episodes (Kaymaz et al., 2008). Therefore, alternative preventive strategies have been developed. For example, Mindfulness-Based Cognitive Therapy (MBCT; Segal et al. (2012)) significantly reduces relapse risk in patients with three or more previous depressive episodes (Piet and Hougaard, 2011) and appears to be at least as effective as mADM in the prevention of relapse (Kuyken et al., 2008; Kuyken et al., 2015; Segal et al., 2010). This suggests that MBCT offers a viable alternative for patients preferring a psychological intervention to prevent relapse.

In general, practice guidelines recommend that patients'

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treatment preferences should play an important role in the selection of a treatment modality (American Psychiatric Association (APA), 2010). In the context of the acute phase of depression treatment, depressed patients have been shown to generally prefer psychological rather than pharmacological treatment (Steidtmann et al., 2012; van Schaik et al., 2004). This suggests that many patients with recurrent depression might prefer psychological treatment, such as MBCT, over mADM to prevent relapse/recurrence.

Treatment preferences seem to be related to treatment expectations and therefore, may contribute to adherence and outcomes as a non-specific therapeutic factor (Rutherford et al., 2010). Although several studies on the acute treatment of depression have examined the impact of preferences on outcome, results are inconclusive. A systematic review on treatment preferences in MDD concluded that preferences may positively affect treatment initiation and the therapeutic alliance, but have minimal impact on depression severity outcomes (Gelhorn et al., 2011). In contrast, a simultaneous meta-analysis indicated a small (Cohen's $d=0.31$) but significant benefit of preference-match in patients with psychiatric problems receiving psychological or pharmacological therapies (Swift et al., 2011). For the subset of studies specifically looking at depression ($k=12$), this effect was also small ($d=0.35$) but significant. The inconsistency in the literature on the effects of preference on treatment outcome may be related to differences in methodology. For example, in an RCT comparing behavioural activation and antidepressant medication, preference for psychotherapy influenced treatment outcome in terms of clinician-rated depression, but not self-rated depression (Moradveisi et al., 2014). In addition, the strength of patient preference on a continuous measure may be more predictive of outcome than preference-match as a categorical predictor (Raue et al., 2009).

Unlike most patient characteristics, preferences cannot be randomly allocated because of their intrinsic relationship with the received treatment. In this way, preferences can affect the external and internal validity of randomised controlled trials (RCTs) (Corrigan and Salzer, 2003). For instance patients with a strong preference for psychological treatment are likely to decline RCTs precluding their preference (van Schaik et al., 2004). Consequently, RCTs may underestimate the effect of preferences on outcome. In addition, preferences may affect the internal validity of a trial, for example because patients who receive a treatment concordant with their preference are less likely to drop out, show higher rates of attendance and have a better working alliance with the therapist (Elkin et al., 1999; Iacoviello et al., 2007; Kwan et al., 2010; Raue et al., 2009). These methodological problems related to preferences may lead to a gap between results obtained in RCTs and routine practice (TenHave et al., 2003).

To our knowledge, no studies have explicitly examined patient preferences and their possible relation with treatment adherence and treatment outcome in relapse/recurrence prevention of MDD. In two parallel randomised controlled trials (the first comparing the combination of MBCT and mADM to MBCT alone, the second comparing the combination to mADM alone), patients could choose to participate in either study, according to their preference for either mADM or MBCT. The current post-hoc study aims to investigate: (a) possible differences in demographic and clinical characteristics between patients with a preference for MBCT and those with a preference for mADM; (b) whether patients' preferences are associated with adherence to MBCT or adherence to mADM; and (c) whether patients' preferences are associated with relapse/recurrence risk, severity of depressive symptoms, or quality of life, over the 15 months follow-up. We had no specific a priori hypotheses with regard to possible differences in patients' baseline characteristics, but we expected MBCT treatment adherence and clinical outcome to be better for patients preferring MBCT than for patients preferring mADM.

## 2. Methods

### 2.1. Study design

The study design and procedures are presented in full in the published study protocol (Huijbers et al., 2012) and are summarised below. Originally we intended to conduct a three-armed RCT of MBCT alone, mADM alone or MBCT+mADM, but due to strong treatment preferences this turned out not to be feasible. Therefore we ended up conducting two parallel RCTs (see Fig. 1). Patients preferring MBCT participated in an RCT comparing the combination of MBCT and mADM to MBCT alone, i.e. with discontinuation of mADM (Huijbers et al., In press). Patients preferring to continue their mADM participated in an RCT comparing the combination of MBCT and mADM to mADM alone (Huijbers et al., 2015). This change in design enabled us to acknowledge patients' preferences while maintaining the experimental rigour of randomisation. In addition, it provided the opportunity to study the possible effect of treatment preference in depression relapse/recurrence prevention.

### 2.2. Participants and procedure

Patients were recruited in 12 secondary and tertiary psychiatric outpatient clinics across the Netherlands between September 2009 and January 2012. Patients were referred by mental health care professionals or recruited by advertisements in the media (TV, magazines and newspapers). Inclusion criteria were a history of at least three previous depressive episodes according to the Diagnostic and Statistical Manual of Mental Disorders-4th edition (DSM-IV), being in full or partial remission; currently treated with mADM for at least 6 months; 18 years of age or older; and Dutch speaking. The study was approved by the Medical Ethics Committee Arnhem-Nijmegen (nr. 2008/242) for all participating sites. After full explanation of the study, written informed consent was obtained from all participants. The study period was 15 months with assessments at 0 (baseline), 3, 6, 9, 12 and 15 months. For the possible differences between patients who preferred to participate in trial A (preference for MBCT) and trial B (preference for medication) we used data of all participants ($n=317$). For all others analyses we only used data from the participants who received the combination of MBCT and mADM ($n=121+33$).

### 2.3. Intervention: MBCT plus maintenance ADM (MBCT+mADM)

MBCT was delivered in 12 different centres across the Netherlands according to the, slightly adapted, protocol by Segal, Williams and Teasdale (Segal et al., 2002). It was delivered in groups of 8–12 participants and consisted of eight weekly sessions of 2.5 h plus one day of silent practice between the 6th and 7th session (Kabat-Zinn, 2013). Participants were encouraged to practice meditation at home for about an hour a day with the support of CDs.

For continuation of mADM, a minimum of one consultation with a psychiatrist was recommended. Psychiatrists were instructed to maintain or reinstate a therapeutic dosage of mADM, and recommendations to manage side effects were provided. Adherence to the mADM protocol was defined as using a therapeutic dose at each follow-up contact during the observed time period (using last observation carried forward for participants who did not complete all assessments).