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Does Mindfulness-Based Cognitive Therapy With Tapering Support Reduce Risk of Relapse/Recurrence in Major Depressive Disorder by Enhancing Positive Affect? A Secondary Analysis of the PREVENT Trial

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Objective: Mindfulness-based cognitive therapy (MBCT) is a viable alternative to maintenance antidepressant medication (M-ADM) to reduce risk of relapse/recurrence (RR) in recurrent depression, but its mechanism of action is not yet fully articulated. This secondary analysis of the PREVENT trial examined if MBCT with support to taper medication (MBCT-TS) reduces risk of RR in part by enhancing positive affect (PA). ***Method:*** In a single-blind, parallel, group randomized controlled trial, adults with ≥3 prior depressive episodes, but not currently in episode and who were taking M-ADM, were randomized to receive either MBCT-TS or ongoing maintenance M-ADM. The primary outcome was RR over 24-month follow-up. Levels of positive affect were assessed at intake and posttreatment. The original PREVENT trial was preregistered (ISRCTN 26666654), but this secondary analysis was not. ***Results:*** Four hundred and twenty-four individuals (predominantly female and of White British ethnicity) were recruited, with 212 randomized to each arm. MBCT-TS led to significantly greater PA relative to M-ADM at posttreatment assessment ($\Delta = 2.78$, 95% CI [1.47, 4.08], $p < .001$). RR was experienced during follow-up by 194 individuals (100 M-ADM; 94 MBCT-TS). Greater intake PA predicted a reduced hazard of RR across treatments ($p < .001$; hazard ratio = .96, 95% CI [0.94, 0.98]). In individuals who had not relapsed by posttreatment with complete data (121 M-ADM; 145 MBCT-TS), greater increase in PA from intake to posttreatment mediated reduced risk of subsequent RR ($p = .04$). ***Conclusions:*** These findings suggest that greater levels of PA predict reduced risk of RR and that MBCT-TS in part acts to protect from RR when withdrawing from M-ADM by increasing PA.

What is the public health significance of this article?

Depression has a chronic relapsing–remitting course for many individuals, and to optimize interventions to minimize the risk of relapse recurrence, it is important to further understand how current preventative treatments work. The current findings show that reduced levels of positive affect (PA) predict an increased risk of relapse/recurrence and that mindfulness-based cognitive therapy with support to taper from antidepressant medication (MBCT-TS) in part acts to reduce risk of relapse/recurrence by increasing levels of PA. This suggests that the protective effects of MBCT-TS could be further enhanced by more systematically targeting PA.

Keywords: mindfulness-based cognitive therapy, depression, positive affect, anhedonia

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Reflecting the fact that PREVENT is a large-scale definitive trial that included an embedded process evaluation within it, a range of other papers have been published from it. These include the trial protocol (Kuyken et al., 2010), the main trial outcome and health economic results (Kuyken et al., 2015a), a detailed report of the overall trial design and findings (Kuyken et al., 2015b), an individual participant data meta-analysis including PREVENT as one of the data sets (Kuyken et al., 2016), and a series of questionnaire validation studies focusing on the mindfulness (Five Facet Mindfulness Questionnaire) and emotion regulation (Cognitive Emotion Regulation Questionnaire) measures (Gu et al., 2016; McKinnon et al., 2022; M. J. Williams et al., 2014). The Dispositional Positive Emotions Scale positive affect data (the core focus of the present analysis) have been included in two previous studies. Dunn et al. (2022) examined how change in Five Facet Mindfulness Questionnaire factors relates to change in positive emotions (a cross-sectional mediation study). Cohen et al. (2023) built a multivariate prognostic model to predict response to mindfulness-based cognitive therapy versus antidepressant medication using a machine learning framework, which ended up including some of the Dispositional Positive Emotions Scale variables within it as part of the algorithm. The present study has a distinct and

continued

Depression is a prevalent, disabling mental health condition that results in significant individual, societal, and economic costs (Kessler et al., 2003; König et al., 2020; Moussavi et al., 2007). For many individuals, depression progresses from a discrete, episodic condition to a longer term condition with a relapsing–remitting course, often with incomplete recovery between episodes (Judd, 1997; Moriarty et al., 2020). There is a pressing need to develop effective preventative interventions that can minimize the risk of relapse/recurrence in those with a history of recurrent depression (RR).[1]

Maintenance antidepressant medication (M-ADM) remains the most common approach to reducing the risk of RR in recurrent depression (Geddes et al., 2003; Moriarty et al., 2020). While M-ADM is effective and acceptable for many, some do not benefit at all, or the benefit diminishes over time; for some the medication is associated with significant side effects; and for some adherence is poor (Cooper et al., 2007; Olfson et al., 2006). Moreover, some individuals have a clear preference to consider nonpharmacological approaches to manage their mental health (van Schaik et al., 2004) or wish to taper antidepressants after a sustained period of being free from depression. When individuals cease to take M-ADM, some are vulnerable to experiencing an RR. For example, the ANTLER trial randomized 478 depressed individuals taking M-ADM to ongoing M-ADM or placebo and found that the odds of experiencing a RR at 1-year follow-up were significantly greater in the placebo group (56%) compared with the M-ADM group (39%; Lewis et al., 2021). Moreover, those in the placebo group reported higher levels of anxiety and depression, a greater number of symptoms potentially related to withdrawal, and reduced mental health-related quality of life.

At the point individuals wish to consider ceasing M-ADM, they may therefore benefit from psychological interventions that can give them additional skills to minimize the risk of RR. One potential approach is mindfulness-based cognitive therapy (MBCT), a psychological group intervention that combines elements from cognitive therapy and mindfulness training to target cognitive mechanisms implicated in RR (Segal et al., 2012). Randomized controlled trials demonstrate that MBCT is effective at reducing the risk of RR in its own right, with equivalent protective effects to continuing with M-ADM (see reviews by Kuyken et al., 2016; Piet & Hougaard, 2011). The PREVENT trial further demonstrated that MBCT can also protect individuals from RR when they choose to stop taking M-ADM (Kuyken et al., 2015a). Four hundred twenty-four individuals with a history of recurrent depression, who were currently well and were taking a therapeutic dose of M-ADM, were randomized either to continue with M-ADM or to receive a course of MBCT with support to taper or discontinue their use of M-ADM. At 2-year follow-up, rates of RR were 47% in M-ADM and 44% in MBCT-TS, with no significant difference between them.

While the PREVENT trial establishes MBCT with tapering support (MBCT-TS) as a viable alternative to M-ADM for those with recurrent depression, many individuals do still experience RR following MBCT-TS, and there is a need to further optimize its efficacy. One way to further refine MBCT-TS is to better understand the mechanisms that bring about RR and to ensure that MBCT-TS successfully targets these mechanisms.

A critical component of depression is a reduced capacity to experience positive affect (PA), with anhedonia (a loss of interest and pleasure in previously enjoyable activities) being a core symptom of the disorder (Dunn, 2012, 2019). More marked anhedonia and/or reduced PA is associated with a greater risk of developing depression in the first place, reduced response to existing acute psychological and pharmacological treatments for depression, and greater depression severity at longer term follow-up (Khazanov & Ruscio, 2016; Shankman et al., 2010; Spijker et al., 2001; Uher et al., 2012). Clients report enhancing PA and reducing anhedonia as a key to full recovery from depression (Zimmerman et al., 2006). Current acute psychological and pharmacological treatments for depression struggle effectively to repair anhedonia and bolster PA (Alsayednasser et al., 2022; Dunn et al., 2020), resulting in individuals often experiencing residual anhedonia features and having PA levels below general population typical values even when they meet formal depression remission and recovery criteria at the end of treatment (e.g., Whiston et al., 2022). These residual anhedonia features are associated with ongoing psychosocial

[1] Historically, a clear distinction was drawn between relapse (reemergence of depressive symptoms after some level of improvement but preceding recovery) and recurrence (onset of a new depressive episode after recovery; Frank et al., 1991), largely based on a duration criterion of how long individuals had remained at subclinical levels before symptoms returned. However, this demarcation lacks empirical support (see systematic review by de Zwart et al., 2019). Therefore, we use the term relapse/recurrence to reflect reemergence of depressive symptoms that meet criteria for a major depressive episode, irrespective of how long after remission this occurred.

unique focus examining if levels of positive affect predict and mediate treatment outcomes. In particular, this is the first data publishing mediation results on PREVENT.

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Barnaby D. Dunn is developing augmented depression therapy, a well-being and positive affect-focused treatment for depression, and receives an honorarium for delivering training workshops and supervision on this approach. Willem Kuyken is the Director of the Oxford Mindfulness Centre, a collaboration between the University of Oxford and not-for-profit charity, the Oxford Mindfulness Foundation.

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impairment (Vinckier et al., 2017) and may make individuals more vulnerable to subsequent RR. According to the broaden and build framework (Fredrickson, 2004), PA results in expanded attentional awareness, improved creative problem-solving, and greater social connection. This in turn may enhance individuals' coping skills and resilience in the face of life challenges. Relatedly, evolutionary frameworks argue that one function of PA is to encourage individuals to rest, renourish, and strengthen affiliative bonds and to seek safety (Gilbert, 2015). This affiliative, affective experience is postulated to protect individuals from psychological suffering. Therefore, reducing residual anhedonia and bolstering PA in individuals with a previous history of depression may build resilience and reduce the risk of RR (Garland et al., 2010).

It has been proposed that the beneficial effects of mindfulness practices in general and MBCT in particular may in part result from improvements in PA (Feldman & Kuyken, 2019; Garland et al., 2015; Martins et al., 2019). While it is not the primary conceptual focus of the original MBCT program, various elements of MBCT for depression do explicitly attend to building PA, meaning this may be a plausible mechanism of action to account for how MBCT-TS reduces the risk of RR. In Week 2 of the MBCT course, individuals are encouraged to engage in everyday activities in a mindful fashion (potentially leading to enhanced pleasure experience), and a pleasant event calendar is set as homework. In the following session, participants are invited to deconstruct their experience during these pleasant events (noticing the situation, bodily sensations, mood, thoughts, and appraisal of recall). It has been demonstrated that MBCT results in increased PA from pre- to posttreatment for those in remission/recovery who show elevated residual depression symptoms. For example, Geschwind et al. (2011) randomized individuals with residual depression symptoms, but not currently in an episode to receive either MBCT or a wait-list control. Using an experience sampling methodology, it was demonstrated that MBCT led to increased momentary PA relative to wait-list control. Similarly, in a previous analysis of the PREVENT trial, it has been demonstrated that in the subset of individuals with residual depressive symptoms, MBCT-TS led to a greater increase in PA relative to M-ADM on a questionnaire measure (Dunn et al., 2022, Study 2). However, both of these analyses were restricted to individuals with residual symptoms. It remains unclear if similar effects will emerge when considering all individuals in current remission from depression (irrespective of the presence or absence of residual symptoms).

The extent to which greater PA protects against the risk of RR in recurrent depression, and the degree to which MBCT-TS acts by bolstering PA, has received little empirical attention in the extant literature. Moreover, we are not aware of any mediation analyses of clinical trials that have examined if the protective effects of MBCT regarding reducing risk RR are in part accounted for by the extent to which MBCT bolsters PA.

As a preliminary exploration of these issues, the present study is a further secondary analysis of the PREVENT trial (Kuyken et al., 2015a), focusing on whether PA is related to the risk of RR when considering the entire sample (not just the subset with residual depression symptoms). The aims of the analysis are as follows: to examine whether findings that MBCT increases PA replicate when using a sample that combines individuals with and without residual symptoms, to evaluate if intake PA predicts risk of RR, and to explore if change in PA during treatment accounts for the protective effects of MBCT-TS.

Based on previous findings on the subset of the sample with residual symptoms (Dunn et al., 2022), we predicted that MBCT-TS would result in greater levels of posttreatment PA than M-ADM when considering the entire sample irrespective of residual symptom status (Hypothesis 1). Influenced by the broaden and build framework (Fredrickson, 2004) and evolutionary accounts (Gilbert, 2015), we predicted that greater levels of PA at intake would predict a reduced risk of RR across conditions (Hypothesis 2). Informed by accounts arguing that mindfulness interventions in part exert their resilience-enhancing effects through bolstering PA (Garland et al., 2015; Martins et al., 2019), we predicted that a greater increase in PA during MBCT-TS should mediate any observed reduction in risk of RR (Hypothesis 3). The M-ADM arm is viewed as a neutral control condition in these analyses, as participants are simply continuing with their existing treatment regime (and so we did not expect to see any increase in PA from intake to posttreatment).

Sensitivity analyses were also conducted to explore if any predictive effects of PA held when adjusting for a range of other constructs linked to PA and/or greater risk of RR in the extant relapse prevention and MBCT literature. These were as follows: earlier age of first depression onset, greater number of previous episodes, greater residual depression symptoms, lower levels of dispositional mindfulness, extent of practice of formal meditation, a history of childhood maltreatment/abuse, higher levels of comorbidity, use of antidepressant medication during the trial follow-up period, age, and gender (Buckman et al., 2018; Kuyken et al., 2016; van der Velden et al., 2015).

Method

Transparency, Openness, Consent, and Approvals

The article aligns to transparency and openness guidelines. All data, program code, and other methods developed by others are cited in the text and listed in the References section. Anonymized source data used in these analyses are available from Prof. Kuyken (willem.kuyken@psych.ox.ac.uk) upon request (release of data is subject to an approved proposal and a signed data access agreement). This is not available on an open-access repository as the trial predated open science practices and consent from participants was not taken to share data in this way. The computer code needed to reproduce the analyses and a copy of the modified DPES scale are included in the supporting online materials. The article complies with the American Psychological Association style journal article reporting standards. The original trial was preregistered (ISRCTN 26666654), the protocol was published prior to completing recruitment (Kuyken et al., 2010), and the primary trial outputs have been described in detail elsewhere (Kuyken et al., 2015a; Kuyken et al., 2015b). This secondary analysis was not preregistered. The participants gave written informed consent before participating in the trial. Multicenter ethical approval for the study was given by the South West Research Ethics Committee (reference number 09/H0206/43; 2009).

Design and Participants

PREVENT was a multicenter, parallel group, definitive randomized controlled trial. Four hundred and twenty-four depressed adult (aged ≥18 years) participants with a diagnosis of recurrent depression (three or more episodes; not currently in an episode) as the primary presenting issue and who were currently taking M-ADM at a therapeutic dose were recruited from three sites across the South West region of the United Kingdom (Bristol; Exeter and East Devon; Mid, North, and South Devon). Participants were randomized in a 1:1 ratio to MBCT with tapering support (MBCT-TS) or M-ADM (212 per arm), stratified by recruitment locality and symptomatic status (asymptomatic [scoring < 8] versus partially symptomatic [scoring ≥ 8] on the 17-item Hamilton Depression Rating Scale [GRID-HAMD]; J. B. W. Williams et al., 2008), via computer-generated random permuted blocks on a password-protected website externally hosted by the Peninsula Clinical Trials Unit. The sample size was set to be able to detect a 10% difference in relapse/remission rates between the two treatment arms. It was not a priori powered for the current analyses examining if PA relates to the risk of RR. Research assessors were not involved in delivering treatment. Baseline assessment occurred prior to randomization, and research assessors were blind to treatment allocation at subsequent follow-ups. The full details of the original trial design and findings are available in the original trial publications (Kuyken et al., 2010; Kuyken et al., 2015a; Kuyken et al., 2015b).

Interventions

In the M-ADM arm, the participants were instructed to continue taking a therapeutic dose of antidepressants for the 2-year trial duration, with support and monitoring from their general practitioner (GP). Seventy-six percent of participants (162/212) followed this regime (i.e., did not discontinue medication or reduce medication below a therapeutic dose during the trial) and so were judged to be treatment adherent.

In the MBCT-TS arm, the participants were invited to attend eight weekly 2.5-hr group sessions and up to four refresher sessions in the following year. Sessions followed the standard MBCT manual, but with more work in later sessions on developing a relapse/recurrence signature response plan that explicitly included consideration of reduction/discontinuation of M-ADM. Those who completed a per-protocol dose of MBCT (at least four sessions) were invited to taper/discontinue medication with the support of their GP within 6 months of the end of the course (being instructed tapering should not start before Session 6 of the course). The study team provided GPs and participants with guidance about typical tapering/discontinuation regimes. A total of 21 MBCT-TS groups were delivered by four experienced MBCT therapists, with coding of session recordings indicating that therapists had delivered groups competently. Eighty-three percent of participants (176/212) in the MBCT-TS arm completed a minimum adequate dose of MBCT and were invited to taper/discontinue medication. Of these 176 participants, 153 individuals (72% of the entire MBCT-TS sample) reduced or discontinued medication at some point during the follow-up and so were judged to be fully treatment adherent.

Outcomes

The primary outcome was the occurrence of (and time to) any depressive relapse/recurrence (according to criteria from the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition*), assessed via the Longitudinal Interval Follow-up Evaluation interview protocol (Keller et al., 1987). This was administered at intake, posttreatment (1 month after the end of the MBCT-TS course or the equivalent time in the M-ADM arm), and at 9, 12, 18, and 24 months after randomization.

Following earlier work (Dunn et al., 2022), PA at intake and posttreatment was assessed by pooling the joy (e.g., "On a typical day, many events make me happy"; six items) and contentment (e.g., "I am generally a contented person"; five items) subscales from the Dispositional Positive Emotions Scale (DPES; Shiota et al., 2006). The PREVENT trial used a modified Likert rating scale for each item on the DPES, asking the participants to state if they *strongly disagreed* (coded 1), *disagreed* (coded 2), *were neutral* (coded 3), *agreed* (coded 4), or *strongly agreed* (coded 5) with each statement. These items were summed to index composite PA (scale scores ranging from 11 to 55). Indicating it is valid to pool these items, at intake in the current sample, the two subscales were highly correlated ($r = .63$, $p < .001$), and the combined scale had excellent internal reliability (Cronbach's $\alpha = .90$).

A range of other variables previously linked to PA and/or risk of RR were also measured, meaning these potential confounders could be adjusted for in secondary sensitivity analyses. At intake and posttreatment, depression severity was indexed using the GRID-HAMD (J. B. W. Williams et al., 2008); dispositional mindfulness was measured using the total score from the 39-item Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006); and amount of formal meditation practice in the past month was indexed (coded on a 4-point scale from 0 = *not at all* to 3 = *regularly and more days than not*). The current age in years, gender (coded as male = 0, female = 1), age in years of first depression onset, number of previous depressive episodes (coded via median split as 3–5 [0] or >5 [1]), and an abusive childhood (coded as no = 0 and yes = 1, following classification used by Kuyken et al., 2015a) were assessed at intake. If participants discontinued M-ADM at any stage during follow-up, this was also indexed (coded as no = 0 and yes = 1).

Analyses

The R software (R Core Team, 2021) was used to conduct analyses. In all analyses, two-tailed statistical tests were reported, α was set at .05, and group was coded as 0 (M-ADM) and 1 (MBCT-TS). All regression and survival analyses were adjusted for the trial stratification variables (GRID-HAMD intake scores coded as 0 if <8 and as 1 if ≥8 to classify the presence of residual symptoms; three dummy variables to code recruitment site). Where the target event (RR) had not occurred by either the last assessment the participant completed or the end of the final follow-up period, right censoring was utilized in all survival models. Censoring was assumed to be noninformative (i.e., participants who dropped out did so for reasons unrelated to the trial or treatment). No analyses adjusted for potential therapist effects in the MBCT-TS arm, given little evidence of therapist effects in the primary trial article (Kuyken et al., 2015a) and because not all survival analyses used could incorporate a frailty

term to model random effects of therapist. Analyses except where otherwise stated had complete data or used multiple imputation to simulate missing data, meaning data were analyzed on an intent-to-treat basis.

To examine if the risk of RR differed as a function of group, a series of Cox proportional hazard regression (survival) models examined if group predicted the hazard of RR at different follow-up assessments. To test Hypothesis 1, a linear regression examined if the treatment groups differed on posttreatment PA, additionally entering intake PA as a covariate. Paired sample *t* tests were also run on each arm separately to examine if there was a change in PA (reporting Cohen's *d* as a measure of effect size; J. Cohen, 1988). To test Hypothesis 2, a Cox proportional hazard regression examined if intake PA predicted the hazard of RR from intake to 24-month follow-up. While we had no a priori predictions regarding a potential moderating role of intake PA on predicting the risk of RR in MBCT-TS relative to M-ADM, we repeated this analysis when entering the interaction term between group and intake PA to assess for possible moderation.

To test Hypothesis 3, counterfactual causal mediation analyses on complete case data were run using the R mediation package (Tingley et al., 2014, following the method proposed by Imai et al., 2010). These analyses estimated the difference in outcome (risk of RR) that would have occurred if participants in the MBCT-TS group had displayed change in the mediator (ΔPA) comparable with those in the M-ADM group. Similarly, they estimated the difference in risk of RR that would have occurred if participants in the M-ADM group had displayed change in PA comparable with those in the MBCT-TS group. In other words, what is being modeled is the difference in effect seen by changing the mediator, as if the treatment had been changed but without actually changing the treatment itself. This difference is referred to as the natural indirect effect and can be interpreted in a similar way to indirect effects in standard regression mediation analyses (see Valente et al., 2020, for a description of counterfactual approaches). To meet the temporal precedence criterion (change in predictor occurs before change in outcome) that underpins causal inferences from mediation models (Lapointe-Shaw et al., 2018), this analysis was restricted to the subset of individuals who had not already relapsed by posttreatment.

To conduct the counterfactual analyses, first, a linear regression modeled the extent to which treatment assignment predicted change in PA from intake to posttreatment (additionally covarying for baseline PA). Second, an accelerated failure time (AFT) survival model (using a Weibull distribution and robust standard errors) was run to model the extent to which change in PA from intake to posttreatment predicted subsequent risk of RR from posttreatment to 24-month assessment (covarying for intake PA).

Results from the linear regression model and the AFT model were then fed into the mediation package (using 10,000 simulations and computing quasi-Bayesian confidence intervals) to estimate the natural indirect effect. The natural indirect effect is reported in days survived. If zero is not included in the 95% confidence interval of the estimate, this indicates significant mediation. It was necessary to use an AFT rather than Cox survival model in the mediation analyses due to the constraints of the mediation package. Moreover, as the mediation package cannot accommodate multiple imputation for survival data, only participants with valid PA data at intake and posttreatment and who had valid survival data at subsequent follow-ups were included. Contemporary mediation guidance argues that sensitivity analyses should be conducted to examine if the indirect effect varies as a function of the treatment group even if the group by interaction term is statistically nonsignificant in the main prediction model (as trials are not typically powered to be able to detect such an interaction; Hesser, 2022, p. 1055). Therefore, the counterfactual analyses were repeated when including the interaction term between PA change and treatment in the main prediction model.

The main and interactive effects of intake PA and PA change on predicting the risk of RR were plotted using the *plot_surv_area* package in R (Denz & Timmesfeld, 2022). As *plot_surv_area* can only incorporate data from Cox regressions, this necessitated repeating the PA change analyses using a Cox model rather than an AFT model.

Sensitivity analyses examined if any observed effects of treatment changing PA and intake PA predicting risk of RR remained significant when adjusting for potential confounding variables measured at intake (age, gender, FFMQ dispositional mindfulness, GRID-HAMD depression severity, number of comorbid conditions, median splot of number of previous depressive episodes, abuse history, age of first onset of depression, amount of meditation practice in month before intake) and if ADM was discontinued at any point during the 2-year follow-up. Moreover, it was examined if any observed effects of change in PA mediating risk of RR held when adjusting for confounding variables. These were the same confounder variables as in the intake prediction analyses, except that to covary for other potential mediators, posttreatment levels in GRID-HAMD depression severity, FFMQ dispositional mindfulness, and formal meditation practice were included. Moreover, the ADM variable indexed if the participant reduced or discontinued ADM at any point prior to the posttreatment follow-up rather than at any point during the 2-year follow-up. This change was necessary to ensure the temporal precedence criterion was met (i.e., that change in the medication use preceded the change in RR outcome).

Results

Clinical and demographic characteristics of participants in each arm are shown in Table 1. The overall sample was predominantly female, of White British ethnic origin, and with some degree of residual depression symptoms as measured on the GRID-HAMD, with no obvious differences between treatment groups.

When focusing on rates of RR that had occurred by the posttreatment assessment (when MBCT-TS had been completed but tapering of medication had yet to start or had only just started), an RR had been experienced by 70/424 (17%) of participants (24/212 [11%] in MBCT-TS and 46/212 [22%] in M-ADM). There was a significant reduction in risk of RR in MBCT-TS relative to M-ADM at this juncture, hazard ratio (HR) = .51 (95% CI [0.31, 0.83]), $p < .01$. As reported in Kuyken et al. (2015a), a RR was experienced by 94/212 (44%) participants in the MBCT-TS arm and 100/212 (47%) of participants in the M-ADM arm over the 2-year follow-up duration of the study (i.e., when MBCT had been delivered and tapering had been completed). There was a numerically lower risk of RR in MBCT-TS relative to M-ADM across this follow-up period, but this difference did not reach statistical significance, Cox regression HR = 0.89 (95% CI [0.67, 1.18]), $p = .43$.

Table 1
Clinical and Demographic Characteristics of Sample

Variable	Pooled	M-ADM	MBCT-TS
Entire sample			
N	424	212	212
Age (years)	49.44 (12.31)	48.71 (12.73)	50.16 (11.85)
Female gender	325/424	174/212	151/212
White British ethnicity	420/424	210/212	210/212
Age of depression first onset (years)	24.70 (11.87)	25.02 (12.28)	24.39 (11.47)
Five or more previous episodes	198/424	106/212	92/212
Number of comorbidities at intake	0.61 (0.91)	0.67 (0.95)	0.54 (0.86)
Suffered abuse in childhood	216/422	111/212	105/201
Residual depression symptoms	99/424	50/212	49/212
Intake depression (GRID-HAMD)	4.69 (4.33)	4.63 (4.34)	4.75 (4.33)
Intake mindfulness (FFMQ)	118.61 (17.97)	117.94 (17.22)	119.26 (18.70)
Intake regular formal meditation	0.16 (0.44)	0.12 (0.38)	0.21 (0.49)
Intake PA (DPES)	31.14 (7.48)	31.44 (7.34)	30.85 (7.61)
Posttreatment PA (DPES)	32.57 (7.91)	31.25 (7.76)	33.90 (7.86)
PA change from intake to post (DPES)	1.26 (6.68)	−0.23 (6.19)	2.70 (6.84)
Mediation subsample			
N	266	121	145
Age (years)	51.12 (12.24)	50.25 (13.12)	51.85 (11.46)
Female gender	201/266	98/121	103/145
White British ethnicity	263/266	119/121	144/145
Age of depression first onset (years)	26.50 (12.52)	27.18 (12.75)	25.94 (12.34)
Five or more previous episodes	112/266	53/121	59/145
Number of comorbidities at intake	0.48 (0.79)	0.54 (0.78)	0.44 (0.80)
Suffered abuse in childhood	120/266	53/121	67/145
Residual depression symptoms	57/266	24/121	33/145
Intake depression (GRID-HAMD)	4.39 (4.11)	4.03 (3.87)	4.68 (4.30)
Posttreatment depression (GRID-HAMD)	5.53 (4.78)	6.05 (5.39)	5.09 (4.18)
Intake mindfulness (FFMQ)	119.92 (17.29)	120.17 (16.38)	119.71(18.06)
Posttreatment mindfulness (FFMQ)	128.37 (18.09)	123.57 (16.39)	132.37 (18.52)
Intake meditation practice	0.17 (0.43)	0.15 (0.44)	0.19 (0.43)
Posttreatment regular formal meditation	1.03 (1.13)	0.24 (0.63)	1.67 (1.05)
Intake PA (DPES)	31.78 (7.42)	32.45 (7.29)	31.23 (7.50)
Posttreatment PA (DPES)	34.03 (7.55)	33.01 (7.38)	34.88 (7.38)
PA change from intake to post (DPES)	2.24 (6.53)	0.56 (5.91)	3.65 (6.71)

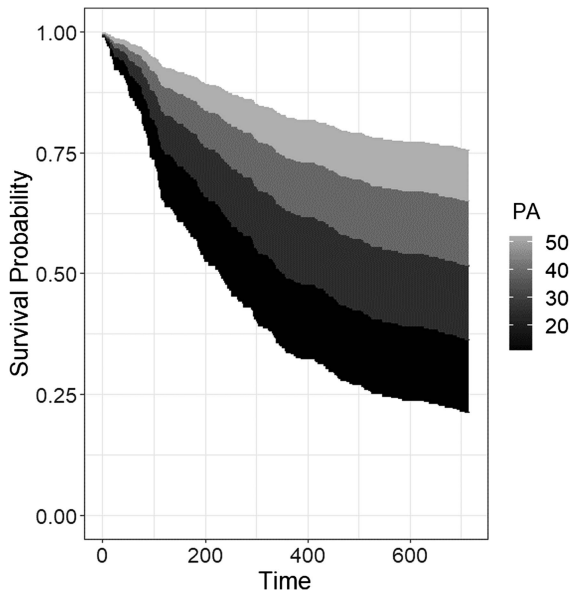
Note. Data are mean (*SD*) or count values. M-ADM = maintenance antidepressant medication; MBCT = mindfulness-based cognitive therapy; MBCT-TS = MBCT with support to taper medication; GRID-HAMD = Hamilton Depression Rating Scale; FFMQ = Five Facet Mindfulness Questionnaire; PA = positive affect; DPES = Dispositional Positive Emotions Scale.

Intake and posttreatment PA data were available for 340/424 individuals (80%; 172/212 individuals [81%] in MBCT-TS and 168/212 individuals [79%] in M-ADM). Supporting Hypothesis 1, linear regression found significantly greater levels of PA posttreatment in the MBCT-TS relative to the M-ADM, $\Delta = 2.84$ (95% CI [1.55, 4.13]), $p < .001$, and this effect held when adjusting for potential confounding variables, $\Delta = 1.78$ (95% CI [0.38, 3.17]), $p = .01$. Paired sample *t* tests showed a significant (small-to-medium effect size) improvement from intake to posttreatment in MBCT-TS, $\Delta PA = 2.93$ (95% CI [2.00, 3.87]), $t = 6.19$, $p < .001$, $d = .42$, and a nonsignificant (negligible effect size) deterioration from intake to posttreatment in M-ADM, $\Delta PA = -0.28$ (95% CI [−1.12, 0.56]), $t = 0.64$, $p = .56$, $d = -.04$. When considering the pooled sample across arms, there was a significant (small effect size) increase in PA from intake to posttreatment, $\Delta PA = 1.29$ (95% CI [0.65, 1.93]), $t = 3.95$, $p < .001$, $d = .19$. Exploratory analyses suggested that PA levels were below general population typical values at intake, while MBCT-TS did improve PA levels, these remained below general population typical levels at posttreatment (see online Supplemental Material Section 1). Moreover, greater PA improvement observed in MBCT-TS relative to M-ADM was (cross-sectionally) mediated by greater increase in dispositional mindfulness, but not changes in medication usage or increases in the frequency of formal meditation practices (see online Supplemental Material Section 2).

Intake PA and survival data were available for 408/424 individuals (96%; 207/212 [98%] in the MBCT-TS arm and 201/212 [95%] in the M-ADM arm). Supporting Hypothesis 2, a Cox regression found that greater intake PA was associated with a reduced hazard of RR across groups, Cox HR = .96 (95% CI [.94, .98]), $p < .001$ (see Figure 1). This effect held when adjusting for potential intake confounding variables, HR = .95 (95% CI [.93, .98]), $p < .001$. Exploratory analyses found no significant moderating effect of intake PA on predicting risk of RR in MBCT-TS relative to M-ADM group by intake PA interaction term, HR = 1.02 (95% CI [.98, 1.06]), $p = .31$. When looking at each group separately at the point no new treatment was being introduced (intake assessment in the M-ADM group; posttreatment in the

Figure 1

Association Between Positive Affect (PA) at Intake and Time to Relapse/Recurrence (in Days) Pooled Across Groups



Note. Graphs plot survival curves as a function of intake PA (from gray greater levels to black lower levels).

MBCT-TS group), greater intake PA continued to significantly predict reduced risk of RR in both cases (see online Supplemental Material Section 3).

The posttreatment assessment was completed by 370/424 individuals (87%; 184/212 individuals [87%] in M-ADM and 186/212 individuals [88%] in MBCT-TS). Of these individuals, 46/184 (25%) in the M-ADM arm and 24/186 (13%) in the MBCT-TS arm had already suffered an RR. This left 138/212 individuals (65%) in the M-ADM and 162/212 individuals (76%) in the MBCT-TS arm potentially eligible for mediation analyses. A further 17 individuals in each arm either did not have complete intake and posttreatment PA data or lacked subsequent follow-up survival data, leaving a final sample of 266/424 (63% of the total sample) for mediation analyses (121/212 [57%] in the M-ADM arm and 145/212 [68%] in the MBCT-TS arm). All subsequent analyses are conducted on this subsample on a complete case basis.

Clinical and demographic characteristics of the mediation analysis subsample were broadly similar to the overall sample, and again there were no obvious differences between treatment groups (bottom half of Table 1). A RR was experienced after posttreatment follow-up in 55/145 (38%) of participants in MBCT-TS and 39/121 (32%) of participants in M-ADM. The risk of RR after posttreatment assessment (at the point when tapering was introduced and followed through for a majority of clients) was numerically greater in MBCT-TS relative to M-ADM, but this difference was not statistically significant, HR = 1.14 (95% CI [0.75, 1.72]), $p = .53$.[2] Linear regression analysis found greater levels of PA posttreatment in MBCT-TS relative to M-ADM, $\Delta = 2.65$ (95% CI [1.23, 4.07]), $p < .001$. This difference in PA between arms remained significant when adjusting for potential confounder variables, $\Delta = 2.91$ (95% CI [1.47, 4.36]), $p < .001$. AFT survival analysis found that a greater increase in PA from intake to posttreatment was associated with a lower risk of subsequent RR across conditions, Weibull coefficient = 0.04 (95% CI [0.00, 0.08]), $p = .03$ (see Figure 2 for an illustration of this effect using a comparable Cox regression analysis). When adding the interaction term between PA change and group, this did not reach statistical significance, Weibull coefficient = 0.05 (95% CI [−0.01, 0.12]), $p = .12$. When adjusting for potential confounder variables, greater PA increase continued to predict reduced risk of RR across treatment arms, Weibull coefficient = 0.06 (95% CI [0.00, 0.11]), $p = .04$, and the interaction between PA change and condition remained nonsignificant, Weibull coefficient = 0.06 (95% CI [−0.02, 0.13]), $p = .13$.

Counterfactual mediation analysis (not including the nonsignificant group by mediator term) revealed a significant natural indirect effect of PA change on the risk of RR, $p = .04$ (difference in days to relapse in MBCT-TS = 184 days (95% CI [9, 483 days]); in M-ADM = 261 days (95% CI [9, 721 days]). When adjusting for potential confounding variables, the natural indirect effect remained significant ($p = .04$). In sensitivity analyses allowing for a nonzero interaction between group and the mediator, there was a significant natural indirect effect of PA change in MBCT-TS, difference in days to relapse = 341 (95% CI [53, 894 days]), $p < .01$, but not M-ADM, difference in days to relapse = 66 (95% CI [−231, 483 days]), $p = .74$. When adjusting for potential confounding variables, the natural indirect effect remained significant in the MBCT-TS arm ($p = .01$) and nonsignificant in the M-ADM arm ($p = .50$).

Discussion

This secondary analysis of the PREVENT randomized controlled trial (Kuyken et al., 2015a) aimed to evaluate the degree to which MBCT-TS increases PA, if greater PA at intake is associated with reduced risk of RR in depression, and to explore if increasing PA partially accounts for the protective effects of MBCT-TS.

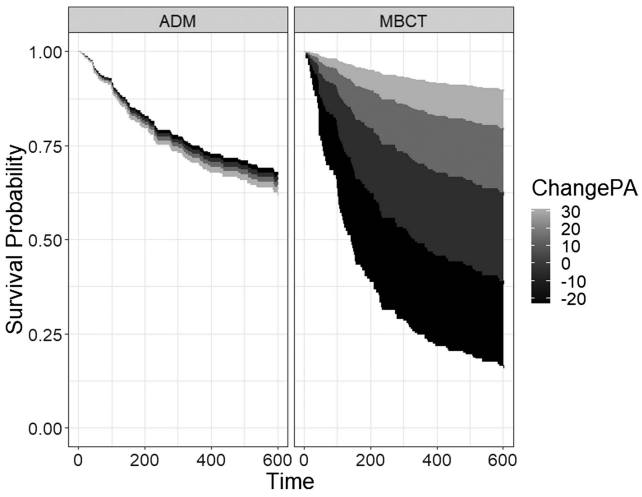
The risk of RR was significantly lower in MBCT-TS relative to M-ADM at the posttreatment assessment (before tapering had been completed) and then did not significantly differ at subsequent follow-up intervals (when tapering was largely complete). This is consistent with findings reported in the main trial article (Kuyken et al., 2015a).

Consistent with Hypothesis 1, individuals in the MBCT-TS arm had greater levels of PA at posttreatment than those in the M-ADM arm. There was a significant improvement from intake to posttreatment following MBCT-TS, but not M-ADM. The conclusion that mindfulness improves PA replicates and extends the previous analysis of the PREVENT data set that was restricted to the subset of individuals with significant residual symptoms (Dunn et al., 2022), demonstrating the same pattern holds when considering the entire sample irrespective of residual symptom status. This finding is also consistent with experience sampling findings showing that MBCT (without tapering support) results in greater levels of momentary

[2] Exploratory analyses revealed that there was a numerically greater but nonsignificant increase in risk of RR in those who had stopped/tapered (vs. continued with) ADM by the posttreatment assessment, HR = 1.43 (95% CI [0.84, 2.45]), $p = .19$.

Figure 2

Association Between Change in Positive Affect (PA) From Intake to Posttreatment and Subsequent Time to Relapse/Recurrence (in Days) as a Function of Treatment Arm



Note. Graphs plot survival curves as a function of change in PA (from gray greater increase to black greater decrease from intake to time one). ADM = antidepressant medication; MBCT = mindfulness-based cognitive therapy.

PA relative to wait-list control in those with residual depression symptoms (Geschwind et al., 2011).

As predicted by Hypothesis 2, greater intake levels of PA predicted reduced risk of RR across treatment arms for the duration of the 24-month follow-up, and this effect held even when controlling for a range of other predictors previously linked to the risk of RR (including tapering/withdrawal from M-ADM and depression severity). This finding identifies PA as a candidate mechanism modulating the risk of RR in recurrent depression, consistent with claims made by the broaden and build framework and evolutionary accounts that greater PA may bolster resilience (cf. Fredrickson, 2004; Gilbert, 2015). It is consistent with previous findings showing that PA and well-being predict future depression symptom severity (Khazanov & Ruscio, 2016; Shankman et al., 2010; Spijker et al., 2001; Uher et al., 2012).

Supporting Hypothesis 3, the capacity of MBCT-TS to protect individuals from subsequent relapse/recurrence was in part mediated by the degree to which MBCT-TS increased PA. A greater increase in PA from intake to posttreatment predicted reduced subsequent risk of RR across arms. Counterfactual mediation analysis revealed a significant natural indirect effect of PA change, and this mediating relationship remained significant when controlling for potential confounding variables, including alternative candidate mediators such as change in depression severity, dispositional mindfulness, mindfulness practice during treatment, and use of M-ADM. When allowing for a nonzero interaction between mediator and group, there was a significant natural indirect effect of PA change in MBCT-TS, but not M-ADM (and this pattern held when adjusting for potential confounding variables). The finding that PA change mediates the protective effects of MBCT-TS is consistent with theoretical accounts arguing that mindfulness practice may bolster resilience by activating the PA system (Garland et al., 2015; Martins et al., 2019). It is unsurprising that the mediating effects of PA change were clearer in MBCT-TS relative to M-ADM, as the M-ADM arm in the present study was effectively an inert control (where no new treatment was introduced).

The conclusion that intake PA in the M-ADM arm and posttreatment PA in the MBCT-TS arm robustly predicted the risk of RR suggests that clinicians should review levels of PA to determine which clients may be at risk of RR. For example, if individuals continue to exhibit lowered levels of PA when stabilized on ADM or following completion of an MBCT course, they may benefit from considering other intervention approaches that specifically target PA.

While MBCT-TS did significantly enhance PA relative to M-ADM, this improvement was of a small-to-medium magnitude, and exploratory analyses suggested that many individuals continued to have levels of PA below general population typical levels posttreatment. This pattern of modest PA improvement is perhaps unsurprising, given that the predominant emphasis in the MBCT curriculum is to help prevent reactivation of unhelpful depressogenic patterns of mind when experiencing negative mood (Dunn et al., 2022). It is conceivable that the capacity of MBCT to reduce the risk of RR could be enhanced if targeting PA is made a more explicit emphasis in the program.

Other interventions that explicitly target PA in depression are being developed, including augmented depression therapy (Dunn et al., 2019, 2023), positive affect treatment (Craske et al., 2019), and positive cognitive behavioural therapy (Geschwind et al., 2019). Other mindfulness approaches beyond MBCT for depression also more explicitly target the cultivation of PA (e.g., mindfulness-based cognitive therapy for life and mindfulness-oriented recovery enhancement; Garland et al., 2021; Strauss et al., 2021). These novel interventions may show promise in their own right as preventative treatments to reduce the risk of RR in recurrent depression, although this possibility requires evaluation in definitive clinical trials. Elements of these approaches could be integrated into the MBCT for depression curriculum to optimize its capacity to target PA (see Kuyken & Dunn, 2022).

We cannot be certain that the findings regarding PA as a mechanism of change in MBCT-TS will generalize to individuals receiving MBCT who choose to continue maintenance medication or to individuals who are not medicated at the time they engaged with MBCT. Therefore, further research is warranted to examine mechanisms of change of MBCT when delivered without tapering support.

There are a number of limitations that should be held in mind with the present study. First, the MBCT arm was asked both to complete the MBCT course and also to taper antidepressant medication, meaning we cannot be certain that it was completing MBCT rather than stopping M-ADM that led to improvements in PA. However, exploratory analysis (see online Supplemental Material Section 2) suggested that this improvement in PA in MBCT-TS was most clearly associated with increases in dispositional mindfulness (rather than the tapering/withdrawal of ADM or formal meditation practice).

Second, the trial was powered to detect a significant difference between treatment arms, not to examine if mechanistic variables like PA are related to treatment outcomes. While we did not conduct a post hoc power calculation for these secondary analyses (cf. Zhang et al., 2019), it is likely that the analyses were underpowered and at risk of Type II error. Despite this potential risk, PA was nevertheless

found to significantly predict the risk of RR. Third, participants were only randomized to treatment group, and change in the putative mediator was observed rather than manipulated, meaning the sequential ignorability assumption of mediation analysis is not fully met (cf. Forastiere et al., 2018). This makes the mediation findings vulnerable to confounding effects of other variables. While steps were taken to adjust analyses for a number of confounders previously linked to the risk of RR, it cannot be ruled out that other unmeasured confounders are biasing results. Due to the constraints of the mediation package in a survival context, it was not possible to implement sensitivity analyses to examine this possibility. Fourth, the analyses were post hoc, not preregistered, and a relatively large number of comparisons were run without corrections being made for multiple comparisons. All results therefore require replication in an independent sample to test a priori hypotheses that are preregistered before viewing them as confirmatory. Fifth, the sample recruited was predominantly of White British ethnic origin. While this is representative of the South West region in which the study was run, it remains an open question as to whether these findings generalize to other ethnic groups. Sixth, we did not have data available as to the extent to which individuals in the MBCT-TS arm attended the (up to four) optional booster sessions scheduled in the year after the course. Engagement with this booster offering could conceivably modulate the pattern of results observed. Finally, the PREVENT trial did not include a measure of negative affect. Therefore, it remains unknown to what extent changes in PA, relative to negative affect, are related to the mechanism of action of MBCT-TS in preventing the risk of RR.

In summary, these findings demonstrate that MBCT-TS increases PA, although the extent of this effect is relatively modest. Greater PA at intake is associated with a reduced risk of RR, consistent with PA being an important protective factor to cultivate to help individuals stay well from depression over the longer term. Moreover, a greater extent of PA improvement during treatment predicted reduced subsequent risk of RR, and this mediated the effects of MBCT-TS in reducing the risk of RR, consistent with the possibility that MBCT-TS in part protects from future depression by bolstering PA levels. There is potential to enhance the protective effects of MBCT and MBCT-TS by increasing the emphasis on practices that foster PA.

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