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Consolidation and prediction of long-term treatment effect of group and online mindfulness-based cognitive therapy for distressed cancer patients

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ABSTRACT

Background: Group face-to-face and individual internet-based mindfulness-based cognitive therapy (MBCT and eMBCT) have been demonstrated to reduce psychological distress for distressed cancer patients in a randomized controlled trial (RCT). This study focused on the long-term effects of this RCT during the nine-month follow-up period, and on possible predictors, moderators and working mechanisms.

Methods: Distressed cancer patients ($n = 245$) were randomized to MBCT or eMBCT. Data were collected at baseline, post-treatment, three- and nine-month follow-up. Data were analyzed with linear mixed effect models and (hierarchical) linear regressions.

Results: Analyses revealed long-term reductions in psychological distress and rumination, and long-term increases in positive mental health and mental health-related quality of life (QoL) in both interventions over the course of the nine-month follow-up. Interestingly, patients reported less psychological distress in the follow-up period after eMBCT in comparison to MBCT. Less psychological distress, rumination and neuroticism, and more extraversion and agreeableness at baseline predicted less psychological distress at the nine-month follow-up after both interventions. Less mindful and conscientious patients at baseline benefited more from eMBCT than from MBCT. Regarding working mechanisms, changes in mindfulness skills, fear of cancer recurrence and rumination during both interventions predicted less psychological distress at follow-up.

Conclusions: Our findings suggest most improvements in cancer patients' increase over time after both interventions. Furthermore, patients seemed to benefit more from eMBCT than MBCT based on psychological distress levels, especially those patients with low levels of mindfulness skills and conscientiousness.

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Introduction

Cancer is one of the leading causes of morbidity and mortality worldwide, and the number of cases is expected to increase by 70% in the upcoming two decades [1]. Receiving a cancer diagnosis and undergoing cancer treatment have a major impact on patients. Not surprisingly, one in three patients experiences significant psychological distress [2,3]. Especially anxiety disorders are common in cancer survivors, with prevalence rates of almost one in five [4]. In turn, psychological distress may result in worse outcomes. For instance, anxiety and depression are related to lower quality of life (QoL) in cancer patients [5], and depression might even predict cancer progression and mortality [6].

In recent years, mindfulness-based cognitive therapy [MBCT; 7] has proven to be an effective intervention to reduce psychological distress in cancer patients [8–10].

Mindfulness is defined as 'paying attention in a particular way: on purpose, in the present moment, and non-judgmentally' [11, p. 4]. MBCT instructs patients in mindfulness skills and is usually delivered as eight-week group training, including a so-called silent day.

The classical format of MBCT, with weekly group meetings, poses a number of challenges for cancer patients. While often suffering from fatigue [12], cancer patients have to travel to the MBCT location on a fixed date and time, resulting in little flexibility and travel costs. Internet-based MBCT (eMBCT), on the other hand, has a number of benefits, like availability, but also flexibility in time and location [13]. A small waitlist randomized-controlled trial (RCT) about an online group mindfulness-based intervention (MBI) for cancer patients revealed positive effects on stress symptoms and mood disturbances [14]. Moreover, an active-controlled study

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showed eMBCT could reduce cancer-related fatigue [15]. Our research group conducted a large RCT (the BeMind project) comparing group MBCT with individual eMBCT, showing that both types of treatments are superior to usual care [16]. However, long-term effects, predictors/moderators and working mechanisms of both MBCT and eMBCT still need to be addressed, which is the goal of this study.

Long-term effects

In a large meta-analysis, Piet et al. [8] found small to moderate effects of MBIs for cancer patients in the long-term (on average six months after the intervention), but concluded this as preliminary evidence, due to the small amount of studies that included long-term results. More recent randomized controlled trials for breast cancer patients showed that intervention effects of MBIs persist, even up to one year after the intervention [17,18].

Prediction/moderation

Although MBCT and eMBCT are beneficial for cancer patients in general, not all patients respond to these interventions. In order to guide clinical practice, research on predictors and moderators is necessary to know what works for whom. Predictors are variables that predict outcomes regardless of treatment allocation, while moderators are variables that influence the relationship between treatment and outcome, answering the question which type of treatment works best for whom [19]. In the field of MBIs for cancer, a small number of studies focused on identifying predictors and moderators of face-to-face MBIs. With regard to the demographic characteristics, earlier research showed higher education predicted stronger improvement from pre to post-treatment, while gender and age did not predict outcomes in MBIs for cancer patients [20]. Personality aspects (neuroticism, extraversion, openness, agreeableness and conscientiousness) did not moderate treatment outcome of a MBI for cancer patients versus supportive-expressive therapy [21]. Presence of mood or anxiety disorder(s) was associated with larger treatment effects in face-to-face MBCT in patients with a range of medical and psychiatric conditions [22]. Moreover, baseline psychological distress and more generally, baseline complaints moderated treatment outcome; patients with more severe complaints benefited more from the intervention compared to control [21,23–25].

Working mechanisms

Another way of advancing treatment research is by gaining a deeper understanding of the working mechanism of an intervention. This can help clinicians to identify the active component of an intervention and tailor the program accordingly. A small number of previous studies focused on this topic in cancer patients. In breast cancer patients, fear of cancer recurrence was a mediator for psychological and physical outcomes [26]. Other studies found rumination and mindfulness skills as mediators of disturbed mood in cancer patients

[27,28], although findings seemed mixed [29]. A large meta-analysis combining psychiatric and medical conditions also found rumination and mindfulness skills as mediators of MBIs [30].

Research questions

This study reports on the long-term effects of MBCT and eMBCT in cancer patients who experience at least mild psychological distress [31]. We expected our primary outcome (psychological distress) and secondary outcomes (fear of cancer recurrence, rumination, positive mental health, health-related QoL) to remain stable over the course of the follow-up, without a difference between MBCT and eMBCT, as they are similar in content. In addition, we studied prediction and moderation of treatment outcome in MBCT versus eMBCT. Potential predictors and moderators were gender, age, level of education, work, anticancer treatment intent, presence of depressive and/or anxiety disorder, personality traits, baseline psychological distress, fear of cancer recurrence, rumination and mindfulness skills. These predictors and moderators were studied exploratory. Finally, this study investigated whether change in fear of cancer recurrence, rumination and mindfulness skills over (e)MBCT, could predict psychological distress at the last follow-up. We expected that decreases in fear of cancer recurrence and rumination, and increases in mindfulness skills during (e)MBCT predict psychological distress at the nine-month follow-up.

Material and methods

This study involved the follow-up data from a three-armed, multicenter and randomized controlled trial. Participants were randomized into one of three conditions; face-to-face group MBCT, individual eMBCT or treatment as usual (TAU). Patients in the TAU condition were randomized to MBCT or eMBCT after they had completed the three-month TAU period, thus, follow-up data is only available for MBCT and eMBCT. Information regarding inclusion of participants and content of the intervention is described in the study protocol [31]. The study was approved by an ethical review board (CMO Arnhem-Nijmegen, registered under number 2013/542).

Participants

Participants were recruited through various online (e.g., Facebook) and offline (e.g., newspapers) media. Interested patients were directed to a study website, containing further information. Inclusion criteria were having any cancer diagnosis; experiencing at least mild psychological distress [a score of ≥ 11 on the Hospital Anxiety and Depression Scale (HADS) that patients could fill out on the study website; 32,33]; computer literacy and internet access; good command of the Dutch language; and willingness to participate in either mindfulness intervention. Potential participants could self-enroll for the study if they fulfilled the inclusion criteria, which were verified in a face-to-face or telephone interview. Exclusion criteria were severe psychiatric morbidity, change

in psychotropic medication within three months of baseline, and current or previous participation in MBCT or MBSR. More details about the recruitment procedure can be found elsewhere [31].

Procedure

Patients eligible for the study were randomized to one of the three arms: MBCT, eMBCT or TAU. Patients in the TAU condition were randomized to the MBCT or eMBCT after a three-month period. Participants filled out questionnaires after randomization (baseline, T0), directly after the intervention (T1), and at three-month (T2) and nine-month (T3) follow-up. Participants in TAU completed an additional assessment (T0b) at the end of the three-month TAU period.

Interventions

The content of the MBCT and eMBCT was similar, and based on the MBCT program of Segal et al. [34]. Minor adaptations were made to the program to suit the needs of cancer patients, in terms of psycho-education (e.g., about cancer-related fatigue) and movement exercises (e.g., suitable for patients with edema). In each MBCT group, a maximum of 12 patients participated. For eight weeks, patients had weekly 2.5 h sessions, and they were requested to practice at home on a daily basis (45 min a day and six days a week). Between session six and seven, there was a silent day. For eMBCT, each participant was provided with information and exercises through a personal, secure webpage containing material for the eight sessions and the silent day. Participants were encouraged to read the information and do the exercises of a session within one week. Participants reflected on their experiences by keeping a personal log. The therapist assigned to the participant gave weekly written feedback based on this log on a set day of the week through a secured, integrated e-mail system, guiding the patient through the program. Therapists could encourage patients and answer their questions, they could ask questions to deepen understanding of patients, and help patients to overcome the obstacles they encountered through the e-mails. Different themes could be discussed, for example, growing awareness about automatic tendencies like perfectionism, or resistance to feel an unpleasant sensation like a headache. Therapists could spend 30 min per patient per week on feedback in eMBCT.

Both MBCT and eMBCT were taught by qualified mindfulness therapists, according to the criteria of the UK Mindfulness-Based Teacher Network [35]. Seven therapists provided both interventions, two provided only MBCT and five provided only eMBCT. All therapists attended three full-day supervision meetings. MBCT sessions were videotaped to rate therapist competency with the Mindfulness-Based Interventions – Teachers Assessment Criteria [MBI-TAC; 36] by two independent therapists (inter-rater reliability was 0.72). Randomly, two sessions of each of the nine MBCT therapists were rated; four were considered 'proficient' ($n=64$ patients), three 'competent' ($n=64$ patients) and two 'beginner' ($n=7$ patients).

Material

Outcome measures

The primary outcome measure was psychological distress, measured with the 14-item Hospital Anxiety and Depression Scale (HADS), developed to measure depression and anxiety [32,33]. The HADS has adequate psychometric properties to detect distress in cancer patients and is a suitable screening instrument for psychiatric disorders in this group [37,38]. Internal consistency in this study was good (Cronbach's α at T0 = 0.87).

The secondary outcome measures were fear of cancer recurrence, rumination, positive mental health and health-related quality of life. Fear of cancer recurrence was measured with the 9-item Severity subscale of the Fear of Cancer Recurrence Inventory [FCRI; 39,40]. Internal consistency was good ($\alpha=0.85$). Rumination was measured with the 12-item rumination subscale of the Rumination and Reflection Questionnaire [RRQ; 41]. Internal consistency was excellent ($\alpha=0.91$). Positive mental health was measured with the 14-item Mental Health Continuum-Short Form [MHC-SF; 42,43]. Internal consistency was excellent ($\alpha=0.92$). Health-related QoL was measured with the 12-item Short Form-12 [SF-12; 44]. Clinical Dutch norms were used to calculate two subscales, physical and mental health-related QoL [45].

Predictors/moderators

Tested predictors/moderators were gender, age, education level, work, anticancer treatment intent, presence of depressive and/or anxiety disorder, personality, baseline psychological distress, fear of cancer recurrence, rumination and mindfulness skills. Sociodemographic and clinical characteristics were assessed via a self-report questionnaire.

Presence of a depressive or anxiety disorder (according to DSM-IV) was assessed with the relevant sections of the Structural Clinical Interview for DSM-IV disorders [SCID-I; 46]. The SCID-I was administered by trained interviewers. Personality was assessed with the NEO Five Factor Inventory [NEO-FFI; 47]. This 60-item self-report questionnaire measures five personality characteristics; openness to experiences, conscientiousness, extraversion, agreeableness and neuroticism. Mindfulness skills were measured with the Five Facet Mindfulness Questionnaire Short Form (FFMQ-SF), a 24-item self-report questionnaire [48]. Internal consistency was good ($\alpha=0.85$).

Working mechanisms

Tested working mechanisms were fear of cancer recurrence (FCRI), rumination (RRQ) and mindfulness skills (FFMQ) (measures described above).

Statistical analyses

To facilitate transparency, the data-analysis plan was pre-registered online at Open Science Framework (<https://osf.io/v9ud8/>). Adaptations to the analysis plan were tracked. All analyses were conducted in SPSS version 22 (IBM SPSS

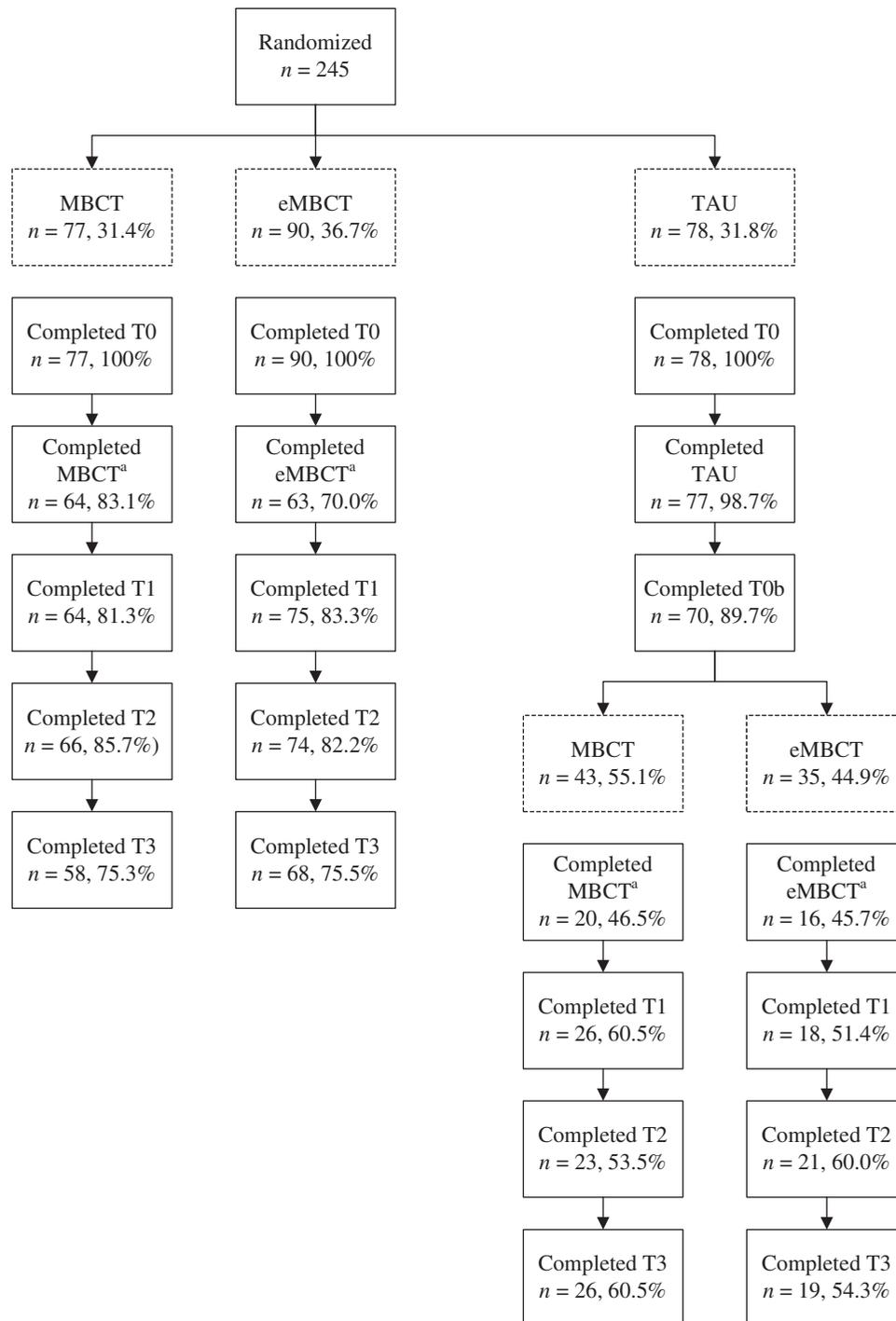


Figure 1. Flowchart indicating randomization, completion of interventions and assessments (based on the primary outcome). ^aCompleted at least four sessions. T0 = pre-measure, T0b = post-TAU measure, T1 = post-intervention; T2 = three-month follow-up; T3 = nine-month follow-up.

Statistics, Armonk, NY, USA) [49]. The mean percentage of missing data for the follow-up assessments of our primary outcome, combining both interventions and TAU, varied between 25 and 30% (see Figure 1 for a flowchart). Participants that missed T3 (primary outcome) had less positive mental health and more fear of cancer recurrence, rumination and neuroticism at T0 and they were more likely to be females. Therefore, we assumed data were not missing completely at random, but missing at random (MAR), allowing procedures to handle missing data, described below. For the TAU group, T0 scores on the primary and secondary outcome measures were replaced with T0b (post-TAU) scores, as

those were closer in time to the start of the intervention. These scores did not differ from T0 of the original MBCT and eMBCT group. In all analyses, data of patients that followed (e)MBCT after TAU were combined with data of patients that were initially randomized to (e)MBCT.

Long-term effects

To examine long-term effects, we used linear mixed effect models with the primary outcome or secondary outcomes at T1, T2 and T3 as dependent variable. Independent variables were time (nested in individuals), intervention (MBCT/

eMBCT), their interaction and the baseline measure (T0) of the outcome. Visual inspection of residual plots revealed linear relationships between time and outcomes, allowing us to treat time as covariate, to draw conclusions regarding general increases and decreases of outcomes over time. In case of a non-significant interaction, the model was rerun without the interaction. Random intercepts for participants were added. A heterogeneous first-order autoregressive (ARH(1)) covariance structure was used, which assumes measurements closer in time are more strongly related. Restricted maximum likelihood was used as estimation method, to handle missing data [50]. In case of a significant difference between interventions, effect sizes (Cohen's *d*) were calculated with the difference between the estimated marginal means of the interventions, corrected for T0, divided by the pooled baseline standard deviation, following the guidelines of Cohen [51].

Prediction/moderation

To examine prediction, we conducted separate linear regression models. Psychological distress at T3 acted as dependent variable. Independent variables were the baseline level of psychological distress, intervention (MBCT/eMBCT) and the baseline characteristic (testing prediction). To test moderation, we used the same model, but added the interaction between the baseline characteristic and the intervention. As these analyses were exploratory, an alpha level of 0.05 was used. Analyses were run on the completer data, and on imputed data, as sensitivity analysis. Missing data were imputed with the Fully Conditional Specification method, based on all variables included in the models, and the stratification variables (gender, location, treatment intention and breast cancer yes/no). Following guidelines of White et al. [52], 30 imputed datasets were created, representing the maximum % of missing data.

Working mechanisms

To examine working mechanisms, data from participants that completed four or more sessions were included. Residual change scores of fear of cancer recurrence, rumination and mindfulness skills from T0 to T1 were calculated. Next,

separate hierarchical linear regression models were run. Step 1 was identical for the three regressions, and included baseline psychological distress and intervention (MBCT/eMBCT). In step 2, the residual change score was added, to test the added contribution in the model. Psychological distress at T3 acted as dependent variable. Analyses were run on the completer data, and on imputed data, as sensitivity analysis. Missing data were imputed following the same procedure as described above.

Results

The final sample consisted of 245 cancer patients with at least mild psychological distress (HADS ≥ 11). Baseline characteristics can be found in Table 1. No baseline differences were found between participants in eMBCT and MBCT, except for mindfulness skills, with significantly higher levels of mindfulness skills in eMBCT.

Long-term effects

The results of the linear mixed effect models regarding the long-term effects of MBCT and eMBCT on the primary and secondary outcomes can be found in Table 2. None of the time \times intervention interactions were significant; therefore, these were excluded from the models. In contrast to our expectations, rather than remaining stable, the level of psychological distress further decreased over the course of the follow-up in both interventions. Furthermore, participants in eMBCT reported less psychological distress during the follow-up period compared to participants in MBCT. The effect size for the difference between groups at T3, corrected for T0, was small (Cohen's *d* = 0.22).

With regard to the secondary outcome measures, rumination significantly decreased over the nine-month follow-up in both MBCT and eMBCT. Furthermore, positive mental health and mental health-related QoL significantly increased over the course of the nine-month follow-up. Fear of cancer recurrence and physical health-related QoL did not significantly change over time. There were no differences between MBCT and eMBCT on the secondary outcomes.

Table 1. Sample characteristics per intervention (MBCT/eMBCT) at T0.

		MBCT (n = 120)	eMBCT (n = 125)	Test-statistic (t or χ^2)	p
Gender (n, %)	Male	19 (15.8%)	16 (12.8%)	0.46	.498
	Female	101 (84.2%)	109 (87.2%)		
Age in years (M; SD)		51.5 (11.1)	51.8 (10.2)	-0.18	.857
Education level (n, %)	Low/middle	35 (29.2%)	44 (35.2%)	1.02	.312
	High	85 (70.8%)	81 (64.8%)		
Type of cancer (n, %)	Breast	75 (62.5%)	76 (60.8%)	0.08	.784
	Other	45 (37.5%)	49 (39.2%)		
Type of treatment (n, %)	Curative	104 (86.7%)	102 (81.6%)	1.17	.279
	Palliative	16 (13.3%)	23 (18.4%)		
Depressive and/or anxiety disorder (n, %)		35 (29.2%)	34 (27.2%)	0.12	.732
Psychological distress HADS (M; SD)		18.2 (6.7)	16.8 (6.9)	1.64	.103
Fear of cancer recurrence severity FRCI (M; SD)		21.2 (6.6)	21.1 (6.3)	0.04	.970
Rumination RRQ (M; SD)		43.6 (8.2)	42.4 (8.4)	1.16	.247
Mindfulness FFMQ-SF (M; SD)		73.5 (10.4)	77.1 (11.2)	-2.55	.011

Both categories include the patients that were initially randomized to the TAU group.

Bold values represent statistically significant differences.

Table 2. Descriptive statistics and effects of time, intervention and baseline on primary and secondary outcomes in separate linear mixed effect models.

	Descriptive statistics						
	M (SD)			Results linear mixed models			
	MBCT	eMBCT		F	df	p	
Primary outcome:							
Psychological distress (HADS)	T1	13.5 (6.5)	11.6 (6.2)	T0 HADS	130.2	1, 199	<.001
	T2	12.9 (7.2)	11.1 (7.0)	Time	14.3	1, 178	<.001
	T3	12.6 (6.7)	9.6 (6.4)	Intervention	3.9	1, 201	.049
Secondary outcomes:							
Fear of cancer recurrence severity (FCRI- severity)	T1	17.9 (6.7)	17.0 (7.5)	T0 FCRI	272.0	1, 196	<.001
	T2	16.7 (5.4)	16.3 (5.5)	Time	1.2	1, 157	.282
	T3	17.3 (6.4)	16.3 (6.7)	Intervention	1.6	1, 191	.201
Rumination (RRQ – rumination)	T1	37.9 (8.6)	36.0 (8.9)	T0 RRQ – rum	146.4	1, 190	<.001
	T2	37.3 (7.6)	35.4 (8.3)	Time	38.4	1,185	<.001
	T3	34.6 (5.8)	33.9 (6.1)	Intervention	0.5	1, 194	.489
Positive mental health (MHC-SF)	T1	40.1 (12.9)	43.4 (13.2)	T0 MHC-SF	191.9	1, 195	<.001
	T2	39.7 (13.7)	46.2 (11.8)	Time	21.7	1, 169	<.001
	T3	43.6 (13.7)	48.3 (12.2)	Intervention	2.7	1, 190	.101
Physical health-related QoL (SF-12 PCS)	T1	48.5 (8.2)	47.8 (10.1)	T0 SF-12 PCS	76.7	1, 198	<.001
	T2	47.2 (9.2)	47.5 (9.3)	Time	0	1, 177	.995
	T3	48.3 (9.4)	47.8 (10.5)	Intervention	0.3	1, 192	.610
Mental health-related QoL (SF-12 MCS)	T1	42.6 (10.2)	43.8 (10.6)	T0 SF-12 MCS	52.9	1, 191	<.001
	T2	45.4 (11.0)	47.0 (11.8)	Time	25.5	1, 172	<.001
	T3	46.5 (11.5)	48.9 (10.6)	Intervention	1.8	1, 197	.182

All time × intervention interactions were non-significant, and, therefore, excluded from the models. T1 = post-treatment; T2 = three-month follow-up; T3 = nine-month follow-up.

Table 3. Relationship between predictor (corrected for baseline psychological distress and the main effect of intervention) and psychological distress at the nine-month follow-up with separate linear regressions (completer data).

Variable	Full model			Predictor		
	F-value (df)	p	Adjusted R ²	B	t	p
Psychological distress (T0)	39.11 (2, 167)	<.001	0.311	0.51	8.16	<.001
Gender	26.59 (3, 166)	<.001	0.312	−1.32	−1.18	.242
Age: younger than 40 years ^a	21.12 (4, 165)	<.001	0.323	−0.68	−0.50	.616
Age: older than 55 years ^a				1.74	1.89	.060
Education level (high/low)	26.02 (3, 166)	<.001	0.308	−0.43	−0.45	.653
Work (3 d or more, less than 3 d)	13.03 (3, 103)	<.001	0.254	−0.19	−0.16	.870
Anticancer treatment intent	25.93 (3, 166)	<.001	0.307	0.18	0.15	.882
DSM depressive/anxiety disorder	26.10 (3, 166)	<.001	0.308	−0.64	−0.60	.550
Personality – openness	25.95 (3, 166)	<.001	0.307	−0.02	−0.25	.800
Personality – conscientiousness	27.57 (3, 166)	<.001	0.320	−0.13	−1.84	.068
Personality – extraversion	30.35 (3, 166)	<.001	0.343	−0.22	−3.01	.003
Personality – agreeableness	31.06 (3, 166)	<.001	0.348	−0.32	−3.24	.001
Personality – neuroticism	30.30 (3, 166)	<.001	0.342	0.22	2.99	.003
Fear of cancer recurrence – severity	25.81 (3, 165)	<.001	0.307	0.02	0.29	.773
Rumination	28.39 (3, 165)	<.001	0.328	0.13	2.32	.022
Mindfulness	26.37 (3, 166)	<.001	0.311	−0.04	−0.96	.338

^aReference category was age 40–55 years.

Bold values represent statistically significant effects.

Prediction/moderation

Table 3 shows the results of the linear regression models to determine prediction of treatment effect. In all analyses, more baseline psychological distress predicted more psychological distress at the nine-month follow-up. With regard to predictors, baseline rumination, extraversion, agreeableness and neuroticism predicted psychological distress at the nine-month follow-up. More rumination and neuroticism were related to more psychological distress at nine-month follow-up. More extraversion and agreeableness were related to less psychological distress at nine-month follow-up. These results were confirmed with sensitivity analyses on the imputed data. No other significant predictors were found. Regarding moderation (Table 4), we found that mindfulness skills and conscientiousness moderated the relationship between the intervention and psychological distress at nine-month follow-

up (controlling for baseline psychological distress). Patients who were less mindful and conscientious at baseline had lower psychological distress at the nine-month follow-up in the eMBCT intervention than in the MBCT intervention. This was confirmed in sensitivity analyses on the imputed data. No other moderators were found.

Working mechanisms

Results of the three hierarchical regressions analyses testing working mechanisms can be found in Table 5. The residual change scores of fear of cancer recurrence, rumination and mindfulness skills all added a significant contribution in step 2. A decrease in rumination and fear of cancer recurrence, and an increase in mindfulness skills over the course of (e)MBCT predicted lower levels of psychological distress at

Table 4. Relationship between moderator (i.e., predictor x intervention interaction; corrected for baseline psychological distress and the main effect of intervention) and psychological distress at the nine-month follow-up with separate linear regressions (completer data).

Variable (x intervention)	Full model			Moderator		
	F-value (df)	p	Adjusted R ²	B	t	p
Psychological distress (T0)	26.36 (3, 166)	<.001	0.310	-0.12	-0.95	.342
Gender	20.61 (4, 165)	<.001	0.317	-3.29	-1.46	.148
Age: younger than 40 years ^a	14.13 (6, 163)	<.001	0.318	-2.53	-0.93	.357
Age: older than 55 years ^a				-0.82	-0.45	.655
Education level (high/low)	19.6 (4, 165)	<.001	0.306	1.40	0.73	.467
Work (3 d or more, less than 3 d)	10.01 (4, 102)	<.001	0.254	-2.36	-0.98	.328
Anticancer treatment intent	19.34 (4, 165)	<.001	0.303	0.31	0.12	.902
DSM depressive/anxiety disorder	19.77 (4, 165)	<.001	0.308	-1.76	-0.92	.357
Personality – openness	19.35 (4, 165)	<.001	0.303	-0.01	-0.06	.953
Personality – conscientiousness	23.07 (4, 165)	<.001	0.343	0.37	2.60	.010
Personality – extraversion	23.30 (4, 165)	<.001	0.345	0.18	1.32	.189
Personality – agreeableness	23.15 (4, 165)	<.001	0.344	-0.01	-0.03	.975
Personality – neuroticism	23.35 (4, 165)	<.001	0.346	-0.16	-1.41	.161
Fear of cancer recurrence – severity	19.25 (4, 164)	<.001	0.303	0.03	0.18	.858
Rumination	22.28 (4, 164)	<.001	0.336	-0.17	-1.71	.088
Mindfulness	21.15 (4, 165)	<.001	0.323	0.16	2.01	.046

^aReference category was age 40–55 years.

Bold values represent statistically significant effects.

Table 5. Effects of change in fear of cancer recurrence/rumination/mindfulness (corrected for psychological distress at baseline and intervention) on psychological distress at the three-month follow-up with hierarchical linear regressions (completer data).

Working mechanism	Step-variable	F	df	p	ΔR ²	B	t	p
All ^a	Step 1	29.63	2, 126	<.001	0.320			
	Psychological distress T0 Intervention (MBCT/eMBCT)					0.49 -3.44	6.77 -3.37	<.001 .001
Fear of cancer	Step 2	6.42	1, 125	.013	0.033			
	Residual change score fear of cancer recurrence T0/T1					1.40	2.53	.013
Rumination	Step 2	16.13	1, 125	<.001	0.078			
	Residual change score rumination T0/T1					1.99	4.02	<.001
Mindfulness	Step 2	15.47	1, 125	<.001	0.075			
	Residual change score mindfulness T0/T1					-2.01	-3.93	<.001

Dependent variable: psychological distress at T3.

^aFor all three working mechanisms, step 1 was identical.

the nine-month follow-up. These results were confirmed with sensitivity analyses on the imputed data.

Discussion

This study focused on long-term outcome, prediction, moderation and working mechanisms of MBCT and eMBCT for distressed cancer patients.

Long-term effects

In contrast to our expectations, psychological distress and rumination further decreased and positive mental health and mental health-related QoL further increased over the duration of the follow-up period in both interventions. A few other studies on MBIs for cancer patients also reported further improvements over the course of follow-up [e.g., 53]. It is possible that the cumulative practice of mindfulness resulted in increased gains over time. This observation fits with the idea of mindfulness as a mental training [54], that keeps improving with practice like a muscle, as suggested by Parsons et al. [55]. Fear of cancer recurrence and physical health-related QoL did not change over time, suggesting improvements gained during the training remain stable over the course of the follow-up, as expected.

Furthermore, eMBCT appeared to be superior to MBCT in the reduction of psychological distress during the follow-up period. So far, research has shown online and face-to-face interventions to produce similar effects, as is reported in a large meta-analysis about the comparison of online and face-to-face cognitive behavioral therapy for patients with somatic and psychiatric disorders [56]. As MBCT and eMBCT were similar in content, the delivery method might explain why eMBCT resulted in a greater reduction of psychological distress during the follow-up. From the start of the training, participants in eMBCT had to be more autonomous. This autonomy might help to form the habit of more actual mindfulness practice [57], which we know is related to better treatment outcomes [55]. Furthermore, the flexibility allowed by eMBCT could result in practice at a time the participant was ready to absorb information, which might also support the efficacy of eMBCT. Finally, it is also possible that the individual nature of eMBCT, compared to group MBCT, contributed to the greater efficacy. The individual attention of a therapist in eMBCT might serve as a catalyst for mindfulness practice or might be more compatible with the individual needs of the cancer patients.

Prediction/moderation

Baseline psychological distress, rumination, neuroticism, extraversion and agreeableness predicted treatment outcome

at nine-month follow-up in both eMBCT and MBCT, controlled for baseline psychological distress. More baseline psychological distress was related to more psychological distress at the nine-month follow-up. More rumination and neuroticism at baseline were related to more psychological distress at the follow-up (even while controlling for baseline psychological distress). Thus, while patients improved after the interventions, it seems that patients with more severe complaints at the start of the intervention had higher levels of distress at the nine-month follow-up compared to their less distressed counterparts. Other studies [e.g., 25] also found that patients with more baseline severity had more severe complaints at the follow-up (even though more severe patients benefit relatively more from MBIs compared to less severe patients). Booster sessions might be indicated for this subgroup of patients.

More extraversion and agreeableness predicted less psychological distress at nine-month follow-up after both interventions. An earlier study found that when working in teams, more extravert and agreeable people were more willing to share what they think [58]. This willingness to share might also occur in context of MBCT (with the therapist and other patients) and eMBCT (with the therapist). By sharing more, one is able to receive more input from others, which could result in deepening of knowledge about mindfulness that might enable more and faster learning. Furthermore, both extraversion and agreeableness are related to more self-compassion [59]. As self-compassion forms a link between mindfulness and positive outcomes [60], more extraverted and agreeable people could benefit more from MBCT and eMBCT, resulting in less psychological distress.

With regard to moderation, patients with less mindfulness skills and less conscientiousness benefited more from eMBCT than MBCT on the long-term. It is possible that the individual attention in eMBCT helped patients who are less mindful and conscientious. Furthermore, while patients in MBCT can refrain from discussing (the lack of) home practice by letting others in the group share their experiences, patients in eMBCT are more acknowledged for their home practice as they receive weekly written feedback from their therapist on it. Thus, eMBCT might encourage the less conscientious and mindful patients to complete their homework. The absence of other moderating variables implies that despite the common belief that older and less-educated patients might benefit less from online interventions like eMBCT, they seemed to do just as well as their younger and higher educated counterparts, although the latter group was more represented in our sample. Future studies are needed to replicate these findings.

Working mechanisms

Finally, we found that a decrease in fear of cancer recurrence and rumination, and an increase in mindfulness skills during (e)MBCT were related to lower psychological distress nine months after (e)MBCT, which confirmed our hypotheses. These results are in accordance with previous research identifying fear of cancer recurrence, rumination and mindfulness

skills as mediators [26,27,30]. Furthermore, these results are in line with the mindfulness-to-meaning theory that explains how mindfulness practice might decrease stress and rumination in adverse circumstances, through positive psychological processes [61], for which evidence was found in cancer patients [62]. Future research on working mechanisms is necessary and should include measuring positive psychological processes in addition to negative psychological processes.

Strengths and limitations

This study has a number of strengths. First of all, it is the first in this field to directly compare MBCT and eMBCT which were similar in content. Second, this study is one of the few to focus on long-term effects of (e)MBCT for cancer patients [8]. Third, due to promotion of the study website through various online and offline media, cancer patients from outside the participating institutes could be reached. This inclusion method might benefit the ecological validity of our study. However, it could also have resulted in a self-selection bias, as patients interested in mindfulness were probably more likely to participate, which can be considered as a drawback. Another limitation of this study is the absence of data about the control condition at the follow-up. Due to ethical constraints, we chose to offer patients randomized to the TAU condition participation in one of the two interventions after three months. This prevented us from testing whether the improvement over time is due to the MBCT interventions or whether this improvement is due to natural recovery or regression to the mean, although we did not observe this tendency in the TAU group during the three-month waiting. Finally, patients that missed the nine-month follow-up had worse complaints at baseline. As we miss the results of this group in the analyses, an underestimation or overestimation of effects is possible, although we used restricted maximum likelihood estimation or imputation procedures to deal with missingness. Finally, as we had no control group, we were not able to do formal mediation analyses, which limit our conclusions regarding working mechanisms.

Conclusions

To the authors' knowledge, this study is the first to directly compare an online and face-to-face version of MBCT for cancer patients. Results showed that patients kept improving over time after both MBCT interventions over the nine-month follow-up period, based on their level of psychological distress, rumination, positive mental health and mental health-related QoL. Furthermore, we found eMBCT to be superior to MBCT in terms of psychological distress reduction at nine-month follow-up, especially for patients with less mindfulness skills and conscientiousness, who seemed to benefit more from eMBCT. No other baseline characteristics were differential moderators between the two conditions, so both MBCT and eMBCT appeared to be suitable for a large range of cancer patients. Future research is necessary to confirm these

claims and to include MBIs in the clinical guidelines for treatment of distressed cancer patients.

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