A parallel-group, randomized controlled trial into the effectiveness of Mindfulness-Based Compassionate Living (MBCL) compared to treatment-as-usual in recurrent depression: Trial design and protocol

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ARTICLE INFO

ABSTRACT

Background: Mindfulness Based Cognitive Therapy (MBCT) has been shown to reduce the risk of relapse in patients with recurrent depression, but relapse rates remain high. To further improve outcome for this group of patients, follow-up interventions may be needed. Compassion training focuses explicitly on developing self-compassion, one of the putative working mechanisms of MBCT. No previous research has been done on the effectiveness of compassion training following MBCT in patients with recurrent depression.
Aims: To investigate the effectiveness of Mindfulness-Based Compassionate Living (MBCL) in reducing (residual) depressive symptoms in patients with recurrent depression who previously participated in MBCT.
Methods/design: A randomized controlled trial comparing MBCL in addition to treatment as usual (TAU) with TAU only, in patients suffering from recurrent depressive episodes who completed an MBCT course in the past. Assessments will take place at baseline, post-treatment and at six months follow-up. After the control period, patients randomized to the TAU condition will be offered MBCL as well.
Outcome measures: Primary outcome measure is severity of depressive symptoms according to the Beck Depression Inventory-II (BDI-II) at post-treatment. Secondary outcome measures are presence or absence of DSM-IV depressive disorder, rumination, self-compassion, mindfulness skills, positive affect, quality of life, experiential avoidance and fear of self-compassion.
Discussion: Our study is the first randomized controlled trial to examine the effectiveness of compassion training following MBCT in a recurrently depressed population.
Trial registration: ClinicalTrials.gov: NCT02059200, registered 30 January 2014.

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1. Background

Major depressive disorder (MDD) is one of the most prevalent psychiatric disorders. It is characterized by high relapse rates [1,2], partly due to persistence of residual symptoms after remission [3]. Given the high psychological as well as social and economic burden associated with MDD, the prevention of relapse is extremely important. To address the need for psychological interventions targeting relapse prevention, Segal, Williams and Teasdale developed Mindfulness-Based Cognitive Therapy (MBCT) [4]. Mindfulness can be defined as paying attention in a particular way: on purpose, in the present moment, and non-judgmentally [5]. MBCT helps patients with recurrent depression to develop non-judgmental awareness in the face of difficult thoughts, feelings, and bodily sensations, and fosters an intentional, skilful response to these experiences instead of avoiding them or reacting 'on automatic pilot'. A meta-analysis [6] showed that MBCT for patients with recurrent depression in remission resulted in a reduction of the risk of a relapse/recurrence of 34%. A growing number of studies indicate that MBCT may also be effective in decreasing residual levels of depression [7–10]. An RCT conducted by our own team in 205 patients with three or more previous depressive episodes showed that patients who were currently depressed benefitted as much from MBCT as those who were in remission in terms of depressive symptoms [11]. These findings were maintained

during a one-year follow-up, showing a similar course of depressive symptoms in depressed and remitted patients [12]. These results were subsequently confirmed by a meta-analysis of $N = 12$ studies on the effectiveness of MBCT for people with a current depression, which found significant improvements of depressive symptoms following MBCT in comparison to control conditions (Hedges $g = -0.39$, 95% CI $= -0.15$ to -0.63) [13].

However, even after MBCT relapse rates remain considerable (38%; [6]) and mild levels of depression (average BDI score of 10) remain present [12]. Therefore, it is important to look for ways to further improve outcomes for this group of recurrently depressed patients. Residual symptoms of depression are an important predictor of relapse [3], and may be a useful target for a follow-up intervention. A possible candidate for such a follow-up intervention is compassion training, a training that focuses explicitly on developing (self-)compassion as one of the putative working mechanisms of MBCT. Kuyken and colleagues [14] showed that the effect of MBCT on relapse/recurrence was mediated by increased self-compassion and mindfulness, along with a decoupling of the relationship between reactivity to depressive thinking and poor outcome. The cultivation of self-compassion was associated with this decoupling in the intervention group.

1.1. Compassion

In 2012, Van den Brink and Koster developed a training in self-compassion as a follow-up intervention for patients who have already attended MBCT or MBSR, Mindfulness-Based Compassionate Living (MBCL) [15,16]. It is based on previous work in compassion research as conducted by Neff, Germer and Gilbert among others [17–20] and is designed to be used in both clinical and non-clinical settings. In contrast to the more implicit teaching of compassion in MBCT, cultivating self-compassion is the primary focus of the training. Throughout the entire curriculum, the invitation is to practice kindness and compassion in the midst of suffering.

Considering the preliminary evidence linking lack of self-compassion to negative self-esteem and depression [17,20–22], MBCT combined with a follow-up training with a more explicit focus on self-compassion may be a fruitful approach to further reduce (residual) symptoms of depression in patients with recurrent depression who previously participated in MBCT. The extent to which this, in turn, contributes to the prevention of relapse and enhancement of psychological wellbeing is the question.

To date, the effectiveness of compassion training has not been studied in a clinical population in a large, adequately powered RCT. As a first step, we investigated the feasibility, acceptability and preliminary effectiveness of the MBCL in a pilot study, showing an increase in self-compassion and mindfulness skills and a trend in reducing depressive symptoms (Schuling et al., submitted). Participants of this study ($N = 17$) were all previous participants of an MBCT course and regular attendees of reunion meetings organized by our centre.

1.2. Aims

The aims of the present study are: 1) to examine the effectiveness of MBCL in adults with recurrent depression who are either in (partial) remission or currently depressed, and who previously participated in MBCT. Considering the effectiveness of MBCT even in patients who are currently depressed [11], we will include patients with and without current depression. For this reason, our primary outcome measure is depressive symptoms and not relapse; 2) to investigate the impact of MBCL on rumination, fear of self-compassion, experiential avoidance, type of positive affect, self-compassion, mindfulness and quality of life; and 3) to investigate the added value of MBCL to only MBCT based on participants' experiences using one-on-one, in-depth, qualitative interviews.

2. Methods

2.1. Design

This study is designed as a parallel-group RCT. Patients will be randomized to [a] MBCL in addition to TAU or [b] TAU only. The protocol was approved by the ethical review board CMO Arnhem-Nijmegen and registered under number 2013/220.

2.2. Study population

The study will be conducted at the Radboud UMC Centre for Mindfulness, Nijmegen, the Netherlands. This centre was founded in 2007 and has a threefold purpose: 1) to provide mindfulness based interventions to patients with either mental health problems, such as recurrent depression, somatic diseases, such as cancer; and subjects from the general population; 2) to conduct and disseminate research on the effectiveness and working mechanisms of mindfulness based interventions; and 3) to offer a teacher training program to become a mindfulness teacher. Approximately 228 patients from all over the Netherlands were taught MBCT in 2015, Mindfulness Based Stress Reduction was taught to 218 health care professionals and subjects from the general population. The centre also hosts fortnightly reunion meetings for attendees of both MBCT and MBSR courses, which were attended by a total of 310 participants in 2015.

The study population will consist of patients with recurrent depression who previously participated in an MBCT course at the Radboud UMC Centre for Mindfulness in Nijmegen, the Netherlands. In order to be eligible to participate in this study, participants must meet the following criteria: 1) recurrent depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders (fourth edition; DSM-IV) criteria, with or without a current depressive episode; and 2) having participated in an MBCT (≥ 4 sessions) training before (≥ 1 year ago). Exclusion criteria are: 1) one or more previous (hypo)manic episodes according to the DSM-IV criteria; 2) primary psychotic disorder; 3) clinically relevant neurological or somatic conditions that could be causally related to the depression; 4) current alcohol and/or drug dependence; 5) recent electro convulsive therapy (<3 months ago); 6) inability to complete interviews and/or self-report questionnaires.

2.3. Interventions

2.3.1. Mindfulness Based Compassionate Living

MBCL is set up as a follow-up intervention to MBSR or MBCT. Its main purpose is to offer those participants with persistent dysfunctional thinking or behavioural patterns a means to practice more explicitly with cultivating a kinder, gentler attitude towards themselves. These patients are often highly self-critical and are tormented by feelings of shame and guilt. As MBSR and MBCT, MBCL is a group intervention, consisting of classes up to 12 participants. The format of the MBCL program is similar to MBSR/MBCT, including eight weekly sessions of 2.5 h, containing a mixture of mindfulness practice, group enquiry and didactic and interactive teaching. However, the content of the practices and focus of the enquiry and didactic teaching is quite different, in the sense that they are actively geared towards the experience of suffering and explicitly focus on developing a kind attitude in the midst of this.

Participants are typically provided with a course folder containing background reading on each session, an explanation or description of practices used and helpful suggestions for practice. They are also given a set of CDs containing audio files with guided meditations. It is recommended that MBCL for patient populations are taught by health care professionals who are also qualified to teach MBCL.

The primary practice is that of Metta, a Pali word generally translated as "loving kindness" and which the MBCL developers translate as "mildness meditation" [16]. In this practice, the participant is gradually

guided through several steps of developing kindness towards self and others, starting with imagining a person by whom they feel unconditionally accepted and formulating intentions for their well-being, continuing with the self, a close other, a neutral person, and a difficult person. An overview of the intervention, as modified by us in the pilot study, is given in Table 1. Specifics of the original program can be found in Koster and Van den Brink [16].

Patients are invited to practice at home for about 30 min on a daily basis, supported by CDs, and to record their experiences on homework forms.

2.3.1.1. Delivery of MBCL. MBCL will be provided at the Radboud University Medical Centre for Mindfulness. Groups will be taught by one of two teachers who both have 7 years of experience with teaching MBCT (>50 groups) and who both meet the UK guidelines for teaching MBCT (good practice guidelines for teaching mindfulness-based courses by the UK Network for Mindfulness-Based Teacher Training Organizations). In two previous trials [24,25], both teachers met level four of the Mindfulness Based Interventions Teaching Assessment Criteria (MBI-TAC) [26]. The teachers are also both trained to teach

MBCL by the developers Frits Koster and Erik van den Brink: 100 h of training in MBCL plus 80 h of supervised teaching of MBCL. Integrity of the program and teaching are assessed by review of two randomly selected videotapes (of each teacher) of training sessions by an experienced MBCL teacher with the MBI:TAC [26] (slightly adapted to be congruent with MBCL instead of MBSR/MBCT).

2.3.2. Treatment as usual

TAU consists of regular medical and psychiatric or psychological treatment. Participants will be requested not to change their medication during the study, if at all possible, and to refrain from other compassion-focused interventions. Health care use of all participants (including necessary changes of medication) will be assessed at baseline, end of treatment/control period and during the six months follow-up using the Client Service Receipt Inventory (CSRI) [27].

2.3.3. Adherence

Participant compliance to the MBCL program will be assessed during the intervention period using a calendar on which participants indicate their adherence to formal and informal exercises on a daily basis.

Table 1
MBCL overview per session.

Theme of the session	Similarities in structure and exercises from MBSR/MBCT	Compassion practice Session 1–4 to self Session 5–8 to self & others	Psycho-education	Homework
1 – Why do we need compassion?	- Compassionate body scan - Compassionate breathing space	- The safe haven [16]	- Introduction compassion - Evolutionary development of the human brain: three emotion regulation systems: threat, drive and soothe system. Exploration of balance between these systems [23]	- Safe haven - Compassionate body scan - Diary: moments of kindness and compassion
2 – Development of self-compassion	- Self compassion and dealing with obstacles - Compassionate breathing space	- Experiencing acceptance from a friendly other	- Obstacles to compassion: confrontation with (old) pain - Five paths to self-compassion	- Soften-soothe-allow - Metta: unconditionally accepting other - Diary: recording moments of experiencing threat
3 – Craving and compassion	- Compensating unpleasant feelings by chasing what we want: recognising automatic patterns - Compassionate breathing space in difficult moments	- Experiencing acceptance from a friendly other and self - Soften-soothe-allow: compassion for self [19]	- Reflection on the inner bully: convictions and behaviour	- Compassionate floor yoga - Metta: unconditionally accepting other and self - Diary: drive system
4 – Aversion and compassion	- Compensating unpleasant feelings by avoiding what we don't want: recognising automatic patterns - Compassionate breathing space with emotional pain	- Experiencing acceptance from a friendly other and self - Soften-soothe-allow: compassion for self	- Exploration of compassionate stance towards unhelpful automatic patterns - Exploration of guilt and shame	- Soften-soothe-allow - Metta: unconditionally accepting other and self - Diary: soothe system
5 – Compassion to others	- Responding to stress - Compassionate breathing space with emotional pain	- Experiencing acceptance from a friendly other, self and important other	- Reflection on what contributes to happiness	- Compassionate standing yoga - Metta: unconditionally accepting other, self and important other - Diary: exploring the possibility to be kind and compassionate
6 – Common humanity	- Responding to stress: forgiving self: the compassionate letter - Compassionate breathing space	- Experiencing acceptance from a friendly other, self, important other, neutral other	- Exploration of forgiving self - Exploration of common humanity	- Metta: unconditionally accepting other, self and neutral person - Compassionate walking - Diary: recording moments of kindness and compassion
7 – Compassion in action	- Responding to stress: forgiving others - Compassionate breathing space in action	- Experiencing acceptance from a friendly other, self, important other, neutral other and difficult other or difficult characteristics of yourself	- Exploration of forgiveness others: five stages of acceptance - Reflection on compassionate qualities and skills	- Metta: unconditionally accepting other, self, neutral person and difficult person or characteristics of yourself you have difficulty with - Soften-soothe-allow - Diary: acting out of compassion
8 – Resourced by compassion	- Responding to stress - Compassionate breathing space	- Experiencing acceptance from a friendly other, self, important other, neutral other and difficult other or difficult characteristics of yourself and including all beings	- Reflection of the four heart qualities: kindness, compassion, joy and equanimity	

2.3.4. Outcome measures

2.3.4.1. Primary outcome measure

2.3.4.1.1. Depressive symptoms. Primary outcome measure will be severity of depressive symptoms as measured by the Beck Depression Inventory-II [28] (Dutch version: BDI-II-NL [29]). This standardized questionnaire contains 21 items, scored on a 0–3 scale. The BDI-II has been validated in psychiatric outpatients. The internal consistency varies from 0.84 to 0.91 and the retest reliability ranged from 0.73 to 0.96 [30,31].

2.3.4.2. Secondary outcome measures

2.3.4.2.1. Depressive disorder. Presence, partial or full remission of depressive disorder will be assessed with the Structured Clinical Interview for DSM-IV disorders (SCID), part 1 [32]. The interview (either face-to-face or, at follow-up, sometimes by telephone) will be administered at baseline, end-of-treatment/end-of-control and six months after completion of treatment. Previous studies on inter-rater reliability of the SCID-I have reported Cronbach's alpha values between 0.61 and 0.80 [33,34]. All interviews will be audio taped and a random sample of $N = 30$ interviews will be second-rated by an independent and blind assessor to assess inter-rater reliability in the current study.

2.3.4.2.2. Rumination. Rumination will be assessed with the Ruminative Response Scale (Dutch translation; [35]), a 26-item, 4-point scale, self-report questionnaire designed to measure ruminative thought in response to (recalled) moments of feeling 'sad, down or depressed'. It consists of two subscales: reflection and brooding. Internal consistencies vary from 0.72 to 0.77 and test-retest reliabilities vary from 0.60 to 0.62 [36]. Rumination seems to be sensitive to change in mindfulness-based interventions [11].

2.3.4.2.3. Experiential avoidance. Experiential avoidance will be measured using the Dutch version of the Acceptance and Action Questionnaire (AAQ-II; [37]), a 7-item questionnaire scored on a 7-point scale. Internal consistency is good (Cronbach's alpha of 0.89) and convergent validity with the BDI-II is high [37]. Items examples include: "My painful experiences and memories make it difficult for me to lead a valuable life" and "I am afraid of my emotions".

2.3.4.2.4. Fear of Compassion. Fear of Compassion will be measured using the Fear of Compassion of self subscale of the Fears of Compassion Scales [38]. This subscale is a 15-item, 5-point scale which was tested on a student and therapist population (Cronbach's alpha respectively 0.92 and 0.85) [38]. Subscale item examples include: "I feel that I don't deserve to be kind and forgiving to myself", "I fear that if I become more self-compassionate, I will become a weak person" and "Getting on in life is about being tough rather than compassionate". As there was no Dutch version available, the list of items was translated and back translated by the authors. Discrepancies between original and translated version of the scale were discussed among the authors upon which a shared decision was made about the best translation.

2.3.4.2.5. Self-compassion. Self-compassion will be measured using the Dutch version of the Self-Compassion Scale (SCS) [39]. The questionnaire consists of 26 items divided over 3 subscales: 1) self-kindness versus self-judgment, 2) common humanity versus isolation, and 3) mindfulness versus over-identification. On a scale of 1 to 5, participants indicate the extent to which they agree with statements such as: "I try to be loving towards myself when I'm feeling emotional pain" (self-kindness), "When things are going badly for me, I see the difficulties as part of life that everyone goes through" (common humanity) and "When I'm feeling down I try to approach my feelings with curiosity and openness" (mindfulness). Internal consistencies of the different subscales vary from 0.75 to 0.81 and test-retest reliabilities vary from 0.80 to 0.93 [39]. The SCS is sensitive to change in MBCT [14].

2.3.4.2.6. Mindfulness skills. Mindfulness skills will be measured using the Five Facet Mindfulness Questionnaire (FFMQ-NL) [40], which has five subscales: observing, describing, acting with awareness, non-judging of inner experience and non-reactivity to inner experience. Internal consistencies of the different subscales vary from 0.72 to 0.93 [40]. The FFMQ is sensitive to change in mindfulness-based interventions [41].

Positive affect will be measured using the Types of Positive Affect Scale [42], an 18-item, 5-point scale which measures the extent to which participants find certain descriptions of positive affect characteristic to themselves. Factor analysis showed three types of positive affect: activated, relaxed and safe. Item examples include lively, tranquil, and secure, respectively. Internal consistency was good (Cronbach's alpha 0.83 for activated and relaxed affect, 0.73 for safe affect) and test retest reliability was good (for safe and activated) to moderate (for relaxed) [42]. As there was no Dutch version available, the list of items was translated in Dutch and translated back in English by the authors.

2.3.4.2.7. Quality of Life. Quality of Life will be measured using the 26-item self-report WHO-QoL short version (WHO-QoL-BREF) [43], which measures subjectively experienced quality of life in four domains: physical, psychological, social, and environmental. Items are scored on a 5-point scale. The internal consistency is satisfactory to good, with an alpha of 0.80 for the domain physical health, 0.74 for psychological health and 0.66 for social relationships [44].

2.3.4.3. Process measures. At the beginning of each session, participants will be asked to fill out weekly questionnaires, consisting of ten items: six items with the highest factor loading for each subscale of the SCS [39], as well as two positive and two negative items with the highest factor loadings from the PANAS [45]. See Table 2 for the schedule of enrolment, interventions and assessments.

2.3.5. Sample size

Based on our pilot study of MBCL in patients with recurrent depression with or without a current depressive episode (Schuling et al., submitted), we estimated the change in Beck Depression Inventory (BDI-II; [28]) scores in the intervention group to be four, with a standard deviation of nine. Using a two-sided alpha of 0.05 and a power of 80%, we would need 162 participants in total. However, using an ANCOVA analysis controlling for baseline levels and assuming the correlation between pre- and post-treatment measures to be 0.5 [11], we could adapt the analysis with the design factor $1 - r^2$ [46], resulting in a required number of participants of 104. Based on the absence of drop-out in the pilot study, we anticipate possible drop-out to be no higher than 15% and therefore aim to recruit $N = 120$ patients for the study.

2.3.6. Recruitment procedure

2.3.6.1. Baseline assessment. Patients with recurrent depression who previously participated in an MBCT course at our centre will be informed about the study by letter and invited to take part. Those interested will be invited for a research interview by the principal investigator, including questions about socio-demographic information, medical and psychiatric treatments over the past six months, medication and the extent to which participants are still practicing mindfulness. The SCID-I will be administered to assess the DSM-IV criteria for current depression, partial or full remission, number of previous depressive episodes and age of onset. All SCID-interviews will be conducted by the principal researcher (RS) who has received SCID training and is supervised by a consultant psychiatrist (AS). A subset of SCID-interviews will be audio taped and rated by a second, independent senior researcher to establish inter-rater reliability. In addition, patients will be requested to fill out a set of questionnaires, including the Childhood Trauma Questionnaire (CTQ) [47], which assesses childhood trauma in terms of sexual and physical abuse, and emotional neglect.

2.3.6.2. Randomization. Those eligible for the study will be asked to sign the informed consent form and are subsequently randomized to MBCL + TAU or TAU only. Randomization will take place by a computerised program, designed by an independent statistician. The randomization will be in blocks of four and minimized for presence,

Table 2
Schedule of enrolment, interventions, and assessments.

Timepoint	Enrolment	Study period			
		Allocation	Post-allocation		
	$-t_1$	0	t_1	t_2	t_3
Enrolment					
Eligibility screen	X				
Informed consent		X			
Allocation		X			
Interventions					
[MBCL + TAU]		●━━━━━━━━●			
[TAU]		●━━━━━━━━●			
Assessments					
Baseline demographics		X			
CTQ		X			
BDI-II		X	X	X	X
SCID-I[a]		X	X	X	X
RRS		X	X	X	X
AAQ-II		X	X	X	X
FoCS		X	X	X	X
TPAS		X	X	X	X
SCS		X	X	X	X
FFMQ		X	X	X	X
WHO-QoL-BREF		X	X	X	X
Calendar (mindfulness adherence)			X	X	
CSRI (use of health care service)		X	X	X	X

t_1: end-of-treatment intervention group/end-of-control control group. t_2: follow-up intervention group/end-of treatment control group. t_3: follow-up control group. CTQ: Childhood Trauma Questionnaire; BDI-II: Beck Depression Inventory-II; SCID-I: Structured Clinical Interview Diagnostics Part I; RRS: Ruminative Response Scale; AAQ-II: Acceptance and Action Questionnaire-II; FoCS: Fear of Compassion Scale; TPAS: Type of Positive Affect Scale; SCS: Self-Compassion Scale; FFMQ: Five Facet Mindfulness Questionnaire; WHO-QoL-BREF: World Health Organization Quality of Life Short Form; CSRI: Client Service Receipt Inventory.

[a] Module depression (current and/or in the past).

partial or full remission of depressive disorder, age of onset, total number of previous depressive episodes (1–2; 3–4; or >5) and presence or absence of either physical or sexual abuse during childhood. After randomization, the principal researcher will inform the participants of the condition they are allocated to.

2.3.7. Blinding

As in most psychological intervention studies, it will be impossible to blind the participants to the intervention they receive. As the principal investigator will be involved in the coordination of the trial, she will not be able to be blind to the assignment of participants either. However, the primary outcome measure and most of the secondary outcome measures are self-report questionnaires which do not involve an assessor at all. The training groups will consist of a mixture of patients allocated to the intervention and patients allocated to the TAU condition participating in the MBCL after completion of the control period. The MBCL teachers will be blinded to who belongs to which group.

2.3.7.1. Follow-up assessments. End-of-treatment/control assessments will place at the end of the intervention/control period. After that, those assigned to the TAU condition will be offered to participate in MBCL. After the TAU group has completed MBCL, they will also have their end-of-treatment assessment. Both those initially assigned to MBCL and those participating in MBCL after the control period will have a follow-up assessment six months after completion of treatment. At end of treatment and six months follow-up, a standardized psychiatric interview will take place (SCID) [32], and health care use since last assessment will be collected for each individual patient using an adapted version of the Client Service Receipt Inventory (CSRI) [48]. Patients will also be asked to complete another set of self-report questionnaires online. A purposive sample of participants will be asked to participate in one-on-one, in-depth interviews about their experiences with MBCL.

2.3.8. Potential harms and dropout

When receiving an indication of harm by the principal investigator or MBCL teachers, contact will be made with the participant to assess the nature of the problem, after which it will be reported to the Medical Ethical Committee appointed to the study. In case of dropout from the intervention, the participants will be asked to state his/her reasons to assess whether the intervention has brought harm to the participant. Subsequently, they will be requested to nevertheless complete the follow-up assessments as the study will be analysed on an intention-to-treat basis.

2.4. Statistical analysis

All analyses will be carried out using both intention to treat (primary) and per protocol samples (secondary). We will use multiple imputation with regard to missing data, and conduct sensitivity analyses using other reasonable scenarios for imputation. Post-treatment BDI-II scores will be compared between the two groups, controlling for baseline levels. All analyses are performed using ANCOVA. A Cohen's *d* effect size will be calculated. SPSS package 20.0 will be used for analyses and graphs.

Results will be reported in accordance with CONSORT guidelines [49]. The one-on-one, in-depth interviews will be analysed using Grounded Theory [50].

In addition to the effectiveness of the MBCL, we will explore possible moderators of treatment effects, such as number of previous episodes [4,51], childhood adversity [47], and early age of onset [10]. As a 'rule of thumb', the number of moderators we will explore will not exceed one per ten participants. In terms of mediation of treatment effect, we will look at possible mediators as adherence to the program, self-compassion, rumination, experiential avoidance and mindfulness [52,53]. For the mediation analysis, we will follow the recommendations of Preachers and Hayes for multiple mediation models [54], whose bootstrapping method can be used on relatively small sample sizes.

2.5. Qualitative study

Lastly, in order to gain more insight into the possible additional value of compassion training after MBCT, we will conduct a qualitative study using one-on-one, in-depth interviews with a purposive sample of the participants. We aim to interview a sample that is as diverse as possible in terms of gender, age and current depressive disorder, and aim to include both completers and non-completers of the intervention. We will analyse the interviews using the constant comparative method in order to be able to establish Grounded Theory [50]. In this method, it is common to include as many participants as is necessary to reach saturation on the subject of the research question, i.e. we will keep on interviewing participants until no more new information is being brought forward by them on the added value of MBCL over MBCT alone. We expect to be interviewing between fifteen and 25 people.

2.6. Data monitoring

The data will be monitored in a number of ways: a random subsample ($N = 30$) of the SCID-interviews will be rated by an independent, senior researcher to assess inter-rater reliability. All MBCL sessions will be recorded on DVD, of which two random sessions per teacher will be reviewed by both the principal researcher and an independent experienced MBI teacher to assess therapist competency and adherence to the MBCL curriculum adherence. All statistical analyses will be reviewed by an independent statistician. No interim analyses will be performed. Lastly, all data collection and analysis will be done independently from the fund that financially supported of the trial.

3. Discussion

To our knowledge, this is the first RCT investigating the effectiveness of compassion training in patients with recurrent depression. Therefore, we have chosen to compare the intervention with TAU. We are aware that this design does not allow us to draw any conclusions about the specificity of compassion training over and above non-specific therapeutic factors such hope, rationale, therapeutic relationship and peer support. Due to the fact that we did not want to disappoint the patients who were interested in participating in the compassion training, we have chosen to offer patients randomized to the TAU condition to participate in the training after the end-of-control assessment. In this way, we have to examine the consolidation of treatment effect in an uncontrolled rather than a controlled sample. Recruitment of the trial started July 2013 and ended December 2014. All data have been collected, the follow-up data on the last cohort of participants was collected in November 2015. Data analysis is currently in progress.

If the findings of this first study are positive, a replication RCT with an active control condition and a longer follow-up period of one year is warranted. Also, future research will be needed to look at the best implementation of compassion training, i.e. should it indeed be a follow-up to a mindfulness-based intervention (MBI) like MBCT, should it be incorporated in existing MBIs or may it even be added to the list of existing MBIs as a stand-alone intervention?

Competing interests

The clinical research team declares it had no part in developing the MBCL program, though Dr. Speckens and Ms. Schuling made modifications to it in collaboration with the original developers following the pilot study (Schuling, 2016, submitted). The team does not gain income from the sale of books on MBCL, nor does it gain income from giving lectures or workshops about it. Dr. Speckens is founder and clinical director of the Radboud UMC Centre for Mindfulness. Ms. Schuling, Ms. Van Ravesteijn and Ms. Huijbers are affiliated with the Radboud UMC Centre for Mindfulness. Dr. Kuyken is director of the Oxford Mindfulness Centre. Dr. Donders is part of the Radboud UMC Department for Health Evidence and declares no competing interests.

Author's contributions

All authors contributed to the design of the study. AS is the principal investigator of the study. RS, MH and AS drafted the paper, which was added to and modified by HR, RD and WK. RS, HR and AS were involved in recruiting participants. RD contributed specifically to the statistical analysis plan. All authors read and approved the final manuscript.

Ethics, consent and permissions

All participants signed a patient consent form, consenting to participation in the research and giving permission to obtain data during research and using it in publication after anonimization.

Acknowledgements

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