MINDFULNESS-BASED INTERVENTIONS FOR DEPRESSION

how does it work and for whom?

Marleen Josien ter Avest
Colophon

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General introduction
1. Depression

Major depressive disorder (MDD) or depression is one of the most prevalent and impairing mental disorders (World Health Organization [WHO], 2017). MDD is characterized by at least five out of nine symptoms, including a minimum of one core symptom. Core symptoms are a depressed mood and a markedly diminished interest or pleasure in most or all activities. Additional symptoms include changes in weight or appetite, insomnia or hypersomnia, psychomotor agitation or retardation, fatigue or loss of energy, feelings of worthlessness or excessive or inappropriate guilt, diminished ability to think or concentrate or indecisiveness and recurrent thoughts of death or suicidal ideation. MDD is diagnosed when these symptoms are present for at least two consecutive weeks, are not attributable to substance use or a medical condition, and cause clinically significant distress or impairment in social, occupational, or other important areas of functioning (American Psychiatric Association, 2013).

Currently, MDD is a leading cause of disease burden worldwide (WHO, 2017). In addition, MDD often runs a chronic and recurrent course, and many individuals experience residual depressive symptoms in the aftermath of a depressive episode (Verduijn et al., 2017; Richards, 2011). The most commonly used treatment to prevent new episodes of depression is the use of antidepressant medication (Spijker et al., 2013). However, the use of antidepressant medication also has its disadvantages (i.a. long-term use and side effects) and many patients prefer psychological interventions (Biesheuvel-Leliefeld et al., 2015). Fortunately, aside from antidepressant medication, numerous psychological interventions have been developed for MDD, among which mindfulness-based cognitive therapy (MBCT; Segal et al., 2002, 2012).

2. Mindfulness-Based Cognitive Therapy

MBCT is a manualized group-based intervention originally developed by Segal et al. (2002) to reduce the risk of relapse/recurrence for individuals with recurrent depression. The underlying theoretical model is the ‘differential activation hypothesis’ (Lau et al., 2004; Teasdale, 1988), which suggests that with each depressive episode, reactivation of dysfunctional thinking happens more easily and as a consequence, risk of relapse/recurrence increases (Segal et al., 2006). During MBCT, one learns to recognize and disengage from these automatic dysfunctional thinking patterns, which may lead to depression, by taking a decentered, non-judging perspective on negative thoughts (Segal et al., 2012). Originally, Jon Kabat-Zinn (1994) defined mindfulness as “paying attention in a particular way: on purpose, in the present moment, and non-judgmentally” (p. 4). A further conceptualization of mindfulness proposed a two-component
model; one involving self-regulation of attention to the present moment experience (i.e., the ‘what’), and the other one involving an open, curious, accepting and non-judgmental attitude towards one’s experience (i.e., the ‘how’; Bear et al., 2019).

MBCT combines elements from the mindfulness-based stress reduction program (MBSR; Kabat-Zinn, 1990) with components of cognitive therapy for depression (Beck et al., 1979). It consists of 8 weekly sessions of 2 - 2.5 hours and 1 day of silent practice (Segal et al., 2012). During the course, participants are encouraged to practice at home on a daily basis for about 45 minutes to further increase their mindfulness skills. Mindfulness practices can be divided into formal practices (e.g., body scan, sitting meditation), and informal practices involving the cultivation of mindfulness in routine daily life activities (Segal et al., 2012).

2.1. Effectiveness
Accumulating evidence shows that MBCT is effective for individuals with recurrent depression, both in reducing their risk of relapse/recurrence and in reducing their level of depressive symptoms when they experience a depressive episode (Thimm & Johnson, 2020). Due to its strong evidence base, MBCT is being recommended in (inter)national guidelines as a treatment choice for relapse prevention in recurrent depression (American Psychological Association, 2019; National Institute for Health and Care Excellence, 2009; Spijker et al., 2013).

Initially, MBCT was not considered suitable for individuals with current depression because of the expectation that fully attending to the present moment might be especially difficult in the midst of depressive symptomatology. One might become preoccupied with negative thoughts and difficulties in concentration might impede effectiveness (Baer et al., 2019; Segal et al., 2012; Strauss et al., 2014). Over time, however, research about the effectiveness of mindfulness-based interventions has started to include currently depressed individuals, and results support the feasibility and effectiveness of MBCT in this population (Goldberg et al., 2018; Hedman-Lagerlof et al., 2018; Lenz et al., 2016; Strauss et al., 2014; Wang et al., 2018). Fewer studies have been conducted on the effectiveness of MBCT in individuals with chronic or treatment-resistant depression. Some of these revealed that MBCT can be effective (Barnhofer et al., 2009; Cladder-Micus et al., 2018; Eisendrath et al., 2016; Kenny & Williams, 2007), whereas Michalak et al. (2015) found that MBCT was not more effective than treatment-as-usual (TAU) in reducing depressive symptoms in this population.

To conclude, MBCT for depression has proven to be effective. However, many individuals who participated in MBCT still experience residual depressive symptoms, which are a predictor for relapse/recurrence to depression (Buckman et al., 2018). To further improve the treatment efficacy and targeting of MBCT for depression, more knowledge is needed on its working mechanisms.
2.2. Working mechanisms

2.2.1. Mediation “How does it work?”

In order to improve the treatment efficacy of MBCT for recurrent depression, a better understanding of the processes which bring about therapeutic change is needed (Dimidjian & Segal, 2015; Kazdin, 2007). There are different concepts involved considering research into possible working mechanisms. According to Kazdin (2007), a mechanism is the basis for an effect, i.e., the processes or events that are responsible for the change; the reasons why change occurred or how change came about. One way to investigate a possible mechanism of change is via investigating possible mediators. A mediator is an intervening variable that may account -statistically- for the relationship between the independent and dependent variable (Kazdin, 2007). However, one should keep in mind that something that mediates change may not necessarily explain the -whole- process of how change came about (Kazdin, 2007).

Research to date proposes various possible mediators for the effect of MBCT in individuals with recurrent depression. A systematic review of 23 studies on MBCT for recurrent MDD, of which 20 were RCTs, provided evidence for increases in mindfulness, self-compassion, and meta-awareness and decreases in rumination and worry to mediate treatment outcome (van der Velden et al., 2015). In addition, the study found preliminary evidence indicating that changes in attention, memory specificity, self-discrepancy, emotional reactivity, and momentary positive affect and negative affect might be among the mechanisms of change in MBCT. However, none of the examined studies included measures of temporal precedence as recommended by Kazdin (2007), where both mediator and symptoms are measured at several simultaneous points throughout the treatment period to uncover whether the mediator variable does in fact change prior to change in the outcome variable.

2.2.1.1. Mindfulness and affect

Emotion regulation plays an important role in MDD (Joormann & Stanton, 2016). Along with the diminished experience of positive emotions, the frequent experience of negative emotions is a key characteristic of depressive symptomatology (American Psychiatric Association, 2013). According to the mindfulness-to-meaning theory (MMT; Garland et al., 2015), mindfulness has been suggested to have a positive reciprocal relationship with positive affect and a negative reciprocal relationship with negative affect. Positive affect is suggested to improve well-being and reduce depressive symptoms and risk of relapse/recurrence depression (Bolier et al., 2013; Khazanov & Ruscio, 2016; Sin & Lyubomirsky, 2009) and residual depressive symptoms (e.g., negative affect) are a predictor for relapse/recurrence depression (Buckman et al., 2018; Watson et al., 1988). Therefore, developing one’s level of mindfulness could lead to an increase in positive affect and a decrease in negative affect, which could lead to
further increases in mindfulness and so on, leading to better outcomes in (recurrently) depressed individuals.

Despite accumulating evidence for mindfulness and emotion (regulation) as possible mediators for the effect of MBCT on mental health outcomes (van der Velden et al., 2015), findings have been largely based on pre-post assessments of mediators so far, and most studies did not take the temporal order of change in mediator and outcome variables into account. This makes it difficult to identify causal links between the intervention, possible mediators and outcome(s) (Kazdin, 2007). More rigorous designs are needed to enable a formal mediation analysis to disentangle the dynamic process and temporal order of changes in recurrently depressed individuals during MBCT.

2.2.1.2. Mindfulness practice
In general, it is assumed that mindfulness practice is an essential element in MBCT (Kabat-Zinn, 1990; Segal et al., 2012) and it is conceptualized as a form of mental training (Tang et al., 2015) with greater amount of practice conferring greater benefit. According to a systematic review and meta-analysis by Parsons et al. (2017), there seems to be a small but significant association between the extent of formal mindfulness home practice and positive intervention outcomes in MBCT and MBSR for a wide range of patients. The strength of this association was similar to that reported in meta-analyses of CBT homework assignments and outcomes (Kazantzis et al., 2010). This finding suggests that it is indeed valuable to support and encourage participants to do formal mindfulness practice in MBCT and MBSR.

However, most studies to date have been conducted in samples without psychiatric diagnosis, who received MBSR rather than MBCT, and most studies have been correlational studies with short-term outcomes (Lloyd et al., 2018; Parsons et al., 2017). In addition, there was substantial heterogeneity in amount of home practice reported across studies and evidence suggested a publication bias, whereby studies with lower practice amounts were less likely to be reported (Parsons et al., 2017).

Only a few studies investigated the association between formal mindfulness practice and short-term treatment outcomes of MBCT in recurrent depression (Parsons et al., 2017), which yielded mostly positive effects (i.e., Hawley et al., 2014; van Aalderen et al., 2012; Geschwind et al., 2012) in addition to non-significant findings (i.e., Crane et al., 2014; Shallcross et al., 2015). Moreover, only two studies examined the association between mindfulness home practice during MBCT and relapse/recurrence rates in individuals with recurrent depression over a longer period, which yielded mixed results. Crane et al. (2014) found a significant effect of daily minutes of formal mindfulness home practice on risk of relapse/recurrence over a 12 month follow-up period after MBCT ($n = 99$, Hazard Ratio (HR): .97, CI: .947 - .995). In addition, those who practiced at
least 3 days a week at home during MBCT were almost half as likely to experience a relapse/recurrence than those who practiced less often (HR: .53, CI: .30 - .94). In contrast, the second study did not find significant associations between frequency of formal mindfulness home practice during 12 months follow-up and risk of relapse/recurrence in individuals with recurrent depression (Bondolfi et al., 2010). In that study, home practice was measured in a more general way: participants were asked to retrospectively report their degree of practice during the intervention, during the first 6 months of follow-up, and during the last 6 months of follow-up. Given the emphasis placed on daily practice and the substantial effort and time commitment required of participants in MBCT, replication and methodologically strong studies are needed into the long-term effects of formal mindfulness practice in MBCT for clinical populations.

Furthermore, little is known about the possibility of a reverse effect: higher levels of depressive symptomatology might act as a barrier to engage in home practices. One could experience difficult or aversive thoughts and feelings (Beck & Clark, 1997), and become more preoccupied by them, for example due to attentional biases associated with depression (Mogg et al., 1995) and increased rumination (Whitmer & Gotlib, 2013). As people typically show a tendency to avoid or suppress unpleasant experiences (Aldao et al., 2010), and depressive symptomatology may further add motivational and concentration difficulties (Keller et al., 2019; Ravizza & Delgado, 2014), it seems plausible to expect a negative influence of depressive symptomatology on home practice. To investigate the course and possible mutual relationships between home practice and depression outcomes, multiple assessments of both constructs over time are needed, preferably during and after the intervention period, and these data need to be analyzed with advanced statistical techniques. The autoregressive latent trajectory (ALT) modeling technique (Bollen & Curran, 2004), used in the current thesis, is appropriate to disentangle dynamic processes and the temporal order of change between constructs over time.

2.2.2. Moderation “For whom does it work?”

Another way to explore possible working mechanisms is via investigating possible moderators, i.e. variables that influence the magnitude and/or direction of the relationship between two variables (Kazdin, 2007). For example, if the effect of MBCT on reducing depressive symptoms is stronger for women compared to men, then gender is a moderator (Kuyken et al., 2010). Moderators are related to mediators and mechanisms because they suggest that different processes might be involved dependent on the value of the moderator (e.g., different in women and men) (Kazdin, 2007).

Considering the heterogeneity of people with depression, an improved understanding of what patient characteristics may moderate MBCT’s treatment effect would enable improved targeting of MBCT in this population (van der
Several studies of MBCT aimed at preventing depressive relapse/recurrence in individuals in remission have shown stronger treatment effects for those with increased vulnerability, including individuals with three or more previous major depressive episodes, earlier onset of MDD (Ma & Teasdale, 2004; Teasdale et al., 2000), a history of early adversity (Kuyken et al., 2015; Williams et al., 2014) and more fluctuation in depressive symptoms (Segal et al., 2010). In an individual patient data (IPD) meta-analysis of existing trials on preventing relapse/recurrence in recurrent depression \((n = 1258; Kuyken et al., 2016)\), higher severity of depression at baseline was associated with a better treatment effect of MBCT. In currently depressed individuals it has been suggested that older individuals benefit more from MBCT in terms of reduction of depressive symptoms (Lenz et al., 2016). With regard to individuals with chronic or treatment-resistant depression, higher baseline levels of rumination appeared to predict a larger decrease in depressive symptoms after MBCT (Cladder-Micus et al., 2018).

There are some issues that need to be addressed concerning moderator analysis in the context of MBCT for depression. At first, most studies investigated populations of depressed individuals with a limited range of depressive symptoms at baseline. Secondly, most research into possible moderators has involved the effect of MBCT on risk of relapse and/or level of depressive symptoms. However, MDD has a huge impact on quality of life (WHO, 2017) and the initial aim of MBCT is not to change or eliminate unpleasant experiences (e.g., negative thoughts or feelings), but rather to relate to them in a different way. To date, there are promising results of the effect of MBCT on quality of life (Cladder-Micus et al., 2018; Kuyken et al., 2008, 2015). However, research into possible moderators including quality of life as outcome measure are still scarce.

Other issues concern the statistical approach to moderator analysis, which is often called treatment-subgroup analysis in the context of differential treatment efficacy research. Most studies into possible moderators of treatment effect assume linear associations. However, this assumption is not in line with current thinking that the relationships between psychological and physical processes and outcome may run an inverted U-curve trajectory (Grant & Schwartz, 2011). For example, it has been suggested that depressive symptoms might have an optimal level in which MBCT is effective, above or below this optimum level the effect might be minimal or undesirable effects might occur (Kuyken et al., 2016; van Dam et al., 2018). In addition, research to date did not make a distinction between quantitative treatment-subgroup interactions (or treatment-covariate interaction) and qualitative treatment-subgroup interactions. Quantitative treatment-subgroup interactions indicate that one treatment is always better than the other but only the magnitude of the effect differs for subgroups. These interactions imply that all people would still be assigned to one and the same treatment. In contrast, qualitative treatment-subgroup
interactions may indicate that for one or more subgroup(s) one treatment (e.g., MBCT) is better than another treatment (e.g., TAU), while for other subgroup(s) the reverse is true. Therefore, to identify for whom MBCT has added value and for whom a different intervention might be more suitable, qualitative treatment-subgroup interactions are needed. Furthermore, most studies only consider two-way interaction effects, while higher order interaction effects may play a role in explaining the variance in treatment efficacy too. Hence, our current knowledge of moderators in the context of MBCT for depression is still limited. More sophisticated examination, such as the qualitative interaction trees method (QUINT; Dusseldorp & van Mechelen, 2014), used in this thesis, is needed.

3. Mindfulness-Based Compassionate Living

In addition to gaining knowledge on how MBCT for recurrent depression works, investigating working mechanisms of promising follow-up interventions may further contribute to the improvement of treatment outcome in this population. Van den Brink and Koster (2015) developed mindfulness-based compassionate living (MBCL) as a follow-up intervention to MBCT or MBSR. In MBCL, one explicitly cultivates self-compassion, which is implicitly conveyed in MBCT and has been shown to mediate the effect of MBCT for recurrent depression (Kuyken et al., 2010). In MBCL, (self-)compassion encompasses the capacity to be sensitive to the suffering of self and others, and the commitment to alleviate and prevent this suffering (Gilbert & Choden, 2013). MBCL shares content with other compassion-based interventions (CBIs), such as compassion-focused therapy (CFT; Gilbert, 2010) and the mindful self-compassion program (MSC; Neff & Germer, 2013). It has been structured in a similar way as MBCT and MBSR (van den Brink & Koster, 2015): it is a group-based intervention consisting of eight sessions of 2.5 hours, a silent day, and daily home practices of 45-60 minutes. The practices are explicitly focused on cultivating compassion and kindness towards the self and others, including informal practices (e.g., breathing space with kindness or compassion) and formal practices (e.g., kindness meditation and compassionate breathing). A recent randomized controlled trial (RCT) showed that MBCL, as follow-up to MBCT, resulted in a greater reduction of depressive symptoms and improvement of quality of life, relative to TAU, in recurrently depressed individuals (Schuling et al., 2020). In addition, self-compassion appeared to mediate the post-intervention effect of MBCL. However, the mediation analyses only used pre-post measurements, therefore inferences about possible causality cannot be made. More research is needed into the (dynamic) process of self-compassion in MBCL for recurrently depressed individuals.
Rather than only focusing on depressive symptoms, changes in self-compassion have also been associated with changes in affect during CBIs. An intervention study in individuals vulnerable to depression ($n = 63$) found that practicing self-compassion resulted in subsequent increases in happiness (Shapira & Mongrain, 2010). In addition, several experimental studies suggested that self-compassion increases positive affect (e.g., Engen & Singer, 2015) and reduces negative affect (e.g., Arimitsu & Hofmann, 2017; Leary, et al., 2007). Only one experimental study has been conducted among individuals with MDD ($n = 48$; Diedrich et al., 2014). Depressed mood was induced at 4 points in time. After each mood induction, participants were instructed to wait, reappraise the situation, accept their negative emotions, or employ self-compassion to regulate their depressed mood. Significant differences in effectiveness were only found between the self-compassion and waitlist condition. Effects of self-compassion on positive/negative affect or reverse effects of positive/negative affect on self-compassion during MBCL for depression has not yet been scientifically researched.

4. Conclusion

To conclude, more knowledge is needed into the working mechanisms of MBCT and MBCL in individuals with recurrent depression. The current thesis aims to contribute to this field by investigating prospective associations between multiple assessments of process measures over both, short- and long-term periods by using advanced structural equation modeling techniques (i.e., ALT modeling). Moreover, the QUINT method was used in order to meet the need for more sophisticated examination of moderators to investigate the differential effectiveness of MBCT for depression.
5. Thesis

5.1. Aims

The overall aim of this thesis is to investigate how MBCT works in individuals with recurrent depression. Given that most previous research into the possible working mechanisms is based on correlational research and on short term-outcome, the current thesis endeavors to further develop this field by including short- and long-term outcomes, and by applying more advanced statistical techniques (i.e., ALT modeling). The ALT modeling technique combines an autoregressive (AR) model with a latent trajectory model (LTM), which is a latent growth model, in order to properly investigate cross-lagged (CL) effects, while controlling for overall trajectories, to prevent spurious CL effects to appear while they essentially do not exist (Voelkle, 2008). Hence, using the ALT modeling technique, one can make more reliable statements about the processes of stability and change during MBCT for recurrent depression.

As part of studying possible mechanisms, this thesis will help shed light on the heterogeneity of individuals with depression. This is achieved by providing an improved understanding of what personal characteristics moderate treatment effect and could be helpful to improve targeting of MBCT in this population. The current thesis aimed to meet the need for more sophisticated examination of possible moderators by applying the QUINT method. Contrary to previous research, which is mostly based on two-way treatment-subgroup interactions and linear associations, QUINT focuses on identifying qualitative treatment-subgroup interactions, considers higher order interaction effects and allows for non-linear relationships. This method identifies subgroups of patients in which one treatment is more beneficial than another, and for whom the reverse holds true. It is especially suited for situations with many potential moderating variables that might interact with the treatment variable without clear a priori hypotheses. The result of an analysis with QUINT is a binary tree from which treatment assignment criteria can be derived, relevant for clinical practice.

Lastly, research into the possible working mechanisms of MBCL for depression is still in its infancy. Therefore, the ALT modeling technique will be used to investigate possible process measures within MBCL, as follow-up to MBCT, for depression.

In sum, this thesis addresses the following research questions:

1. How does MBCT for depression work?
2. For whom does MBCT for depression work?
3. How does MBCL for depression work?
5.2. Outline
This thesis is divided into six chapters. Following this general introduction, Chapter 1, results of the research questions will be described in Chapter 2-6.

1. “How does MBCT for depression work?”
Chapter 2 describes the course, and possible interplay between mindfulness and both, positive and negative affect during MBCT for depression in individuals with recurrent depression in (partial) remission (n = 235), based on data from two multicenter RCTs. Prior to each MBCT session, self-reports were obtained on mindfulness, positive affect, and negative affect. The overall course and week-to-week associations of mindfulness and positive/negative affect during MBCT for recurrent depression were analyzed by the ALT modeling technique. Based on two multicenter RCTs on MBCT for recurrent depression (n = 200).

Chapter 3 describes the prospective associations between the extent of formal mindfulness practice and subsequent depression severity, and vice versa, during 15 months of follow-up. Depressive symptoms were assessed at 3-month intervals: 0 (baseline), 3 (post-treatment), 6, 9, 12, and 15 months. Formal mindfulness practice frequency was calculated for each 3-month period. ALT modeling was applied.

2. “For whom does MBCT for depression work?”
Chapter 4 describes the results of an individual patient data-analysis on three randomized-controlled trials, investigating the effect MBCT + TAU versus TAU alone (n = 292). Patients are either in (partial) remission, currently depressed or have chronic, treatment-resistant depression. Outcomes are depressive symptoms and quality of life. The QUINT method will be used to identify subgroups that benefit more from either condition.

3. “How does MBCL for depression work?”
With the use of the ALT-modeling technique, Chapter 5 describes the course and possible interplay between self-compassion and both, positive and negative affect during MBCL for depression in individuals with recurrent depression in (partial) remission and currently depressed individuals (n = 104). Self-reports of self-compassion and positive/negative affect were obtained at the start of each of the eight MBCL sessions.

Finally, Chapter 6 provides a summary of the above mentioned studies, followed by a general discussion, scientific and clinical implications, and directions for future research.
References


Mindfulness and Affect During Mindfulness-Based Cognitive Therapy for Recurrent Depression: an Autoregressive Latent Trajectory Analysis
Abstract

Objectives. Gaining knowledge of dynamic processes of mechanisms underlying mindfulness-based cognitive therapy (MBCT) for recurrent depression could help to improve treatment efficacy. The current study examined the overall course and week-to-week associations of mindfulness and positive/negative affect during MBCT for recurrent depression.

Methods. Using data from the MOMENT study, 235 patients with recurrent depression in (partial) remission allocated to MBCT were included. Prior to each MBCT session, self-reports were obtained on mindfulness, positive affect, and negative affect.

Results. Autoregressive latent trajectory (ALT) modeling revealed that, across the MBCT course, larger increases in mindfulness were associated with larger increases in positive affect ($r = .80, p < .050$). Higher general levels of negative affect were associated with smaller increases in mindfulness over time ($r = -.26, p < .001$). Week-to-week effects showed no reciprocal cross-lagged effects between mindfulness and positive affect or negative affect, except for positive affect at session 2 which was positively associated with mindfulness at session 3 ($r = .11, p < .050$).

Conclusions. The current study supports a positive association in strength of increase between mindfulness and positive affect, while higher general levels of negative affect might be associated with smaller increases of mindfulness during MBCT for recurrent depression. For future research, experience sampling methods (ESMs) are recommended to capture dynamics on a smaller time scale. ALT modeling techniques are advised to be better able to interpret the processes of stability and change during MBCT for recurrent depression.
1. Introduction

Major depressive disorder (MDD) is a common psychiatric disorder in which emotion regulation plays an important role (Joormann and Stanton, 2016; World Health Organization, 2017). Along with the diminished experience of positive emotions, the frequent experience of negative emotions is a key characteristic of depressive symptomatology (American Psychiatric Association, 2013). MDD often runs a chronic and recurrent course, and many patients experience residual depressive symptoms (Nierenberg, 2015; Richards, 2011). Currently, MDD is a leading cause of disease burden worldwide (World Health Organization, 2017).

Mindfulness-based cognitive therapy (MBCT; Segal et al., 2002) has been shown to be effective for relapse prevention in recurrent depression (Kuyken et al., 2016). MBCT consists of 8 weekly group sessions of 2.5hrs and a silent day (Segal et al., 2012). The intervention includes mindfulness practices and elements from cognitive therapy for depression (Beck et al., 1979). Mindfulness, in the context of mindfulness-based interventions, is most often referred to as paying attention, on purpose, in the present moment and non-judgmentally (Kabat-Zinn, 1994) and is considered a skill that can be trained (Segal et al., 2012; Tang et al., 2015).

In order to improve the treatment efficacy of MBCT for recurrent depression, a better understanding of the processes which bring about therapeutic change is needed (Dimidjian & Segal, 2015; Kazdin, 2007). Research to date proposes various possible mediators for the effect of MBIs on mental health outcomes. A systematic review and meta-analysis of 20 studies, of which 15 randomized controlled trials (RCTs), aimed to identify potential psychological mediating mechanisms underlying the effects of MBIs in mixed samples (Gu et al., 2015). The study found moderate evidence that an increase in mindfulness and a reduction of rumination and worry mediated treatment outcome. Evidence for reduction of cognitive and emotional reactivity and for increases in self-compassion and psychological flexibility mediating treatment outcome was preliminary but insufficient. Another systematic review of 23 studies on MBCT for recurrent MDD, of which there were 20 RCTs, provided evidence for increases in mindfulness, self-compassion, and meta-awareness and decreases in rumination and worry to mediate treatment outcome (van der Velden et al., 2015). In addition, the study found preliminary evidence indicating that changes in attention, memory specificity, self-discrepancy, emotional reactivity, and momentary positive affect and negative affect might be possible mediating mechanisms of change. Despite accumulating evidence for mindfulness and emotion (regulation) as possible mediators for the effect of MBCT on mental health outcomes, findings have been largely based on pre-post assessments of mediators so far, and most studies did not take the temporal order of mediator and outcome variables into account. This makes it difficult to identify causal links between the intervention,
the outcome(s), and possible mediators (Kazdin, 2007). More rigorous designs are needed to disentangle causal and mutual associations of possibly mediating factors during MBCT.

According to the mindfulness-to-meaning theory (MMT), mindfulness has been suggested to have a negative reciprocal relationship with negative affect and a positive reciprocal relationship with positive affect (Garland et al., 2015). As residual depressive symptoms (e.g., negative affect) are a predictor for relapse/recurrence depression (Buckman et al., 2018; Watson et al., 1988) and positive affect is suggested to improve well-being and reduce depressive symptoms and risk of relapse/recurrence depression (Bolier et al., 2013; Khazanov and Ruscio, 2016; Sin & Lyubomirsky, 2009), developing one’s level of mindfulness could lead to decreases in negative affect and increases in positive affect, further leading to better outcomes in (recurrent) depressed patients.

Research to date with more advanced methodological approaches, such as experience sampling methods (ESMs; Larson & Csikszentmihalyi, 1983), suggests these positive associations between mindfulness and positive affect and, to a lesser extent, negative associations between mindfulness and negative affect during MBCT in recurrently depressed patients. For example, an open-label RCT of MBCT for adults with residual depressive symptoms ($n = 120$) used experience sampling methodology during 6 consecutive days before and after MBCT or waitlist control period. The results showed that MBCT was associated with increased experience of momentary positive affect compared to waitlist control (Geschwind et al., 2011). Another ESM study of mainly patients with recurrent MDD ($n = 29$) showed that a mindful walking intervention resulted in an overall increase of both levels of mindfulness and positive affect and a decrease in negative affect. In addition, time-specific moment-to-moment effects showed that increased mindfulness was associated with subsequent increases in positive affect and decreases in negative affect the next moment during the day and vice versa (Gotink et al., 2016).

In short, overall increases in mindfulness appear to be associated with overall increases in positive affect and decreases in negative affect. However, knowledge of the dynamic process and temporal order of these changes in recurrently depressed patients is still scant. The dynamic interplay between levels of mindfulness, positive affect, and negative affect during MBCT for recurrent depression has not been investigated yet. The present study expands the previous literature by investigating the course and mutual associations of mindfulness and both positive affect and negative affect in patients with recurrent depression following MBCT based on a large sample originating from two multicenter RCTs (Huijbers et al., 2012). Moreover, assessments of mindfulness, positive affect, and negative affect took place prior to each MBCT session. Finally, the current study uses autoregressive latent trajectory (ALT) modeling to analyze the data, which permits a distinction between overall
trajectories across the entire intervention and week-to-week effects of mindfulness, positive affect, and negative affect. This makes it highly suitable for analyzing dynamic processes. Over the course of the MBCT, it is expected that mindfulness and positive affect increase, while negative affect decreases. In addition, the strength of increase in mindfulness is expected to be associated with the strength of increase in positive affect and decrease in negative affect. Finally, reciprocal week-to-week associations are expected between mindfulness and affect. Specifically, higher levels of mindfulness at a certain week are expected to precede higher levels of positive affect and lower levels of negative affect in the subsequent week. Meanwhile, higher levels of positive affect and lower levels of negative affect at a certain week are expected to precede higher levels of mindfulness in the subsequent week.

2. Methods

2.1. Participants
Adult patients were recruited via direct referral from mental health professionals and media advertisements between September 2009 and January 2012 at 12 different secondary and tertiary psychiatric outpatient clinics across the Netherlands. Native Dutch-speaking patients with recurrent depression (≥ 3 prior episodes) according to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000) using the Structured Clinical Interview for DSM Axis I Disorders (SCID-I; \( \kappa = 0.70, p = .001, 95\% \text{ CI: } 0.46 - 0.94; \) First et al., 1996), who were on a stable dose of antidepressant medication (≥ 6 months) and currently in (partial) remission, were included after written informed consent had been obtained. Exclusion criteria were as follows: bipolar disorder, psychotic disorder, neurological disorder, somatic disorder, current alcohol and/or drug dependency as assessed by the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 1998), use of a high dose of benzodiazepines, electric convulsive therapy ≤ 3 months, previous mindfulness training or considerable meditation experience, current psychological treatment (≥ 1×/3 weeks), and visual hearing/cognitive impairments impeding full participation. Patients were included only after written informed consent had been obtained. Participants from both multicenter trials who received an adequate dose of the intervention, i.e., at least 4 MBCT sessions (Kuyken et al., 2010; Teasdale et al., 2000), were included in the current study (\( n = 235 \)). Table 1 contains a detailed description of the demographic and clinical characteristics of the participants of the current study. Participants participated, on average, 7.16 sessions (range: 4 - 8, \( SD = 1.08 \)) and performed 58% (range: 0 - 1, \( SD = 0.23 \)) of the given formal homework exercises.
2.2. Procedures
The current study used data from the MOMENT study which consists of two related multicenter RCTs. The first RCT was a non-inferiority trial that compared the combination of MBCT and maintenance of antidepressant medication (ADM) with MBCT alone (Huijbers et al., 2016). The second RCT was a superiority trial that compared the combination of MBCT and ADM with ADM alone (Huijbers et al., 2015). For study details, participants’ demographic and clinical characteristics, and outcomes of both RCTs, see the respective papers (Huijbers et al., 2015, 2016).

MBCT was delivered in a real-life setting, from university hospitals to community mental health centers across the Netherlands. Participants attended MBCT classes together with non-trial participants, i.e., patients with recurrent depression from regular clinical practice. MBCT was largely based on the protocol of Segal et al. (2002) with some adaptations (2.5hrs instead of 2hrs sessions and additionally 1 silent day between the 6th and 7th sessions). Adding the silent day has been suggested in the most recent version of the MBCT protocol (Segal et al., 2012). Groups consisted of 8 to 12 patients during 8 weekly sessions. MBCT included formal meditation exercises, such as the body scan, sitting meditation, walking meditation, and mindful movement as well as informal exercises, such as bringing present-moment awareness to everyday activities. Cognitive behavioral techniques included education, monitoring and scheduling of activities, identification of negative automatic thoughts, and devising a relapse prevention plan. Participants were encouraged to practice meditation at home for about an hour a day using CDs. At the start of each weekly session, questionnaires were filled out by participants. A total number of 21 teachers recruited from regular clinical practice participated in both trials. Videotapes were available for 15 primary teachers and examined with the mindfulness-based interventions: Teaching Assessment Criteria (MBI:TAC; Crane et al., 2013). Teacher ratings were ‘proficient’ (n = 3), ‘competent’ (n = 4), ‘advanced beginner’ (n = 6), and ‘beginner’ (n = 2). The mean teacher competency score was 3.53 (SD = 0.92, range: 2.00 - 5.15). Seven of the 15 teachers met the advanced criteria of the association of mindfulness-based teachers in the Netherland and Flanders (www.vmbn.nl), which are in accordance with the UK good practice guidelines (UK Network of Mindfulness-Based Teachers, 2015).

2.3. Measures
2.3.1. Mindfulness
The Mindful Attention Awareness Scale (MAAS) was administered to assess the characteristic of dispositional mindfulness, namely open or receptive awareness of and attention to what is taking place in the present (Brown & Ryan, 2003). This questionnaire consists of 15 items formulated in a negative way (e.g., “I find it difficult to stay focused on what’s happening in the present”). Items are rated on
a 6-point Likert scale ranging from ‘almost always’ to ‘almost never’. Higher values represent higher levels of mindfulness. In this study, participants were instructed to choose the answers for each statement that best reflected their experiences of the past week, including the current day. The average scale score was used in this study. The Dutch version of the MAAS has shown the expected

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>157 (67)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>55 (24)</td>
<td></td>
</tr>
<tr>
<td>Married or Cohabiting</td>
<td>137 (60)</td>
<td></td>
</tr>
<tr>
<td>Divorced or Widowed</td>
<td>38 (16)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>5 (2)</td>
<td></td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>19 (8)</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>65 (29)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>144 (63)</td>
<td></td>
</tr>
<tr>
<td>Missing</td>
<td>7 (3)</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>155 (66)</td>
<td></td>
</tr>
<tr>
<td>Previous CBT</td>
<td>137 (58)</td>
<td></td>
</tr>
<tr>
<td>Type of mADM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SSRI</td>
<td>162 (69)</td>
<td></td>
</tr>
<tr>
<td>TCA</td>
<td>46 (20)</td>
<td></td>
</tr>
<tr>
<td>Other a</td>
<td>27 (11)</td>
<td></td>
</tr>
<tr>
<td>Remission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full (IDS-C30 ≤ 11)</td>
<td>125 (53)</td>
<td></td>
</tr>
<tr>
<td>Partial (IDS-C30 &gt;11)</td>
<td>110 (47)</td>
<td></td>
</tr>
<tr>
<td>Suicide attempt (lifetime)</td>
<td>43 (18)</td>
<td></td>
</tr>
<tr>
<td>Age in years</td>
<td>50.70 (10.81)</td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms (IDS-C30)</td>
<td>12.58 (9.74)</td>
<td></td>
</tr>
<tr>
<td>Previous MDEs</td>
<td>5.91 (5.72)</td>
<td></td>
</tr>
<tr>
<td>Age at MDD onset b</td>
<td>25.89 (11.84)</td>
<td></td>
</tr>
</tbody>
</table>

Note. CBT = cognitive behavioral therapy; mADM = maintenance antidepressant medication; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant; IDS-C30 = Dutch inventory of depressive symptomatology-clinician rated; MDEs = major depressive episodes; MDD = major depressive disorder. a Including serotonin-norepinephrine reuptake inhibitors, monoamine oxidase-inhibitors, and mirtazapine. b Based on self-report.

Table 1. Baseline demographic and clinical characteristics of patients with recurrent depression receiving mindfulness-based cognitive therapy (n = 235)
1-factor structure, a good internal consistency, and theoretically coherent correlations with, e.g., wellbeing and stress among a Dutch non-clinical population (Schroevers et al., 2008). The internal consistency in the current study was excellent ($\alpha = .95$).

2.3.2. Affect
Positive affect and negative affect were assessed with the International Positive and Negative Affect Schedule Short-Form (I-PANAS-SF; Thompson, 2007). This questionnaire consists of ten items of which 5 assess positive affective states (e.g., enthusiastic, excited) and 5 assess negative affective states (e.g., irritable, nervous) relating to the last week, including the day itself. The items are scored using a 5-point Likert scale anchored from ‘never’ to ‘always’. Higher values indicate higher levels of positive/negative affective states. Thompson (2007) investigated the cross-sample stability, internal reliability, temporal stability, and convergent and criterion-related validities of the scale and found the scale to be psychometrically acceptable. The average scale score was used in the current study. The internal consistency in the current study was excellent for positive affect ($\alpha = .93$) and good for negative affect ($\alpha = .89$).

2.4. Data analyses
The current study used the ALT modeling technique which combines a latent trajectory model (LTM) with an autoregressive (AR) model. The LTM allows each individual in the sample to have a different overall trajectory as marked by a different (subject-specific) intercept and slope when tracked over time. The intercept can be interpreted as a general level of a variable and is constant over time. Its variance represents differences in general levels between individuals. The slope can be interpreted as an overall rate of change (positive or negative) of a variable over the intervention period, and its variance represents inter-individual differences in the rate of change. However, reciprocal week-to-week associations between variables during the intervention period are not captured with a LTM. AR models can investigate reciprocal week-to-week associations between variables, so-called cross-lagged (CL) effects, while allowing the prior value of a variable to determine the current value of the same variable (AR effects). Although AR models allow investigating reciprocal CL effects, caution is warranted. Indeed, when not accounting for the (differences in) overall trajectories in the variable(s) over the intervention period, spurious CL effects might appear while they actually do not exist (Voelkle, 2008). Therefore, combining both the AR model and LTM into an ALT model makes it possible to study reciprocal CL effects properly while controlling for overall trajectories. This enables a better interpretation of the processes of stability and change during MBCT for recurrent depression.
The analytical strategy followed Bollen and Curran’s (2004) recommendations. At first, univariate unconditional AR models, LTMs, and several ALT models were estimated separately for each variable - mindfulness, positive affect, and negative affect - and compared to identify which model best represented the course of these variables separately during MBCT. Secondly, bivariate unconditional AR models, LTMs, and various ALT models were fitted and compared for both mindfulness and positive affect as well as negative affect to examine which model best represented the course and possible mutual associations of mindfulness and positive/negative affect during MBCT. For a detailed description of the model building steps of both the univariate and bivariate models, model fit, and data handling, see Supplementary Material 1. Descriptive analyses were performed with SPSS, version 22 (IBM Corporation, 2013). All structural equation models (SEMs) were estimated by using IBM Amos SPSS, version 25.0 (Arbuckle, 2017). As significance level, a two-sided alpha level of .050 was used.

3. Results

The descriptive statistics of and correlations between all studied variables are presented in Supplementary Material 2, Tables 2.1 and 2.2. Mindfulness and positive affect steadily increased over the intervention period, while negative affect showed a more irregular course. See Figure 1 for a visual representation of the overall means of these variables per session. In addition, mindfulness had high autocorrelations between the weekly sessions, whereas these autocorrelations were moderate for positive affect and negative affect. At each session separately, mindfulness correlated positively with positive affect and negatively with negative affect. As the assumption of normality was violated for negative affect, a logarithmic transformation was applied to all measurement points of this variable before further analyses were performed. For a detailed description of the univariate and bivariate models that were fitted and the results of the final univariate ALT models, see Supplementary Material 2. To improve readability and interpretation, only the results of the final bivariate ALT model of both mindfulness and positive affect as well as negative affect are presented below.

3.1. Mindfulness and positive affect

The final bivariate ALT model showed an excellent model fit ($\chi^2 = 83.51, df = 84, p = .495$; comparative fit index (CFI) = 1.000; Tucker-Lewis index (TLI) = 1.000; root-mean-square error of approximation (RMSEA) < 0.001). The significant parameter estimates are depicted in Figure 2, with the (co)variance and correlation estimates being reported in Table 2. A positive covariance was observed between both intercepts ($\Psi_{\alpha_{MFN,\alpha_{PA}}} = 0.077, s.e. = 0.031, p = .013$) and
between both slopes ($\Psi_{\beta_{\text{MFN},\beta_{\text{PA}}}} = 0.002, \text{s.e.} = 0.001, p = .047$). This indicates that participants with higher general levels of mindfulness showed higher general levels of positive affect. In addition, participants with larger increases in mindfulness showed larger increases in positive affect. In addition to these general trajectories over the MBCT course, week-to-week effects were found. Both mindfulness ($\rho_{\text{AR}(1)} = 0.327, \text{s.e.} = 0.051, p < .001$) and positive affect ($\rho_{\text{AR}(1)} = 0.187, \text{s.e.} = 0.048, p < .001$) had a clear stable AR component. This indicates that higher levels of mindfulness respectively positive affect on a given session predicted higher levels of mindfulness respectively positive affect on the following session. The CL parameter estimates showed that the CL effect from positive affect at session 2 to mindfulness at session 3 was positive and significant ($b_{\text{PA}(t2),\text{MFN}(t3)} = 0.118, \text{s.e.} = 0.046, p = .011$), whereas this effect was not significant for other sessions ($-0.044 < b_{\text{PA}(t-t1),\text{MFN}(t)} < 0.057, p > .174$). No CL effects were found from mindfulness to positive affect ($b_{\text{MFN}(t-t1),\text{PA}(t)} = 0.049, \text{s.e.} = 0.061, p = .423$).

3.2. Mindfulness and negative affect

The final bivariate ALT model showed a good model fit ($\chi^2 = 106.67, df = 102, p = .356; \text{CFI} = 0.998; \text{TLI} = 0.998; \text{RMSEA} = 0.014$). The significant parameter estimates are graphically represented in Figure 3, with the (co)variance and

![Figure 1](image.png)

**Figure 1.** Evolution of the mean score of mindfulness, positive affect, and negative affect over time during MBCT for recurrent depression, including 95% confidence interval bars.
Figure 2. Standardized parameter estimates of the final unconditional bivariate ALT model of mindfulness and positive affect. Estimates of (error). Correlations and autoregressive and cross-lagged parameters that are non-significant are not shown. Significant paths are depicted by solid lines. Double-headed arrows represent correlations.
Figure 3. Standardized parameter estimates of the final unconditional bivariate ALT model of mindfulness and negative affect (logarithmic transformed). Estimates of (error) correlations and autoregressive and cross-lagged parameters that are non-significant are not shown. Significant paths are depicted by solid lines. Double-headed arrows represent correlations.
Table 2. Variances, covariances and correlations between the first measurements (session 1) and the intercepts and slopes of mindfulness and positive (upper part) and negative (lower part) affect based on the final bivariate ALT models

<table>
<thead>
<tr>
<th></th>
<th>S1 MFN</th>
<th>S1 PA</th>
<th>Intercept MFN</th>
<th>Intercept PA</th>
<th>Slope MFN</th>
<th>Slope PA</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 MFN</td>
<td>0.423 (0.040)**</td>
<td>.368</td>
<td>.773</td>
<td>.391</td>
<td>-.209</td>
<td>-.193</td>
</tr>
<tr>
<td>S1 PA</td>
<td>0.163 (0.032)**</td>
<td>0.465 (0.044)**</td>
<td>.330</td>
<td>.758</td>
<td>.091</td>
<td>.085</td>
</tr>
<tr>
<td>Intercept MFN</td>
<td>0.189 (0.032)**</td>
<td>0.085 (0.030)*</td>
<td>0.142 (0.034)**</td>
<td>.528</td>
<td>.100</td>
<td>-.344</td>
</tr>
<tr>
<td>Intercept PA</td>
<td>0.099 (0.034)**</td>
<td>0.201 (0.034)**</td>
<td>0.077 (0.031)*</td>
<td>0.151 (0.043)**</td>
<td>.200</td>
<td>.013</td>
</tr>
<tr>
<td>Slope MFN</td>
<td>-0.006 (0.004)ns</td>
<td>0.003 (0.005)ns</td>
<td>0.002 (0.003)ns</td>
<td>0.003 (0.004)ns</td>
<td>0.002 (0.001)ns</td>
<td>.800</td>
</tr>
<tr>
<td>Slope PA</td>
<td>-0.007 (0.005)ns</td>
<td>0.003 (0.005)ns</td>
<td>-0.007 (0.004)ns</td>
<td>&lt;0.001 (0.005)ns</td>
<td>0.002 (0.001)*</td>
<td>0.003 (0.001)*</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>S1 MFN</th>
<th>S1 NA</th>
<th>Intercept MFN</th>
<th>Intercept NA</th>
<th>Slope MFN</th>
</tr>
</thead>
<tbody>
<tr>
<td>S1 MFN</td>
<td>0.423 (0.040)**</td>
<td>- .272</td>
<td>.781</td>
<td>-.262</td>
<td>-.229</td>
</tr>
<tr>
<td>S1 NA</td>
<td>-0.026 (0.007)**</td>
<td>0.021 (0.002)**</td>
<td>- .238</td>
<td>.734</td>
<td>-.108</td>
</tr>
<tr>
<td>Intercept MFN</td>
<td>0.201 (0.030)**</td>
<td>-0.014 (0.005)**</td>
<td>0.156 (0.033)**</td>
<td>-.315</td>
<td>.040</td>
</tr>
<tr>
<td>Intercept NA</td>
<td>-0.016 (0.005)**</td>
<td>0.010 (0.001)**</td>
<td>-0.012 (0.004)**</td>
<td>0.009 (0.001)**</td>
<td>-.258</td>
</tr>
<tr>
<td>Slope MFN</td>
<td>-0.007 (0.003)ns</td>
<td>-0.001 (0.001) ** ns</td>
<td>0.001 (0.003) ns</td>
<td>-0.001 (0.001) **</td>
<td>0.002 (0.001) **</td>
</tr>
</tbody>
</table>

Note. S1 = observed variable of the first session; MFN = mindfulness; PA = positive affect; NA = negative affect (logarithmic transformed). Variances are depicted on the diagonal, covariances below and correlations above the diagonal. Standard errors are shown between parenthesis. Level of significance is indicated for the covariances and variances only. ns p ≥ .050, * p < .050, ** p < .010, *** p < .001.
correlation estimates being displayed in Table 2. A negative covariance was observed between the intercepts of mindfulness and negative affect (Ψ_{\alpha MFN,\alpha NA} = -0.012, s.e. = 0.004, p = .009), which indicates that higher general levels of mindfulness were associated with lower general levels of negative affect. The final model did not contain a slope for negative affect, which implies that there was no increase or decrease of negative affect over the course of the MBCT. A negative covariance was observed between the intercept for negative affect and the slope for mindfulness (Ψ_{\beta MFN,\alpha NA} = -0.001, s.e. = 0.001, p = .036), which suggests that patients with higher general levels of negative affect showed smaller increases in mindfulness over the MBCT course. Week-to-week effects showed substantial AR effects for mindfulness ($\rho_{AR(1)} = 0.303, s.e. = 0.049, p < .001$) and negative affect ($\rho_{AR(1)} = 0.218, s.e. = 0.037, p < .001$) which were stable over time. No CL effects were found from mindfulness towards negative affect ($b_{MFN(t-1),NA(t)} = -0.010, s.e. = 0.010, p = .291$) or vice versa ($b_{NA(t-1),MFN(t)} = -0.137, s.e. = 0.102, p = .181$). As such, the level of mindfulness at a certain session did not predict the level of negative affect at the next session or vice versa.

4. Discussion

The current study was based on data from patients with recurrent depression in (partial) remission receiving an 8-week MBCT as part of two multicenter RCTs. The overall trajectory and week-to-week associations of mindfulness and positive/negative affect were investigated across the intervention period by using the ALT modeling technique. When looking at overall trajectories, mindfulness and positive affect significantly increased, while the overall decrease of negative affect was non-significant. Patients with larger increases in mindfulness showed significantly larger increases in positive affect. In addition, patients with higher general levels of negative affect showed significantly smaller increases in mindfulness. Week-to-week effects showed no significant reciprocal CL effects between mindfulness and positive affect or negative affect, except for positive affect at session 2 which was positively associated with mindfulness at session 3.

4.1. Mindfulness and positive affect

As expected, patients with larger increases in mindfulness showed significantly larger increases in positive affect over the MBCT course. This is in accordance with existing theories (e.g., Garland et al., 2009, 2015) suggesting positive (reciprocal) associations between mindfulness and positive affect. In addition, it is in line with previous research showing effects of MBIs on increasing positive affect (e.g., Geschwind et al., 2011; Schroevers & Brandsma, 2010). However, the current study did not find significant effects between mindfulness and subsequent
positive affect on a weekly basis, while only positive affect at session 2 positively significantly predicted mindfulness at session 3. The latter might be explained by the given home practice during session 2 for the coming week, namely registering one pleasant event on a daily basis with accompanied thoughts, emotions, and bodily sensations. However, this is speculative. Another study investigating mindfulness and positive affect in a community sample also did not find changes in positive affect on a certain day to predict changes in mindfulness the following day, although reverse associations were found (Snippe et al., 2015). In contrast, positive moment-to-moment relations between mindfulness and subsequent positive affect, and vice versa, were found in patients with recurrent MDD during a mindful walking intervention using experience sampling methodology (Gotink et al., 2016). Perhaps, the time span used in the current study was not fine-grained enough to detect these CL effects. More importantly, however, the differences in outcomes could be explained by the different analytic techniques adopted. When not taking overall changes during the intervention period and inter-individual differences therein into account (i.e., fitting intercept-only models while interindividual differences in slopes exist), unmodeled overall changes could “show up” as spurious CL (and AR) effects, rendering the substantive interpretation of these effects impossible. Simulation studies show that ignoring or misspecifying (i.e., assuming linearity when true changes are non-linear) the overall change over time results in incorrect estimates for CL and AR effects (Voelkle, 2008). Indeed, when a bivariate intercept-only ALT model was fitted for mindfulness and positive affect in the current study, instead of a bivariate intercept and slope model, CL effects from mindfulness to positive affect became significant, as half of the CL effects from positive affect to mindfulness. It is therefore very important to carefully build a model that captures the overall trajectories of the variables correctly and that simultaneously accounts for time-specific effects.

4.2. Mindfulness and negative affect
Against expectations, negative affect did not significantly decrease over the MBCT course, which is contrary to previous studies (van der Velden et al., 2015). However, it seems in line with the absence of a clear main effect of MBCT on depression severity found in the clinical trials from which the current data were derived. Another explanation could be that participants were more able to accept negative affect rather than engaging in elaboration or rumination (Garland et al., 2015), therefore having more room for positive affect. Across the intervention period, higher general levels of negative affect were associated with significantly smaller increases in mindfulness, which suggests that negative affect might act as a barrier to develop mindfulness during MBCT. This is in line with the mindfulness-to-meaning theory (Garland et al., 2015), which asserts that negative emotions narrow the scope of awareness. Week-to-week CL
associations between mindfulness and subsequent negative affect were non-significant. This is inconsistent with previous research by Gotink et al. (2016), which found moment-to-moment negative associations between mindfulness and subsequent negative affect during a mindful walking intervention in mainly recurrently depressed patients. However, in an ESM study in a general sample, increases in mindfulness on a certain day preceded decreases in negative affect the next day, but not the other way around (Snippe et al., 2015). One explanation could be that the current study included participants who were (partly) in remission which may have resulted in a restriction of a range of negative affect. More pronounced effects of mindfulness on negative effect or vice versa might be found when MBCT targets acutely depressed individuals. In addition, the relatively low average level of teacher competence compared to previous studies (e.g., Kuyken et al., 2015) may have attenuated the effect of MBCT on negative affect in general. Finally, the same methodological shortcomings apply to these findings as mentioned above (i.e., time span used and differences in analytical techniques adopted).

4.3. Strengths
The current study is the first to investigate the mutual associations of mindfulness and positive affect and negative affect during MBCT for recurrent depression. It included weekly assessments during the intervention in 235 patients and used an advanced analysis technique which enables to make a distinction between the overall trajectories across the entire MBCT course and week-to-week effects of mindfulness, positive affect, and negative affect. This made it possible to study processes of mindfulness and affect in much more detail compared with pre-post studies and increased the statistical power to find potential associations between them. Finally, data from the present study were based on two highly ecologically valid RCTs which were embedded in a standard clinical care setting. This real-life setting increases generalization of our findings to patients with remitted recurrent depression in both secondary care and tertiary care.

4.4. Limitations and future research
There were also some limitations. First, no weekly assessments took place in the control group, which makes it unclear whether similar effects would be observed with the passing of time or in any other group activity. In subsequent research, MBCT should be compared to both passive and active control groups in order to determine whether changes in mindfulness and affect are specific for MBCT. Second, results of the current study are limited to patients with remitted depression and cannot be generalized to patients with acute depression. For future research, it is recommended to investigate changes in mindfulness and affect across individuals with different mental health problems with different levels of severity receiving MBCT (e.g., anxiety disorder) in order to determine
the specificity of changes in mindfulness and affect. Third, another possible methodological problem concerns the questionnaires that were used in the current study. Mindfulness was assessed with the MAAS (Brown & Ryan, 2003), which has been questioned in terms of its validity and ability to measure mindfulness (van Dam et al., 2010). The MAAS taps into one aspect of mindfulness: (lack of) “attention towards the present moment”. The “purposeful orientation to one’s experience with a non-judgmental attitude” is not captured by the MAAS. In addition, the I-PANAS-SF (Thompson, 2007) might have limitations in terms of representing only highly aroused forms of positive and negative feelings (Diener et al., 2009). Moreover, the negative affect scale of the I-PANASSF includes a wide range of different emotions (e.g., anger, fear), which each might follow a different course during MBCT for recurrent depression.

In future research, it would be recommended to include regular measurements administering different facets of mindfulness such as the facets from the Five-Facet Mindfulness Questionnaire short form (FFMQ-15; Baer et al., 2008). With regard to momentary affect measures, it seems important to include more subtle emotions too (e.g., calm, relaxed), considering that, particularly, these emotions are assumed to increase during meditation (Jones et al., 2018). Furthermore, it would be valuable to repeatedly assess depressive symptoms to further determine changes in mindfulness and affect as the possible mechanisms of change in MBCT for depression. Moreover, it is encouraged to use ESMs, in order to capture dynamics on a smaller time scale. Finally, it is very important to carefully build a model that captures the overall trajectories of the variables correctly and that simultaneously accounts for time-specific effects. Authors should aim to provide ample insight into the analysis techniques and methods that were used, in order to increase the chance to replicate findings and properly compare results.

In summary, the current study supports a positive association in strength of increase between mindfulness and positive affect during MBCT for recurrent depression. Negative affect might run a more irregular course and might be associated with a smaller increase in mindfulness during MBCT for recurrent depression. Reciprocal CL associations between mindfulness and positive/negative affect that were established in previous research were generally not confirmed, possibly due to the more rigorous methodology of the current study and the time frame used. For future research, it is encouraged to use ESM in order to capture dynamics on a smaller time scale. In addition, the use of the ALT modeling technique is highly recommended to enable a better interpretation of the processes of stability and change during MBCT for recurrent depression.
References


Supplementary Material 1 - Method section

Detailed description of the model building steps of both the univariate and bivariate models, model fit and data handling

1. Model building univariate models

Separate unconditional univariate models were fitted for mindfulness, positive and negative affect to examine at the same time week-to-week autoregressive (AR) effects and stable, general trajectories over time during MBCT. To this end, successively a univariate unconditional AR model, a latent trajectory model (LTM), and several autoregressive latent trajectory (ALT) models were fitted and compared to determine which model best fitted the data and provided at the same time a parsimonious representation of the data. The univariate AR model used the 8 measurements corresponding to the 8 weekly MBCT sessions. A lag 1-AR model was adopted implying that the score for each session -except for the first one- was regressed on the score of its predecessor. Error-terms were added to the score of sessions 2-8. This AR model was used to measure week-to-week AR effects, however, without taking into account general trajectories over time during MBCT. To test for these general trajectories, LTMs were fitted in which the 8 weekly measurements were modeled with a latent intercept and slope factor which were allowed to covary. The intercept factor loadings of all sessions were fixed to 1 and a linear slope factor was estimated with factor loadings set to 0, 1, 2, 3, 4, 5, 6, and 7 for sessions 1-8 respectively. In order to get identifiable LTM models, the means of the latent factors were set to 0 (Wiggins, 2011). Note that the LTM captures general trajectories over time during the entire intervention but does not account for week-to-week AR effects.

Next, to model week-to-week AR effects and general trajectories over time during MBCT simultaneously, a number of ALT models were estimated. First, the ALT-full model was estimated which models the 8 weekly measurements with a latent intercept and slope factor and with AR effects. A ‘predetermined model’ specification was adopted in which the measurement of the first session did not load on the latent intercept and slope factor but was allowed to covary with both latent growth factors. The loadings of the intercept and slope factors were chosen analogue to the loadings used for the LTM model, except for session 1 (i.e. all measurements -except for session 1- load 1 on the intercept factor and loadings 1-7 were used for sessions 2-8 respectively). The latent intercept and slope factor were allowed to covary and sessions 2-8 contained error-terms. This ‘predetermined model’ specification prevents parameter bias as it controls for prior unmeasured levels of the construct under study (Bollen & Curran, 2004). As a consequence, the intercept factor is no longer the expected initial value but refers to this value accounted for the first wave of data. To facilitate readability, this will be referred to as general level. Second, a series of restricted ALT models were fitted in order to gradually simplify the model but without significantly
decreasing the model fit. In particular, the following restrictions were tested: (1) fixing the AR parameters to 0 (ALT-LTM), (2) fixing the slope factor variance to 0 (ALT-no slope variance), (3) excluding the slope factor (ALT-no slope), and (4) constraining the AR parameters to equal each other over time (ALT-AR constraints). Because these restricted models are nested within the ALT-full model, a direct comparison becomes possible between the ALT-full model and these restricted models.

2. Model building bivariate models
To examine how mindfulness and positive/negative affect influence one another over time during MBCT for recurrent depression, several unconditional bivariate models were estimated and compared to determine which model best fitted the data and provided at the same time a parsimonious representation of the data. The repeated measures consisted of 8 measurements corresponding to the 8 weekly MBCT sessions. First, the bivariate AR model was fitted which contained AR effects, cross-lagged (CL) effects and error-terms added to the scores of sessions 2-8 of both variables (mindfulness and positive/negative affect). The first measurements were allowed to correlate. Second, the LTM was fitted in which the 8 weekly measurements were modeled with error terms. In addition, latent intercept and slope factors were fitted which were allowed to covary. The intercept factor loadings were fixed to 1 and linear slope factors were estimated with factor loadings set to 0-7 for sessions 1-8 respectively. In order to get identifiable LTM models, the means of the latent factors were set to 0 (Wiggins, 2011). Third, a number of ALT models were estimated starting with a bivariate ALT-full model. This model contained (for both variables) the 8 weekly measurements with error-terms added to sessions 2-8, AR as well as CL effects were estimated, and latent intercept and slope factors were fitted which were allowed to covary. A predetermined model specification was adopted to prevent parameter bias from being introduced by not accounting for prior, unassessed levels of the variables. Hereby, all possible correlations between the intercept and slope factors and the first session’s score of each variable were estimated. The following restrictions were subsequently added to the model in order to simplify the model without significantly decreasing its fit to the data: (1) setting AR and CL parameters to 0 (ALT-LTM), (2) fixing the variance of the slope factor to 0 (ALT-no slope variance), (3) excluding the slope factor (ALT-no slope), (4) setting the time-specific error correlations to 0 (ALT-no time-specific error correlations), (5) constraining the time-specific error correlations to be equal to each other over time (ALT-time-specific error constraints), (6) constraining the AR parameters to equality over time (ALT-AR constraints), (7) setting the CL parameters equal to each other over time (ALT-CL constraints). The constraints 2, 3, 6 and 7 were tested for each variable (mindfulness or negative/positive affect) in turn, whereas constraint 1 was applied to both variables simultaneously.
3. Model fit
Model fit was evaluated based on the chi-square ($\chi^2$) to degrees of freedom (df) ratio. Values between 2 to 3 were considered as an acceptable and ≤ 2 as a preferable fit (Carmines & McIver, 1981; Marsh & Hocevar, 1985). Since the $\chi^2$ statistic is sensitive to sample size, other model fit indices were considered to be of greater value (Cheung & Rensvold 2002). The root-mean-square error of approximation (RMSEA; Steiger, 1998) was evaluated where values between 0.05 and 0.08 indicated a reasonable and values < 0.05 a good fit (Browne & Cudeck, 1992). In addition, the comparative fit index (CFI; Bentler, 1990) and Tucker-Lewis index (TLI; Tucker & Lewis, 1973) were evaluated of which values > 0.90 indicated an adequate fit and values > 0.95 a very good fit (Bollen, 1989; Hu & Bentler, 1999). Nested models were compared through the $\chi^2$ difference test ($\Delta \chi^2$; Bollen, 1989). Significant differences between two nested models suggested that the more complex model fitted the data significantly better than the simpler model. When two nested models were not significantly different, the more parsimonious model was preferred as it fitted the data as good as the more complex model. Non-nested models were compared through inspecting the difference in the Akaike information criterion (AIC; Akaike, 1973) between these models. The model with the lowest AIC was favored. Differences on the AIC of ≤ 2 indicated that both models fit the data equally well (Wagenmakers & Farrell, 2004).

4. Data handling
As the data contained missing values (i.e. ranging from 5.5% to 19.1% for each variable at each time point), full maximum likelihood estimation (FIML) procedures were applied. The FIML estimator takes all available observed values into account when estimating model parameters and is suitable for the comparison of multiple structural equation models (Enders & Bandalos, 2001). Before running the analyses, the assumption of normality was evaluated for each variable at each time point by inspecting the quantile-quantile (Q-Q) plots, kurtosis and skewness values. A logarithmic transformation was applied to all time points of the variable that showed non-normality (Ghasemi & Zahediasl, 2012).
References


Supplementary Material 2 - Result section

Detailed description of the studied variables, univariate and bivariate models that were fitted and the results of the final univariate ALT models

1. Descriptive statistics
The descriptive statistics of and correlations between all studied variables are presented in Tables 2.1 and 2.2.

2. Univariate models
The model fit indices of the estimated unconditional univariate models for mindfulness and positive/negative affect are shown in Table 2.3. The estimated variances and covariances/correlations of the final univariate models are presented in Table 2.4. Only the final univariate models are discussed below.

For mindfulness, as indicated in Table 2.3, the results show that -based on AIC- the ALT-full model (model 3) substantially fitted the data better than the AR (model 1) and LTM (model 2) model. The ALT-LTM model (model 4) fitted the data significantly worse than the ALT-full model. Removing the slope variance (model 5) or the slope at all (model 6) resulted in a significant decrement in model fit -according to the Δχ² statistic- compared to the ALT-full model. Finally, constraining the AR effects to be equal to each other over time (model 7) yielded a more parsimonious model that fitted the data as good as the ALT-full model. Therefore, the model with AR constraints was considered as the final model; it had a very good fit to the data (χ² = 28.21, df = 22, p = .169; CFI = 0.997; TLI = 0.995; RMSEA = 0.035). The results indicate that there was a slight variability between individuals in the strength of increase in mindfulness over the entire intervention period, represented by the significant slope variance (σ = 0.002, s.e. = 0.001, p = .040). Besides, individuals differed moderately in their general level of mindfulness, depicted by the significant intercept variance (σ = 0.158, s.e. = 0.035, p < .001). In addition to this overall trajectory, week-to-week AR parameters were positive and significant (ρAR(1) = 0.32, s.e. = 0.05, p < .001) which means that higher levels of mindfulness on a session predicted higher levels of mindfulness on the following session. The ability of mindfulness to predict later levels of mindfulness was stable over time during MBCT due to (univariate) constraint (4).

For positive affect, the AR model (model 1) fitted poorly to the data, whereas the ALT-full model (model 3) showed a better fit to the data than the LTM model (model 2) according to the AIC, see Table 2.3. The ALT-LTM model (model 4) yielded a significant decrease in model fit compared to the ALT-full model according to the Δχ² statistic. The same is true for the model in which the slope variance was fixed to 0 (model 5) and for the model with no slope factor at all (model 6). Imposing constraints to the AR parameters (model 7) resulted in a good fitting model (χ² = 29.50, df = 22, p = .131; CFI = 0.994; TLI = 0.986; RMSEA =
that fitted the data as good as the more complex ALT-full model. As such, the model with AR restrictions was retained as the final model. Inspecting the parameter estimates of this final model, there was a significant positive intercept variance ($\sigma = 0.171$, $s.e. = 0.044$, $p < .001$), indicating inter-individual variability regarding the general level of positive affect. In addition, inter-individual variability was found regarding the strength of increase in positive affect over the entire intervention, represented by a positive significant slope variance ($\sigma = 0.004$, $s.e. = 0.001$, $p = .014$). Week-to-week AR effects show that higher levels of positive affect on a given session predicted higher levels of positive affect on the following session ($\rho_{AR(1)} = 0.19$, $s.e. = 0.05$, $p < .001$). The equality constraint (4) implies that the strength of the AR effects for positive affect stayed the same during the whole MBCT course.

Finally, as can be seen in Table 2.3, the results for negative affect (logarithmic transformed) show that -based on AIC- the AR (model 1) and LTM (model 2) model fitted poorer to the data than the ALT-full model (model 3). Chi-square difference testing shows that the ALT-LTM model (model 4) and the model without slope variance (model 5) fitted the data significantly worse than the ALT-full model. Removing the slope factor (model 6), however, did not result in a worse fitting model, implying that model 6 was preferred over the ALT-full model. Also making the AR effects constant over time (model 7) did not lead to a significant decrease in model fit. Therefore, model 7 was chosen as the final model. This model, which only had an intercept but no slope factor, had a good fit to the data ($\chi^2 = 31.62$, $df = 25$, $p = .169$; CFI = 0.992; TLI = 0.989; RMSEA = 0.034). The omission of the slope factor implies that negative affect was constant over time and that this was true for all subjects. The significant -but small- variance of the intercept factor indicates that individuals varied in their general level of negative affect ($\sigma = 0.009$, $s.e. = 0.001$, $p < .001$). Finally, week-to-week AR effects were observed which had the same strength over time: lower levels of negative affect on one session predicted lower levels of negative affect on the following session ($\rho_{AR(1)} = 0.23$, $s.e. = 0.04$, $p < .001$) in addition to the overall trajectory of negative affect.

3. Bivariate models
Multiple bivariate models were fitted to examine how mindfulness and positive affect influence one another over time during MBCT. As can be seen in Table 2.5, which presents fit indices for the estimated models, the ALT-full model (model 3) better captured the data than the AR (model 1) and the LTM model (model 2) according to the AIC. Further, the ALT-full model showed a good model fit (CFI/TLI > 0.995) and was clearly superior to the ALT-LTM model (model 4; $\Delta\chi^2 = 267.91$, df = 40, $p < .001$). Imposing constraints (2)-(5) (model 5-10) resulted in models that fitted significantly worse, as shown by the accompanied significant $\chi^2$-difference tests. Constraining the AR parameters to be equal to each other
over time for mindfulness (model 11) and subsequently also for positive affect (model 12) yielded simpler models that fitted the data as good as the ALT-full model; these more parsimonious models were therefore preferred over the ALT-full model. Finally, restricting CL relations from mindfulness to positive affect to be equal across time (model 13) yielded a more optimal model, whereas constraining the CL parameters from positive affect to mindfulness equal to each other over time (model 14) did not. As such, model 13 was retained as the final model. This final model showed an excellent model fit ($\chi^2 = 83.51$, $df = 84$, $p = .495$; CFI = 1.000; TLI = 1.000; RMSEA < 0.001).

Multiple bivariate ALT models were fitted to investigate the interplay of mindfulness and negative affect over time during MBCT for recurrent depression. The corresponding model fit indices can be found in Table 2.5. The AIC clearly showed that the ALT-full model (model 3) fitted the data better than the AR (model 1) and the LTM model (model 2). Based on a chi-square difference test, it was concluded that the ALT-full model was preferred over the ALT-LTM model (model 4). Removing the slope factor variance for negative affect (model 5) and next removing the negative affect slope factor at all (model 6) did not significantly decrease model fit. As model 6 was the most parsimonious model among these three models, it was preferred over the other two models. A significant decrease in model fit was observed when the slope factor for mindfulness (model 8) and its variance (model 7) were removed from the model. Also removing the time-specific error correlations (model 9) resulted in a worse fitting model. However, making time-specific error correlations equal to each other over time did not significantly make the model fit worse (model 10). Setting AR (model 11 and 12) and CL parameters (model 13 and 14) equal to each other over time led to more parsimonious models that fitted the data equally well. Model 14 was therefore retained as the final model and it showed a good model fit ($\chi^2 = 106.67$, $df = 102$, $p = .356$; CFI = 0.998; TLI = 0.998; RMSEA = 0.014).
Table 2.1. Correlations between and univariate statistics of mindfulness and positive affect during 8 sessions of mindfulness-based cognitive therapy

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M = mean; SD = standard deviation; $\gamma_1$ = skewness; $\gamma_2$ = kurtosis. Level of significance is indicated for the correlations only. $^a$ Available n decreases from 222 to 164 across S1-8. $^b$ Available n decreases from 218 to 162 across S1-8. ns $p \geq .050$, $^* p < .050$, $^{**} p < .010$. 

Note. MFN = mindfulness; PA = positive affect; S1-8 = session 1-8; M = mean; SD = standard deviation; $\gamma_1$ = skewness; $\gamma_2$ = kurtosis. Level of significance is indicated for the correlations only. $^a$ Available n decreases from 222 to 164 across S1-8. $^b$ Available n decreases from 218 to 162 across S1-8. ns $p \geq .050$, $^* p < .050$, $^{**} p < .010$. 

Table 2.2. Correlations between and univariate statistics of mindfulness and negative affect during 8 sessions of mindfulness-based cognitive therapy

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M = mean; SD = standard deviation; $\gamma_1$ = skewness; $\gamma_2$ = kurtosis. Level of significance is indicated for the correlations only. $^a$ The original, untransformed variable of negative affect is used. $^b$ Available n decreases from 218 to 163 across S1-8. ns $p \geq .050$, $^* p < .050$, $^{**} p < .010$. 

Note. MFN = mindfulness; NA = negative affect; S1-8 = session 1-8; M = mean; SD = standard deviation; $\gamma_1$ = skewness; $\gamma_2$ = kurtosis. Level of significance is indicated for the correlations only. $^a$ Available n decreases from 222 to 164 across S1-8. $^b$ Available n decreases from 218 to 162 across S1-8. ns $p \geq .050$, $^* p < .050$, $^{**} p < .010$. 

Note. MFN = mindfulness; PA = positive affect; S1-8 = session 1-8; M = mean; SD = standard deviation; $\gamma_1$ = skewness; $\gamma_2$ = kurtosis. Level of significance is indicated for the correlations only. $^a$ Available n decreases from 222 to 164 across S1-8. $^b$ Available n decreases from 218 to 162 across S1-8. ns $p \geq .050$, $^* p < .050$, $^{**} p < .010$. 
Table 2.1. Correlations between and univariate statistics of mindfulness and positive affect during 8 sessions of mindfulness-based cognitive therapy

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<td>.314**</td>
<td>.411**</td>
<td>.429**</td>
<td>.541**</td>
</tr>
</tbody>
</table>

Note. MFN = mindfulness; PA = positive affect; S1-8 = session 1-8; M = mean; SD = standard deviation; \( \gamma_1 \) = skewness; \( \gamma_2 \) = kurtosis. Level of significance is indicated for the correlations only. \( a \) Available n decreases from 222 to 164 across S1-8. \( b \) Available n decreases from 218 to 162 across S1-8. \( * p \geq .050, ** p < .050, *** p < .010. \)

Table 2.2. Correlations between and univariate statistics of mindfulness and negative affect during 8 sessions of mindfulness-based cognitive therapy

<table>
<thead>
<tr>
<th></th>
<th>S1</th>
<th>S2</th>
<th>S3</th>
<th>S4</th>
<th>S5</th>
<th>S6</th>
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<td>NA S7</td>
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<td>NA S8</td>
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<tr>
<td>M</td>
<td>2.14</td>
<td>2.01</td>
<td>2.05</td>
<td>2.14</td>
<td>1.97</td>
<td>2.02</td>
<td>1.97</td>
<td>1.89</td>
</tr>
<tr>
<td>SD</td>
<td>0.74</td>
<td>0.76</td>
<td>0.87</td>
<td>0.82</td>
<td>0.75</td>
<td>0.83</td>
<td>0.76</td>
<td>0.75</td>
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<tr>
<td>( \gamma_1 )</td>
<td>0.79</td>
<td>0.85</td>
<td>1.02</td>
<td>0.66</td>
<td>0.89</td>
<td>1.06</td>
<td>0.82</td>
<td>1.11</td>
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<tr>
<td>( \gamma_2 )</td>
<td>0.17</td>
<td>0.37</td>
<td>0.56</td>
<td>-0.35</td>
<td>0.23</td>
<td>1.10</td>
<td>0.29</td>
<td>1.16</td>
</tr>
</tbody>
</table>

Note. MFN = mindfulness; NA = negative affect; S1-8 = session 1-8; M = mean; SD = standard deviation; \( \gamma_1 \) = skewness; \( \gamma_2 \) = kurtosis. Level of significance is indicated for the correlations only. \( a \) The original, untransformed variable of negative affect is used. \( b \) Available n decreases from 218 to 163 across S1-8. \( * p \geq .050, ** p < .050, *** p < .010. \)
### Table 2.3. Model fit indices for the unconditional univariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for mindfulness, positive affect and negative affect

<table>
<thead>
<tr>
<th></th>
<th>χ² (df)</th>
<th>CM</th>
<th>Δχ² (df)</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mindfulness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 AR model</td>
<td>116.12 (21)***</td>
<td>0.949</td>
<td>0.913</td>
<td>0.139</td>
<td>162.116</td>
<td></td>
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</tr>
<tr>
<td>2 LTM model</td>
<td>97.38 (25)***</td>
<td>0.961</td>
<td>0.944</td>
<td>0.111</td>
<td>135.383</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 ALT-full model</td>
<td>21.83 (16) ns</td>
<td>0.997</td>
<td>0.993</td>
<td>0.039</td>
<td>77.829</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 ALT-LTM model</td>
<td>86.98 (23)***</td>
<td>65.15 (7)***</td>
<td>0.966</td>
<td>0.947</td>
<td>0.109</td>
<td>128.983</td>
<td></td>
</tr>
<tr>
<td>5 ALT-no slope variance</td>
<td>26.93 (17) ns</td>
<td>5.10 (1)*</td>
<td>0.995</td>
<td>0.989</td>
<td>0.050</td>
<td>80.931</td>
<td></td>
</tr>
<tr>
<td>6 ALT-no slope</td>
<td>43.18 (19)***</td>
<td>21.35 (3)***</td>
<td>0.987</td>
<td>0.976</td>
<td>0.074</td>
<td>93.178</td>
<td></td>
</tr>
<tr>
<td>7 ALT-autoregressive constraints</td>
<td>28.21 (22) ns</td>
<td>6.38 (6) ns</td>
<td>0.997</td>
<td>0.995</td>
<td>0.035</td>
<td>72.212</td>
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<tr>
<td><strong>Positive affect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 AR model</td>
<td>172.96 (21)***</td>
<td>0.848</td>
<td>0.739</td>
<td>0.176</td>
<td>218.956</td>
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<tr>
<td>2 LTM model</td>
<td>49.30 (25)**</td>
<td>0.976</td>
<td>0.965</td>
<td>0.064</td>
<td>87.304</td>
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</tr>
<tr>
<td>3 ALT-full model</td>
<td>22.17 (16) ns</td>
<td>0.994</td>
<td>0.986</td>
<td>0.041</td>
<td>78.170</td>
<td></td>
<td></td>
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<tr>
<td>4 ALT-LTM model</td>
<td>45.71 (23)**</td>
<td>23.54 (7)**</td>
<td>0.977</td>
<td>0.964</td>
<td>0.065</td>
<td>87.713</td>
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<tr>
<td>5 ALT-no slope variance</td>
<td>31.58 (17)*</td>
<td>9.41 (1)*</td>
<td>0.985</td>
<td>0.969</td>
<td>0.061</td>
<td>85.578</td>
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<tr>
<td>6 ALT-no slope</td>
<td>33.87 (19)*</td>
<td>11.70 (3)**</td>
<td>0.985</td>
<td>0.972</td>
<td>0.058</td>
<td>83.868</td>
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<tr>
<td>7 ALT-autoregressive constraints</td>
<td>29.50 (22) ns</td>
<td>7.33 (6) ns</td>
<td>0.994</td>
<td>0.986</td>
<td>0.038</td>
<td>73.501</td>
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<tr>
<td><strong>Negative affect</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1 AR model</td>
<td>192.45 (21)***</td>
<td>0.804</td>
<td>0.663</td>
<td>0.187</td>
<td>238.453</td>
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<tr>
<td>2 LTM model</td>
<td>50.11 (25)**</td>
<td>0.971</td>
<td>0.959</td>
<td>0.066</td>
<td>88.109</td>
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</tr>
<tr>
<td>3 ALT-full model</td>
<td>20.09 (16) ns</td>
<td>0.995</td>
<td>0.989</td>
<td>0.033</td>
<td>76.085</td>
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<tr>
<td>4 ALT-LTM model</td>
<td>41.74 (23)*</td>
<td>21.65 (7)**</td>
<td>0.979</td>
<td>0.966</td>
<td>0.059</td>
<td>83.738</td>
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<tr>
<td>5 ALT-no slope variance</td>
<td>24.04 (17) ns</td>
<td>3.96 (1)*</td>
<td>0.992</td>
<td>0.983</td>
<td>0.042</td>
<td>78.044</td>
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<tr>
<td>6 ALT-no slope</td>
<td>25.50 (19) ns</td>
<td>5.42 (3) ns</td>
<td>0.993</td>
<td>0.986</td>
<td>0.038</td>
<td>75.504</td>
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<tr>
<td>7 ALT-autoregressive constraints</td>
<td>31.62 (25) ns</td>
<td>6.12 (6) ns</td>
<td>0.992</td>
<td>0.989</td>
<td>0.034</td>
<td>69.619</td>
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</tr>
</tbody>
</table>

*Note.* χ² = chi-square test of model fit; df = degrees of freedom; Δχ² = chi-square difference test; CM = comparison model in the Δχ²; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; AIC = Akaike information criterion. The final model is shown in bold. * Negative affect is on a logarithmic scale. ns p ≥ .050, * p < .050, ** p < .010, *** p < .001.
Table 2.3. Model fit indices for the unconditional univariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for mindfulness, positive affect and negative affect

<table>
<thead>
<tr>
<th></th>
<th>Session 1</th>
<th>Intercept</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mindfulness</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>0.423***</td>
<td>0.775</td>
<td>-0.266</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.200***</td>
<td>0.158***</td>
<td>0.014</td>
</tr>
<tr>
<td>Slope</td>
<td>-0.007*</td>
<td>&lt; 0.001 ns</td>
<td>0.002*</td>
</tr>
<tr>
<td><strong>Positive affect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>0.466***</td>
<td>0.741</td>
<td>0.070</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.209***</td>
<td>0.171***</td>
<td>-0.070</td>
</tr>
<tr>
<td>Slope</td>
<td>0.003 ns</td>
<td>&lt; 0.002 ns</td>
<td>0.004*</td>
</tr>
<tr>
<td><strong>Negative affect</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>0.021***</td>
<td>0.734</td>
<td>-</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.010***</td>
<td>0.009***</td>
<td>-</td>
</tr>
<tr>
<td>Slope</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note. χ² = chi-square test of model fit; df = degrees of freedom; Δχ² = chi-square difference test; CM = comparison model in the Δχ²; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; AIC = Akaike information criterion. The final model is shown in bold.

Table 2.4. Variances, covariances and correlations between the first measurement (session 1) and the intercept and slope factor for mindfulness, positive and negative affect based on the final univariate ALT model

<table>
<thead>
<tr>
<th></th>
<th>Session 1</th>
<th>Intercept</th>
<th>Slope</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mindfulness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>0.423***</td>
<td>0.775</td>
<td>-0.266</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.200***</td>
<td>0.158***</td>
<td>0.014</td>
</tr>
<tr>
<td>Slope</td>
<td>-0.007*</td>
<td>&lt; 0.001 ns</td>
<td>0.002*</td>
</tr>
<tr>
<td><strong>Positive affect</strong></td>
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<td></td>
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</tr>
<tr>
<td>Session 1</td>
<td>0.466***</td>
<td>0.741</td>
<td>0.070</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.209***</td>
<td>0.171***</td>
<td>-0.070</td>
</tr>
<tr>
<td>Slope</td>
<td>0.003 ns</td>
<td>&lt; 0.002 ns</td>
<td>0.004*</td>
</tr>
<tr>
<td><strong>Negative affect</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>0.021***</td>
<td>0.734</td>
<td>-</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.010***</td>
<td>0.009***</td>
<td>-</td>
</tr>
<tr>
<td>Slope</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note. Variances are depicted on the diagonal, covariances below and correlations above the diagonal for each variable separately. Standard errors are shown between parenthesis. Level of significance is indicated for the covariances and variances only. * Negative affect is on a logarithmic scale. ns p ≥ .050, * p < .050, ** p < .010, *** p < .001.
Table 2.5. Model fit indices for the unconditional bivariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for mindfulness and positive and negative affect

<table>
<thead>
<tr>
<th>Mindfulness and positive affect</th>
<th>$\chi^2$ (df)</th>
<th>CM</th>
<th>$\Delta \chi^2$ (df)</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 AR model</td>
<td>342.63 (84)***</td>
<td></td>
<td></td>
<td>0.917</td>
<td>0.866</td>
<td>0.115</td>
<td>478.630</td>
</tr>
<tr>
<td>2 LTM model</td>
<td>333.92 (110)***</td>
<td></td>
<td></td>
<td>0.928</td>
<td>0.912</td>
<td>0.093</td>
<td>417.917</td>
</tr>
<tr>
<td>3 ALT-full model</td>
<td>70.39 (66) ns</td>
<td></td>
<td></td>
<td>0.999</td>
<td>0.997</td>
<td>0.017</td>
<td>242.394</td>
</tr>
<tr>
<td>4 ALT-LTM model</td>
<td>338.30 (106)***</td>
<td>3</td>
<td>267.91 (40)***</td>
<td>0.926</td>
<td>0.905</td>
<td>0.097</td>
<td>430.302</td>
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<tr>
<td>5 ALT-no slope variance on PA</td>
<td>78.32 (67) ns</td>
<td>3</td>
<td>7.93 (1)**</td>
<td>0.996</td>
<td>0.993</td>
<td>0.027</td>
<td>248.232</td>
</tr>
<tr>
<td>6 ALT-no slope on PA</td>
<td>83.91 (72) ns</td>
<td>3</td>
<td>13.52 (6)*</td>
<td>0.996</td>
<td>0.993</td>
<td>0.027</td>
<td>243.914</td>
</tr>
<tr>
<td>7 ALT-no slope variance on MFN</td>
<td>87.90 (73) ns</td>
<td>3</td>
<td>17.51 (7)*</td>
<td>0.995</td>
<td>0.991</td>
<td>0.030</td>
<td>245.904</td>
</tr>
<tr>
<td>8 ALT-no slope on MFN</td>
<td>109.98 (77)**</td>
<td>3</td>
<td>39.59 (11)**</td>
<td>0.989</td>
<td>0.981</td>
<td>0.043</td>
<td>259.979</td>
</tr>
<tr>
<td>9 ALT-no time-specific error correlations</td>
<td>131.00 (73)***</td>
<td>3</td>
<td>60.61 (7)**</td>
<td>0.981</td>
<td>0.965</td>
<td>0.058</td>
<td>289.001</td>
</tr>
<tr>
<td>10 ALT-time-specific error correlation constraints</td>
<td>84.13 (72) ns</td>
<td>3</td>
<td>13.74 (6)*</td>
<td>0.996</td>
<td>0.993</td>
<td>0.027</td>
<td>244.134</td>
</tr>
<tr>
<td>11 ALT-autoregression constraints for MFN</td>
<td>72.96 (72) ns</td>
<td>3</td>
<td>2.57 (6) ns</td>
<td>1.000</td>
<td>0.999</td>
<td>0.008</td>
<td>232.962</td>
</tr>
<tr>
<td>12 ALT-autoregression constraints for PA</td>
<td>79.42 (78) ns</td>
<td>11</td>
<td>6.46 (6) ns</td>
<td>1.000</td>
<td>0.999</td>
<td>0.009</td>
<td>227.417</td>
</tr>
<tr>
<td>13 ALT-cross-lagged constraints for MFN $\rightarrow$ PA</td>
<td>83.51 (84) ns</td>
<td>12</td>
<td>4.09 (6) ns</td>
<td>1.000</td>
<td>1.000</td>
<td>&lt; 0.001</td>
<td>219.509</td>
</tr>
<tr>
<td>14 ALT-cross-lagged constraints for PA $\rightarrow$ MFN</td>
<td>97.96 (90) ns</td>
<td>13</td>
<td>14.45 (6)*</td>
<td>0.997</td>
<td>0.996</td>
<td>0.019</td>
<td>221.962</td>
</tr>
</tbody>
</table>
| Note. MFN = mindfulness; PA = positive affect; NA = negative affect (logarithmic transformed); $\chi^2$ = chi-square test of model fit; df = degrees of freedom; $\Delta \chi^2$ = chi-square difference test; CM = comparison model in the $\Delta \chi^2$; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; AIC = Akaike information criterion. The final model is shown in bold. ns $p$ $\geq$ .050, * $p$ < .050, ** $p$ < .010, *** $p$ < .001.
<table>
<thead>
<tr>
<th></th>
<th>Mindfulness and negative affect</th>
<th>( \chi^2 (df) )</th>
<th>CM</th>
<th>( \Delta \chi^2 (df) )</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>AIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>AR model</td>
<td>339.92 (84)**</td>
<td>0.921</td>
<td>0.858</td>
<td>0.114</td>
<td>475.920</td>
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<tr>
<td>2</td>
<td>LTM model</td>
<td>314.52 (110)**</td>
<td>0.930</td>
<td>0.913</td>
<td>0.089</td>
<td>398.523</td>
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<tr>
<td>3</td>
<td>ALT-full model</td>
<td>74.29 (66) ns</td>
<td>0.997</td>
<td>0.994</td>
<td>0.023</td>
<td>246.286</td>
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</tr>
<tr>
<td>4</td>
<td>ALT-LTM model</td>
<td>309.02 (106)**</td>
<td>3</td>
<td>234.74 (40)**</td>
<td>0.931</td>
<td>0.991</td>
<td>0.090</td>
<td>401.024</td>
</tr>
<tr>
<td>5</td>
<td>ALT-no slope variance on NA</td>
<td>77.69 (67) ns</td>
<td>3</td>
<td>3.41 (1) ns</td>
<td>0.996</td>
<td>0.993</td>
<td>0.026</td>
<td>247.694</td>
</tr>
<tr>
<td>6</td>
<td>ALT-no slope on NA</td>
<td>79.70 (72) ns</td>
<td>5</td>
<td>2.00 (5) ns</td>
<td>0.997</td>
<td>0.995</td>
<td>0.021</td>
<td>239.699</td>
</tr>
<tr>
<td>7</td>
<td>ALT-no slope variance on MFN</td>
<td>87.46 (73) ns</td>
<td>6</td>
<td>7.77 (1) **</td>
<td>0.995</td>
<td>0.991</td>
<td>0.029</td>
<td>245.464</td>
</tr>
<tr>
<td>8</td>
<td>ALT-no slope on MFN</td>
<td>107.05 (77)*</td>
<td>6</td>
<td>27.35 (5) ***</td>
<td>0.990</td>
<td>0.982</td>
<td>0.041</td>
<td>257.053</td>
</tr>
<tr>
<td>9</td>
<td>ALT-no time-specific error correlations</td>
<td>215.26 (79)**</td>
<td>6</td>
<td>135.56 (7) ***</td>
<td>0.953</td>
<td>0.920</td>
<td>0.086</td>
<td>361.260</td>
</tr>
<tr>
<td>10</td>
<td>ALT-time-specific error correlation constraints</td>
<td>89.65 (78) ns</td>
<td>6</td>
<td>9.55 (6) ns</td>
<td>0.996</td>
<td>0.993</td>
<td>0.025</td>
<td>237.645</td>
</tr>
<tr>
<td>11</td>
<td>ALT-autoregression constraints for MFN</td>
<td>96.44 (84) ns</td>
<td>10</td>
<td>6.79 (6) ns</td>
<td>0.996</td>
<td>0.993</td>
<td>0.025</td>
<td>232.439</td>
</tr>
<tr>
<td>12</td>
<td>ALT-autoregression constraints for NA</td>
<td>100.94 (90) ns</td>
<td>11</td>
<td>4.50 (6) ns</td>
<td>0.996</td>
<td>0.994</td>
<td>0.023</td>
<td>224.944</td>
</tr>
<tr>
<td>13</td>
<td>ALT-cross-lagged constraints MFN ( \rightarrow ) NA</td>
<td>104.67 (96) ns</td>
<td>12</td>
<td>3.73 (6) ns</td>
<td>0.997</td>
<td>0.996</td>
<td>0.020</td>
<td>216.671</td>
</tr>
<tr>
<td>14</td>
<td>ALT-cross-lagged constraints NA ( \rightarrow ) MFN</td>
<td>106.67 (102) ns</td>
<td>13</td>
<td>2.00 (6) ns</td>
<td>0.998</td>
<td>0.998</td>
<td>0.014</td>
<td>206.668</td>
</tr>
</tbody>
</table>

**Note.** MFN = mindfulness; PA = positive affect; NA = negative affect (logarithmic transformed); \( \chi^2 \) = chi-square test of model fit; \( df \) = degrees of freedom; \( \Delta \chi^2 \) = chi-square difference test; CM = comparison model in the \( \Delta \chi^2 \); CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; AIC = Akaike information criterion. The final model is shown in bold. \( ^{**} p \geq .050, ^{*} p < .050, ^{**} p < .010, ^{***} p < .001. \)
Prospective Associations Between Home Practice and Depressive Symptoms in Mindfulness-Based Cognitive Therapy for Recurrent Depression: A 15 Months Follow-Up Study
Abstract

**Background.** Home practice is considered a key element in increasing treatment effectiveness of Mindfulness-based cognitive therapy (MBCT) for depression. However, long-term longitudinal research into the associations between home practice and depression outcomes is scarce. The current study examined the prospective associations between the extent of formal home practice and subsequent depression severity during 15 months of follow-up.

**Methods.** Data from two randomized-controlled trials on MBCT for recurrent depression were used (n = 200). Depressive symptoms were assessed at 3-month intervals: 0 (baseline), 3 (post-treatment), 6, 9, 12, and 15 months. Formal home practice frequency was calculated for each 3-month period. Autoregressive latent trajectory (ALT) modeling was applied.

**Results.** Participants practiced formal exercises on 57% (SD = 0.22, range: 0 - 1) of the days during MBCT, equivalent to an average of 4 days per week, which showed a rapid decline after MBCT. The level of depressive symptoms did not change over the full study period. A small positive association was found between formal home practice frequency during each 3-month period on subsequent depressive symptoms, but sensitivity analyses did not confirm this. More robust, a small negative association was found between levels of depressive symptoms at each measurement point and formal home practice frequency during the subsequent 3-month periods.

**Conclusions.** The hypothesis that more frequent home practice would lead to reductions in depressive symptoms was not confirmed in the current study. Rather, it seems that patients with higher levels of depression may subsequently practice less frequently at home. The interplay between home practice and outcome might not be as straightforward as expected. However, these results are preliminary and should be replicated first before recommendations for clinical practice can be formulated.
1. Introduction

Major depressive disorder (MDD) is the most common form of depressive disorders, and the leading cause of disease burden worldwide (American Psychiatric Association, 2013; World Health Organization, 2017). MDD often runs a chronic and recurrent course (Richards, 2011). Many patients experience residual depressive symptoms, which are a predictor of relapse/recurrence (Buckman et al., 2018; Nierenberg, 2015). Aside from antidepressant medication, numerous psychological interventions have been developed for MDD, among which mindfulness-based cognitive therapy (MBCT; Segal et al., 2002). Accumulating evidence suggests that MBCT is effective in both reducing relapse/recurrence and depressive symptoms in recurrently depressed patients (Kuyken et al. 2016; Strauss et al., 2014).

MBCT is a group-based training, consisting of 8 weekly sessions, and includes both mindfulness meditation and cognitive behavioral therapy (Segal et al., 2012). Mindfulness is frequently defined as the awareness that emerges by purposefully paying attention to the present experiences with a non-judgmental stance (Kabat-Zinn, 1994). It is also considered a skill that can be further developed through regular practice (Segal et al., 2012; Tang et al., 2015). Therefore, home practice is considered an essential element in MBCT (Alsubaie et al., 2017). Formal home practice, as part of the MBCT protocol, takes about 45 min a day and includes practices such as the body scan, sitting meditation, and mindful movement. In addition, various short informal home exercises are given involving the cultivation of mindfulness in routine daily life activities (Segal et al., 2012).

Previous research suggests that more formal home practice during mindfulness-based interventions is associated with better post-treatment outcomes. A recent systematic review and meta-analysis, including over 1400 clinical and non-clinical participants (Parsons et al., 2017), found a pooled estimate for participants’ formal home practice of 64% of the assigned amount (i.e., percentage of minutes/day or days/week) during MBCT/MBSR. Twenty-eight studies investigated the association between formal home practice and post-treatment outcomes of which 15 were randomized controlled trials (RCTs). A small to moderate significant association between formal home practice during MBCT/MBSR and positive post-treatment outcomes was found ($n = 898; r = .26, 95\% CI .19 - .34$). This was confirmed by the analysis restricted to RCTs only ($r = .26, 95\% CI .14 - .38, z = 4.21, p < .001$). However, most studies investigated MBSR rather than MBCT and only a few studies investigated the associations between formal home practice and outcome of MBCT in patients with recurrent depression.

Research into the effects of MBCT formal home practice on depression at long-term outcome is limited. Crane et al. (2014) investigated the effect of formal home practice in MBCT on relapse/recurrence depression in 99 recurrently
depressed patients during a 12 month follow-up period, and found a significant effect of average daily minutes of formal home practice on the risk of relapse to major depression ($HR: .97; CI: .947 - .995$). In contrast, Bondolfi et al. (2010) did not find significant associations of formal home practice frequency during and after MBCT, up to 12 months of follow-up, with risk of relapse/recurrence in patients with recurrent depression. However, they suggested that these non-significant findings might be due to retrospective measurements of formal home practice, and the small sample size ($n = 26$), which resulted in limited statistical power.

Furthermore, higher levels of depressive symptomatology might act as a barrier to carry out home practices. One could experience more difficult or aversive thoughts and feelings (Beck & Clark, 1997), and become more preoccupied by them, for example due to attentional biases associated with depression (Mogg et al., 1995) and increased rumination (Whitmer & Gotlib, 2013). As people typically show a tendency to avoid or suppress unpleasant experiences (Aldao et al., 2010), and depressive symptomatology may further add motivational and concentration difficulties (Keller et al., 2019; Ravizza & Delgado, 2014), it seems reasonable to expect a negative influence on home practice. To date, little is known about the possibility of such a reverse effect. To investigate the course and possible mutual relationships between home practice and depression outcomes, multiple assessments of both constructs over time, preferably also after the intervention period, and the use of advanced analytical techniques are needed.

Therefore, the current study examined the prospective associations between multiple assessments of formal home practice frequency and depressive symptoms over a period of 15 months in MBCT for recurrent depression. The autoregressive latent trajectory (ALT) modeling technique used in this study allows an investigation of effects of formal home practice frequency on subsequent depressive symptoms and vice versa while at the same time accounting for the overall trajectories for both variables across the entire study period. Therefore, ALT is perceived as highly suitable for analyzing dynamic processes. We hypothesized that more formal home practice would be associated with subsequent less depressive symptoms. In addition, we hypothesized that more depressive symptoms would be associated with less subsequent formal home practice frequency.

2. Methods

2.1. Design

This study was based on data from the MOMENT study which consists of two RCTs that investigated the effectiveness of MBCT, maintenance antidepressant medication (mADM) and the combination of both to prevent relapse/recurrence
in patients with recurrent depression in remission during 15 months of follow-up (Huijbers et al., 2015, 2016). The first RCT was a non-inferiority trial comparing the combination of MBCT and mADM with MBCT followed by discontinuation of mADM (Huijbers et al., 2016). The second RCT was a superiority trial comparing the combination of MBCT and mADM with mADM alone (Huijbers et al., 2015). The current study used data from the subset of participants ($n = 282$) allocated to MBCT (with or without tapering off mADM) in both trials. The protocol has been approved by the Medical Ethics Committee of Arnhem-Nijmegen (CMO, no. 2008/242; Huijbers et al., 2012).

2.2. Participants

Patients with recurrent depression in (partial) remission ($n = 317$) were recruited between September 2009 and January 2012 at secondary and tertiary psychiatric outpatient clinics across the Netherlands. Inclusion criteria were: (a) ≥ three prior major depressive episodes according to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000) assessed by the Structured Clinical Interview for DSM disorders I (SCID-I; First, Gibbon et al., 1996); (b) ≥ 6 months on a stable dose of antidepressant medication; (c) full or partial remission, not meeting the criteria for a depressive episode using the SCID-I; (d) native Dutch speaking. Exclusion criteria were: bipolar disorder, psychotic disorder, neurological disorder, somatic disorder, current alcohol and/or drug dependency, high dose of benzodiazepines, electric convulsive therapy within the past three months, previous MBCT/MBSR, and current psychotherapy more than once per three weeks. All participants were included only after written informed consent had been obtained.

2.3. Intervention

MBCT was delivered largely according to the protocol of Segal et al. (2002, 2012). The training was delivered in groups of 8 - 12 participants during eight weekly sessions of 2.5hrs and one day of silent practice between the 6th and 7th session. MBCT home practice included daily formal home practices using a compact disk (CD) for 45 min (e.g., the body scan, sitting, walking meditation and mindful movement) and daily informal exercises such as bringing present moment awareness in everyday activities. Videotapes were available for 15 teachers and examined with the Mindfulness-Based Interventions Teaching Assessment Criteria (MBI:TAC; Crane et al., 2013). The teacher competency ratings showed that none of the teachers were incompetent, two teachers (13%) were characterized as beginners, six (40%) as advanced beginners, four (27%) as competent, three (20%) as proficient, and none as advanced. The mean teacher competency score was 3.5 ($SD = 0.9$, range: 2.0 - 5.2). Of these teachers, eight were psychologists, three occupational therapists, three psychiatric nurses and one psychiatrist.
Their mean clinical experience was 21 years ($SD = 6.5$, range: 11.5 - 31.0), with a mean of 23 MBCT courses taught ($SD = 16$, range: 6 - 60). Teachers’ personal experience with meditation included on average 9 years of personal meditation practice ($SD = 8.0$, range: 3.0 - 35.0), with a mean amount of 57 days spent in retreat ($SD = 95$, range: 0 - 282), and mean meditation practice of 4.3hrs a week ($SD = 3.3$, range: 0.5 - 14.0).

2.4. Measures

2.4.1. Depression severity
Depression severity was assessed with the Dutch version of the Inventory of Depressive Symptomatology-Clinician rated (IDS-C; Akkerhuis, 1997) at 3-month intervals: 0 (baseline), 3 (post-treatment), 6, 9, 12, and 15 months. These measurement points are referred to as $t_0$, $t_3$, $t_6$, $t_9$, $t_{12}$, and $t_{15}$, see Figure 1. The IDS-C consists of 30 multiple choice questions on a 4-point Likert-scale assessing depressive symptoms over the last seven days designated by the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR; American Psychiatric Association, 2000). The IDS-C is scored by summing responses of 28 out of 30 items (two sets of items are mutually exclusive) to obtain a total score ranging from 0 to 84. Higher scores indicate greater symptom severity. The internal consistency of the current study was good to excellent at all measurement points ($\alpha$ range: .86 - .91).

2.4.2. Home practice frequency
Home practice frequency was assessed using monthly calendars, specifically designed for this study, on which participants could indicate via tick boxes whether or not they had completed their assigned daily formal home practice (i.e., body scan, sitting meditation, mindful walking or movement exercises). Data on formal home practice frequency was collected across 15 months by asking participants to return their calendars each month using a return postage envelope. The average percentage of days practiced per three months was calculated (1-3, 4-6, 7-9, 10-12, and 13-15 months). These measurement points are referred to as $t_{1.5}$, $t_{4.5}$, $t_{7.5}$, $t_{10.5}$, and $t_{13.5}$. The time period of formal home practice applies to the period between two assessments of depressive symptoms, see Figure 1.

2.5. Statistical analyses

2.5.1. Home practice
Given the fact that participants did hand in monthly calendars indicating that they did not carry out their formal home practices, we assumed that there was not a huge barrier in reporting non-adherence to formal home practice. When a calendar was missing however, we did not know whether a participant did or did not practiced during that month. Therefore, in order to provide a more
accurate estimate of average formal home practice frequency in each 3-monthly period, person mean imputation was applied in case one out of three monthly calendars was missing by using the data of the other two calendars for that time period. When two or three calendars were missing for a certain period, this was coded as a missing value for that period. In addition, participants with less than two out of three monthly calendars for each 3-month period ($n = 82$) were excluded - as these participants had missing values for each period.

2.5.2. ALT modeling technique

To investigate the prospective associations between formal home practice and depressive symptoms during 15 months of follow-up, the ALT modeling technique was used, which combines a latent trajectory model (LTM) with an autoregressive (AR) model. The LTM model allows a different overall trajectory per participant as marked by a different (subject-specific) intercept and slope. The intercept displays a general level of a variable. The intercept variance represents differences in general levels between participants. The slope can be interpreted as an overall magnitude of change (positive or negative) of a variable over the full study period (15 months). Its variance depicts inter-individual differences in the magnitude of change. Interrelationships between two variables from measurement-to-measurement are not captured by a LTM. AR models do investigate associations between two different variables across subsequent measurement points, so called cross-lagged (CL) effects, while taking the effect of the prior value of the same variable on the current value into account. However, when not accounting for the overall trajectories of the variables over time, spurious CL effects might appear while they essentially do not exist (Voelkle, 2008). Hence, by combining the LTM with an AR model into an ALT model it is possible to properly interpret CL effects while controlling for overall trajectories. Several bivariate structural equation models (SEM) were fitted, following the recommendations of Bollen and Curran (2004), which led to a final bivariate ALT model. When fitting the SEM models, robust maximum likelihood (MLR; Satorra & Bentler, 2010) was employed in order to account for skewed

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**Figure 1.** Schematic overview of the measurement points of depressive symptoms (DEP) and formal home practice (HP). $t_0 =$ baseline; $t_1.5 =$ 1-3 months; $t_3 =$ 3 months; $t_4.5 =$ 4-6 months; $t_6 =$ 6 months; $t_7.5 =$ 7-9 months; $t_9 =$ 9 months; $t_{10.5} =$ 10-12 months; $t_{12} =$ 12 months; $t_{13.5} =$ 13-15 months; and $t_{15} =$ 15 months of follow-up.
variables. For the model building steps of the various bivariate SEM models that were fit, see Supplementary Material.

2.5.3. Model fit
Several fit indices were used to evaluate model fit: (1) chi-square ($\chi^2$) to degrees of freedom ($df$) ratio, values close to 1 were considered good, values between 2 and 3 as acceptable and less than 2 as preferable fit (Carmines & McIver, 1981; Marsh & Hocevar, 1985); (2) the Tucker-Lewis index (TLI; Tucker & Lewis, 1973) and comparative fit index (CFI; Bentler, 1990) of which values higher than 0.90 were considered an adequate and higher than 0.95 a very good fit (Bollen, 1989; Hu & Bentler, 1999); (3) root-mean-square error of approximation (RMSEA; Steiger, 1998) of which values below 0.07 were indicative of good fit, while for standardized root-mean-square residual values below 0.08 were adequate and below 0.05 were considered good (SRMR; Hooper et al., 2008). Model comparisons were evaluated with the Satorra-Bentler scaled chi-square difference test for nested models (Satorra & Bentler, 2001, 2010), which takes into account that the MLR estimator was used to fit the SEM models (see above). In case a significant difference between two models existed, the more complex model (i.e., the model with less degrees of freedom) was retained, otherwise the simpler model was chosen. For non-nested models, the model with the lowest Bayesian information criterion (BIC; Raftery, 1995) was favored in which differences between 2-6 points were considered as small, 6-10 points as medium strong and > 10 points as very strong evidence of differences in model fit. Differences of ≤ 2 on the BIC indicated that both models fitted the data equally well and the most parsimonious model was favored (Raftery, 1995).

2.5.4. Sensitivity analyses
At first, the final bivariate ALT model was fitted including a zero imputed variable for formal home practice (i.e., in which no data on formal home practice was interpreted as not having practiced at all) among the same participants included in the current study ($n = 200$). Second, the final bivariate ALT model including a zero imputed variable for formal home practice was fitted among all participants who were allocated to MBCT ($n = 282$). The results of both sensitivity analyses were compared to the results of the final bivariate ALT model of the current study ($n = 200$) including the original (mean imputed) formal home practice variable.

2.5.5. Computational note
Descriptive analyses were performed using IBM SPSS Statistics version 22.0 (IBM Corporation, 2013). The structural equation modeling analyses were carried out by using Mplus version 6.11 (Muthén & Muthén, 1998-2011). Probability values lower than .050 (two-tailed) were considered significant for all analyses.
3. Results

3.1. Descriptives
There were no baseline differences in demographic and clinical characteristics between participants included and excluded from the primary analysis of the current study, see Table 1. Figure 2 portrays the overall course of formal home practice across 15 months of follow-up. Participants practiced on average 57% of the days during MBCT ($SD = 0.22$, range: 0 - 1) which equals an average of 4 days a week. A rapid decline of formal home practice frequency was found during the follow-up periods, where formal home practice reached a plateau at 21% of the available number of days to practice, equivalent to an average of about 1.5 days a week. Depressive symptoms showed a stable course over time. Table 2 presents detailed descriptives and correlations of the variables under study.

3.2. Bivariate ALT modeling
In Table 3 the model fit indices are presented of the consecutive bivariate SEM models that were fit. For detailed results of the bivariate model building process, see Supplementary Material. The bivariate ALT model that demonstrated the best fit had no slope variance and intercept variance for formal home practice, equal AR effects over time for formal home practice, and equality constraints of CL effects over time for both formal home practice to subsequent depressive symptoms and vice versa. This model provided a very good model fit ($\chi^2 = 49.698$, $df = 45$, $p = .292$; $CFI = 0.993$; $TLI = 0.992$; $RMSEA = 0.023$; $SRMR = 0.057$).

Figure 3 graphically displays the standardized parameter estimates of the final bivariate ALT model. The overall trajectory of formal home practice indicated that, on average, formal home practice frequency decreased over time; i.e., a negative and significant slope parameter ($\mu_{\beta_{HP}} = -0.530$, $s.e. = 0.023$, $p < .001$), accompanied by a positive and significant intercept parameter ($\mu_{\alpha_{HP}} = 0.586$, $s.e. = 0.017$, $p < .001$). The variance of the intercept and slope factor of formal home practice could be set to 0, meaning that there was no significant difference between participants in their general formal home practice frequency level nor in their decline of formal home practice frequency over time. The intercept factor and the first measurement point of depressive symptoms were positive and significant ($\mu_{DEP} = 10.261$, $s.e. = 1.866$, $p < .001$; $\mu_{DEP(t0)} = 12.700$, $s.e. = 0.701$, $p < .001$) and positively correlated with each other ($r = .644$, $s.e. = 0.132$, $p < .001$). The variance of the intercept factor of depressive symptoms was non-significant ($\sigma_{\alpha_{DEP}} = 33.291$, $s.e. = 32.220$, $p = .301$), while the variance of the first measurement point of depressive symptoms was positive and significant ($\sigma_{DEP(t0)} = 98.320$, $s.e. = 10.995$, $p < .001$). This indicates that participants did not differ in their general level, but did differ in their baseline levels of depressive symptoms. The slope of depressive symptoms was not correlated with both the first measurement ($p = .275$) and the intercept factor of depressive symptoms ($p = .498$). Both the slope
factor of depressive symptoms and its variance were non-significant ($p = .075$, respectively $p = .086$), which means that, in general, over the full study period, no significant increase or decrease in depressive symptoms was found, with this being true for all participants.

Looking at measurement-to-measurement effects, the AR paths for formal home practice were equally strong and statistically significant across all measurement points ($\rho_{AR(1)HP} = 0.810$, s.e. = 0.036, $p < .001$), inferring that individual differences in formal home practice was stable from one measurement to the next. Autoregressive effects were not present for depressive symptoms,
apart from the period between 12 and 15 months. With regard to the CL effects, which are equal over time, higher average percentages of formal home practice frequency over each 3-month period, predicted subsequent higher levels of depressive symptoms \( (b_{\text{HP}(t-1.5),\text{DEP}(t)} = 3.298, \text{s.e.} = 1.632, p = .043) \). Vice versa, higher levels of depressive symptoms at each assessment predicted, on average, less formal home practice frequency across the subsequent 3-month periods \( (b_{\text{DEP}(t-1.5),\text{HP}(t)} = -0.001, \text{s.e.} < 0.001, p = .005) \).

### 3.3. Sensitivity analyses

The final bivariate ALT model including the zero imputed variable of formal home practice (i.e., missing calendar meaning no formal home practice performed) on the same sample as the primary analysis \( (n = 200) \) yielded similar results, except that some effects became non-significant. This included the CL effects from formal home practice to subsequent depressive symptoms \( (b_{\text{HP}(t-1.5),\text{DEP}(t)} = 1.971, \text{s.e.} = 1.573, p = .210) \) and the AR effect between depressive symptoms at 12 and 15 months of follow-up \( (\rho_{\text{AR,DEP}(t12),\text{DEP}(t15)} = -0.211, \text{s.e.} = 0.112, p = .060) \). These results were also found when fitting the final bivariate ALT model with the zero imputed variable of formal home practice including all participants randomized to MBCT \( (n = 282) \).

Figure 2. The overall course of formal home practice across the full study period (15 months). The x-axis represents time in which \( t1.5 = 1-3 \) months, \( t4.5 = 4-6 \) months, \( t7.5 = 7-9 \) months, \( t10.5 = 10-12 \) months, and \( t13.5 = 13-15 \) months of follow-up. The y-axis represents the average percentage of days that participants adhered to the assigned daily formal home practice.
Table 2. Correlations between formal home practice (HP) and depressive symptoms (DEP) and their descriptives

<table>
<thead>
<tr>
<th></th>
<th>Formal home practice</th>
<th>Depressive symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t1.5</td>
<td>t4.5</td>
</tr>
<tr>
<td>HP t1.5</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>HP t4.5</td>
<td>.71**</td>
<td>1</td>
</tr>
<tr>
<td>HP t7.5</td>
<td>.55**</td>
<td>.81**</td>
</tr>
<tr>
<td>HP t10.5</td>
<td>.55**</td>
<td>.67**</td>
</tr>
<tr>
<td>HP t13.5</td>
<td>.53**</td>
<td>.57**</td>
</tr>
<tr>
<td>DEP t0</td>
<td>- .10</td>
<td>- .10</td>
</tr>
<tr>
<td>DEP t3</td>
<td>.11</td>
<td>.11</td>
</tr>
<tr>
<td>DEP t6</td>
<td>.08</td>
<td>.06</td>
</tr>
<tr>
<td>DEP t9</td>
<td>- .09</td>
<td>- .15</td>
</tr>
<tr>
<td>DEP t12</td>
<td>- .07</td>
<td>-.002</td>
</tr>
<tr>
<td>Mean</td>
<td>0.57</td>
<td>0.32</td>
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<tr>
<td>Standard deviation</td>
<td>0.22</td>
<td>0.02</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>- 0.37</td>
<td>- 0.15</td>
</tr>
<tr>
<td>Skewness</td>
<td>- 0.17</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Note. * p < .05, ** p < .01.
Table 3. Model fit indices for the bivariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for formal home practice (HP) and depressive symptoms (DEP)

<table>
<thead>
<tr>
<th>Formal home practice \ and depressive symptoms</th>
<th>$\chi^2$ (df)</th>
<th>CM</th>
<th>$\Delta \chi^2$ (df)</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>SRMR</th>
<th>BIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 AR model</td>
<td>102.035 (36)**</td>
<td></td>
<td></td>
<td>0.907</td>
<td>0.859</td>
<td>0.096</td>
<td>0.104</td>
<td>7683.834</td>
</tr>
<tr>
<td>2 LTM model</td>
<td>108.832 (49)**</td>
<td></td>
<td></td>
<td>0.916</td>
<td>0.906</td>
<td>0.078</td>
<td>0.072</td>
<td>7609.851</td>
</tr>
<tr>
<td>3 ALT - full model</td>
<td>22.274 (25)*ns</td>
<td></td>
<td></td>
<td>1.000</td>
<td>1.008</td>
<td>&lt; 0.001</td>
<td>0.028</td>
<td>7652.367</td>
</tr>
<tr>
<td>4 ALT - LTM model</td>
<td>103.220 (44)**</td>
<td>3</td>
<td>71.380 (19)**</td>
<td>0.917</td>
<td>0.896</td>
<td>0.082</td>
<td>0.071</td>
<td>7631.041</td>
</tr>
<tr>
<td>5 ALT - no slope variance DEP</td>
<td>35.186 (30)*ns</td>
<td>3</td>
<td>12.155 (5)*</td>
<td>0.993</td>
<td>0.987</td>
<td>0.029</td>
<td>0.038</td>
<td>7639.300</td>
</tr>
<tr>
<td>6 ALT - no slope on DEP</td>
<td>37.413 (31)*ns</td>
<td>3</td>
<td>14.138 (6)*</td>
<td>0.991</td>
<td>0.984</td>
<td>0.032</td>
<td>0.041</td>
<td>7636.064</td>
</tr>
<tr>
<td>7 ALT - no slope variance HP</td>
<td>28.635 (30)*ns</td>
<td>3</td>
<td>6.485 (5)*</td>
<td>1.000</td>
<td>1.004</td>
<td>&lt; 0.001</td>
<td>0.029</td>
<td>7634.182</td>
</tr>
<tr>
<td>8 ALT7 - no slope on HP</td>
<td>231.403 (34)**</td>
<td>7</td>
<td>164.776 (4)**</td>
<td>0.723</td>
<td>0.552</td>
<td>0.170</td>
<td>0.290</td>
<td>7830.822</td>
</tr>
<tr>
<td>9 ALT7 - AR constraints for HP</td>
<td>33.523 (33)*ns</td>
<td>7</td>
<td>4.609 (3)*</td>
<td>0.999</td>
<td>0.999</td>
<td>0.009</td>
<td>0.041</td>
<td>7623.172</td>
</tr>
<tr>
<td>10 ALT9 - AR constraints for DEP</td>
<td>44.696 (37)*ns</td>
<td>9</td>
<td>9.643 (4)*</td>
<td>0.989</td>
<td>0.984</td>
<td>0.032</td>
<td>0.050</td>
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</tr>
<tr>
<td>11 ALT9 - CL constraints for DEP &gt; HP</td>
<td>38.202 (37)*ns</td>
<td>9</td>
<td>4.569 (4)*</td>
<td>0.998</td>
<td>0.997</td>
<td>0.013</td>
<td>0.044</td>
<td>7606.357</td>
</tr>
<tr>
<td>12 ALT11 - CL constraints for HP &gt; DEP</td>
<td>46.685 (41)*ns</td>
<td>11</td>
<td>7.787 (4)*</td>
<td>0.992</td>
<td>0.989</td>
<td>0.026</td>
<td>0.056</td>
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</tr>
<tr>
<td>13 ALT12 - no intercept variance HP</td>
<td>49.698 (45)*ns</td>
<td>12</td>
<td>3.093 (4)*</td>
<td>0.993</td>
<td>0.992</td>
<td>0.023</td>
<td>0.057</td>
<td>7577.015</td>
</tr>
</tbody>
</table>

Note. HP = formal home practice; DEP = depressive symptoms; $\chi^2$ = Satorra-Bentler scaled chi-square difference test; df = degrees of freedom; $\Delta \chi^2$ = chi-square difference test; CM = comparison model in the $\Delta \chi^2$; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean-square residual; BIC = Bayesian information criterion. The final model is shown in bold. * Including free slope parameter estimates (0, *, *, *, 1). ** Including linear slope parameter estimates (0, 1, 2, 3, 4) and predetermined specification. *** Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^a$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^b$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^c$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^d$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^e$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^f$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^g$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model. $^h$ Due to a non-significant (small) negative intercept variance of formal home practice in the previous model.
Figure 3. Standardized parameter estimates of the final bivariate ALT model. Significant estimates are depicted by solid black lines, non-significant estimates are not shown. Double-headed arrows represent correlations. The 2nd, 3rd, and 4th factor loadings of the slope factor of formal home practice were freely estimated. The autoregressive effects of formal home practice were set equal to each other; the same applies to the cross-lagged effects of formal home practice to depressive symptoms, and from depressive symptoms to formal home practice. Note that standardizing the parameters may disrupt the equality constraints. $t_0 =$ baseline; $t_{1.5} =$ 1-3 months; $t_3 =$ 3 months; $t_{4.5} =$ 4-6 months; $t_6 =$ 6 months; $t_{7.5} =$ 7-9 months; $t_9 =$ 9 months; $t_{10.5} =$ 10-12 months; $t_{12} =$ 12 months; $t_{13.5} =$ 13-15 months; and $t_{15} =$ 15 months of follow-up. DEP = depressive symptoms; HP = formal home practice.
4. Discussion

The current study used autoregressive latent trajectory (ALT) modeling to investigate the prospective associations between formal home practice frequency and depression severity during 15 months of follow-up in recurrently depressed patients participating in MBCT. Overall trajectories showed a rapid decline of formal home practice frequency and a stable course of depressive symptoms over time. The hypothesis that more frequent formal home practice would lead to reductions in depressive symptoms was not confirmed in the current study. In contrast, we found a small effect of more practice being associated with higher levels of subsequent depressive symptoms. However, this was not confirmed by both sensitivity analyses. The current study did find support for a reversed effect; patients with higher levels of depression subsequently performed formal exercises less frequently at home.

Non-compliance with formal home practice remains a persistent problem in clinical practice. The overall formal home practice compliance rate of the current study during MBCT (57%) was slightly lower compared to rates found by Parsons et al. (2017), who reported a pooled estimate of 64% (95% CI: 60 - 69%) of what is typically suggested in MBCT/MBSR formats (Kabat-Zinn, 1990; Segal et al., 2012). Moreover, compliance rates rapidly declined after the intervention period, which is in line with previous research (Bondolfi et al., 2010). The finding that depressive symptoms did not decrease over the study period might be inherent to the participants included in the current study, namely patients in remission at start of the study.

Against expectations, no robust associations between formal home practice frequency and subsequent reduction of depressive symptoms were found. This is in contrast to previous research suggesting that more formal home practice during MBCT/MBSR is associated with better post-treatment outcomes (Parsons et al., 2017; van Aalderen et al., 2012) and reduced long-term relapse/recurrence rates (Crane et al., 2014) in recurrently depressed patients. The relatively low average frequency of formal home practice and the rapid decline of formal home practice frequency after the intervention period might have resulted in the marginal to non-significant findings of the current study. In addition, the relative stability of the outcome measure over time may have resulted in a restriction of range. More pronounced effects of formal home practice on depressive symptoms might be found when MBCT targets acutely depressed individuals. On the other hand, based on the findings of the current study, higher levels of depression might actually impede formal home practice itself.

Support for a reversed effect was found in the current study. Patients with more depressive symptoms subsequently performed formal exercises less frequently at home. As previous studies investigating the association between formal home practice and outcome were mostly correlational (Parsons et al.,
2017) and to our knowledge, a reverse effect has not yet been investigated, this might shed a new light on the association between formal home practice and depressive symptoms in MBCT for recurrent depression. One possible interpretation could be that difficulties with motivation and concentration, or a tendency to avoid negative thoughts, feelings and possibly bodily sensations, might make it more challenging to engage in mindfulness practice. Qualitative research into the specific barriers and facilitators to engage in mindfulness practice could provide more insight in the underlying processes.

The current study addresses two important gaps in the literature on MBCT home practice and depression outcomes (Parsons et al., 2017). First, by using ALT modeling techniques, we were able to disentangle the dynamic relationship between formal home practice frequency and depression severity over time. Second, by including long-term follow-up data, we were able to gain more insight into this relationship beyond the intervention period. In addition, a continuous outcome measure was used, allowing more subtle changes to be detected compared with a binary measure (e.g., relapse). Moreover, the data in this study was drawn from two multicenter RCTs, in which MBCT was delivered in university hospitals and community mental health centers across The Netherlands. Therefore, this study has drawn a rather realistic picture of compliance in patients from secondary and tertiary care with recurrent depression with mild levels of depressive symptoms.

Of course, the current study is not without limitations. At first, selection bias might have taken place because 82 participants were excluded from the primary analyses in the current study due to missing data on formal home practice. We handled this by performing sensitivity analyses with zero imputation (i.e. no calendar data meaning no home practice) both on the same data set, as well as on the data of all participants randomized to MBCT. In addition, the primary excluded patients did not differ on baseline characteristics and depression outcomes compared to the included patients, however, they may differ in other aspects that are related to adherence that were not assessed in the current study. Second, the analyses presented in the current study did not correct for individuals tapering off their antidepressant medication (tADM) nor teacher competency/experience, because running a conditional bivariate ALT-full model including tADM did not affect results and led to a decrease in model fit. In addition, previous research on the same dataset by Huijbers et al. (2017) found that teacher competency/experience was not associated with MBCT treatment outcomes (e.g., depressive symptoms). However, other possible confounding factors that were not assessed cannot be ruled out (e.g., childhood trauma). Third, a methodological limitation is that the current study was observational in terms of formal home practice and outcomes and did not manipulate formal home practice as a predictor. Random assignment of participants in MBCT with or without experiential cultivation of mindfulness
practice (including home practice) has been previously done by Williams et al. (2014), who compared MBCT with both cognitive psychological education (CPE) and treatment-as-usual (TAU) in preventing relapse to MDD in people currently in remission. CPE was modeled on MBCT, but without experiential training in meditation. MBCT provided significant protection against relapse for participants with increased vulnerability due to history of childhood trauma, but showed no significant advantage in comparison to CPE or usual care over the whole group of patients with recurrent depression. Lastly, a limitation of the current study is that the effect of informal home exercises was not included. Informal exercises are typically shorter exercises that bring present-moment awareness into everyday activities (e.g., consciously performing a daily routine activity). Perhaps over time, formal home practices are used less frequently, while informal exercises become more embedded in participants’ daily life (Bondolfi et al., 2010). However, it seems challenging to quantify the frequency and duration of informal exercises due to their more integrated nature, as a result of which they have been studied less often (Vettese et al., 2009). Research to date did not find associations between informal home exercises in MBCT/MBSR in patients with recurrent depression and intervention outcomes (e.g., Bondolfi et al., 2010; Crane et al., 2014; Hawley et al., 2014).

For future studies, it is important to operationalize home practice, both formal and informal, in the same way across studies and to avoid drop-out as much as possible. Improving the methodology, the use of smartphone applications to record real-time home practice and outcomes could be a great way forward. Data on both frequency and amount of time spend on each practice can easily be collected in this way. In addition, next to negative outcome measures, it would be valuable to include repeatedly administered positive health measures (e.g., quality of life, positive mental health). Moreover, notes on the quality of practice could be collected, which may be another relevant aspect of the relation between practice and outcomes (Del Re et al., 2013; Goldberg et al., 2020). Finally, qualitative in-depth interviews could provide valuable information about the views that people have on the importance of regular practice, and about specific barriers and facilitators that affect the engagement in mindfulness practices.

In conclusion, the interplay between home practice and outcome might not be as straightforward as expected. The current study shows support for depressive symptoms to have a negative influence on home practice, but not the other way around. However, these results are preliminary and should be replicated first before recommendations for clinical practice can be formulated.
References


Supplementary Material - Bivariate model building

1. Steps
At first, a bivariate AR model was fitted, which contained 6 observed variables of depressive symptoms (t0, t3, t6, t9, t12, and t15) and five observed variables of formal home practice (t1.5, t4.5, t7.5, t10.5, and t13.5), with AR effects included for both variables. See Figure 1 for the definition of the measurement points of both variables over time. In addition, each observed variable was regressed on the former measurement point of the other variable (CL effects). Secondly, a bivariate LTM model was fitted including the observed variables of depressive symptoms and formal home practice, and an intercept for both variables with all factor loadings set to 1. A linear slope was fitted for depressive symptoms (0, 1, 2, 3, 4, and 5), while for formal home practice, both a linear slope (0, 1, 2, 3, and 4) and a free slope (0, *, *, *, 1) were fitted and compared to each other based on model fit (see further). The slope specification for formal home practice that showed the best fit, was then held for all subsequent models that were fitted. In addition, the intercept and slope factors were allowed to covary. Thirdly, the ALT-full model was fitted. This model contained the observed variables of both depressive symptoms and formal home practice. For both variables, an intercept, AR effects, and CL effects were included. Again, a linear slope was estimated for depressive symptoms, while the slope specification that fitted the data best (linear or free) based on previous results from the bivariate LTM models was held for formal home practice. Considering the time frame, see Figure 1, only baseline depressive symptoms was allowed to covary with the intercept and slope factors of both variables (i.e., a predetermined specification) and no time-specific error correlations were estimated (i.e., assumption of 0 correlation). Note that because of the predetermined specification, the intercept factor of depressive symptoms no longer represent an initial baseline value, but resembles the value of the second measurement which is not yet explained by the first measurement point. However, in the remainder, we refer to the intercept as the general level of a construct. To check for possible influences of individuals tapering off their antidepressant medication (tADM) on the results, the bivariate ALT-full model was fitted with and without tADM as predictor for baseline depressive symptoms, and both the intercept and slope of depressive symptoms. In case including tADM led to changes in results and/or significant increases in model fit, it was included as a predictor for all subsequent bivariate ALT models. When including tADM did not result in changes in results and model fit did not significantly improve, subsequent bivariate ALT models were fitted without tADM as predictor. Subsequently, in order to simplify the model, the following restrictions were imposed on the bivariate ALT-full model and it was tested whether these restrictions did not significantly worsened the model fit: (a)
exclude AR and CL effects (ALT-LTM), (b) exclude the variance of the slope (ALT-no slope variance), (c) exclude the slope (ALT-no slope), (d) constrain the AR effects over time to equality, if these effects are still present in the model (ALT-AR constraints), and (e) set CL effects over time equal to each other (ALT-CL constraints). Constraint (a) was applied to both variables simultaneously, whereas constraints (b)-(e) were tested for each variable in turn.

2. Results
For formal home practice, a free slope specification fitted significantly better than a linear slope specification ($\Delta \chi^2 = 1577.09, df = 3, p < .001$) and was therefore held for all subsequent models. In addition, when including tADM as a predictor into the bivariate ALT-full model, results were not affected and a decrease in model fit was found ($\Delta \text{BIC} = 11.125$). Therefore, all subsequent analyses were fitted excluding tADM as a predictor. Results showed that the bivariate ALT-full model had a better model fit compared to the bivariate AR, LTM and ALT-LTM models. The model fit significantly worsened when the slope (variance) of depressive symptoms was removed. Excluding the slope variance of formal home practice was possible without significantly decreasing model fit. However, removing the slope of formal home practice entirely from the model resulted in a clear significant worsening of model fit. Constraining the AR effects of formal home practice over time was possible without significantly decreasing model fit, in contrast to constraining the AR effects over time of depressive symptoms. Cross-lagged effects for both depressive symptoms to formal home practice and vice versa could be constrained over time without this resulting in a significant decrease in model fit. To prevent the intercept variance of formal home practice becoming estimated as negative, as an additional step, this variance was set to 0; this did not result in a significant decrease in model fit.
Added value of Mindfulness-Based Cognitive Therapy for Depression: A Tree-based Qualitative Interaction Analysis
Abstract

**Aim.** To identify moderators of treatment effect for mindfulness-based cognitive therapy (MBCT) versus treatment-as-usual (TAU) in depressed patients.

**Methods.** An individual patient data-analysis was performed on three randomized-controlled trials, investigating the effect of MBCT + TAU versus TAU alone \((n = 292)\). Patients were either in (partial) remission, currently depressed or had chronic, treatment-resistant depression. Outcomes were depressive symptoms and quality of life. The qualitative interaction trees (QUINT) method was used to identify subgroups that benefited more from either condition.

**Results.** MBCT + TAU outperformed TAU in reducing depressive symptoms. For both conditions, the effect of baseline depressive symptoms on post-treatment depressive symptoms was curvilinear. QUINT analyses revealed that MBCT + TAU was more beneficial than TAU for patients with an earlier onset and higher rumination levels in terms of depressive symptom reduction and for patients with a lower quality of life in terms of improving quality of life.

**Conclusions.** The results suggest that MBCT might be more beneficial for those with earlier onset and higher levels of rumination and for patients with a lower quality of life. Sophisticated analytical techniques such as QUINT can be used in future research to improve personalized assignment of MBCT to patients. Long-term outcome could also be integrated in this.
1. Introduction

Major depressive disorder (MDD) is a common and severe psychiatric disorder and a leading cause of disease burden worldwide (World Health Organization [WHO], 2017). Aside from antidepressant medication, numerous psychological interventions have been developed for MDD among which mindfulness-based cognitive therapy (MBCT; Segal et al., 2002).

Mindfulness is defined as the awareness that emerges by purposefully paying attention to the present experiences with a curious, open, accepting, non-judgmental, and friendly attitude (Kabat-zinn, 1994). MBCT consists of 8 weekly group sessions of 2.5hrs and a silent day (Segal et al., 2012). The intervention includes training in mindfulness skills and elements from cognitive therapy for depression (Beck et al., 1979). Originally, MBCT was designed to prevent relapse for recurrently depressed patients who are in (partial) remission, and it has been shown to be effective for this patient group (Kuyken et al., 2016).

Initially, MBCT was not considered suitable for patients with current depression because of the expectation that fully attending to the present moment might be especially difficult in the midst of depressive symptomatology. One might become preoccupied with negative thoughts and difficulties in concentration might impede effectiveness (Baer et al., 2019; Segal et al., 2012; Strauss et al., 2014).

More recently, however, research about the effectiveness of mindfulness-based interventions has started to include currently depressed patients, and results support the feasibility and effectiveness of MBCT in this population (Goldberg et al., 2018; Hedman-Lagerlof et al., 2018; Lenz et al., 2016; Strauss et al., 2014; Wang et al., 2018). Fewer studies have been conducted on the effectiveness of MBCT in patients with chronic or treatment-resistant depression. Some of these revealed that MBCT can be effective in this population too (Barnhofer et al., 2009; Cladder-Micus et al., 2018; Eisendrath et al., 2016; Kenny & Williams, 2007), whereas Michalak et al. (2015) found that MBCT was not more effective than treatment-as-usual (TAU) in reducing depressive symptoms.

Considering the heterogeneity of patients with depression, an improved understanding of what patient characteristics moderate treatment effect could enable improved targeting of MBCT in this population (van der Velden et al., 2015). Several studies of MBCT aimed at preventing depressive relapse/recurrence in remitted patients have shown stronger treatment effects for those with increased vulnerability, including patients with three or more previous major depressive episodes, earlier onset of MDD (Ma & Teasdale, 2004; Teasdale et al., 2000), a history of early adversity (Kuyken et al., 2015; Williams et al., 2014) and more fluctuation in depressive symptoms (Segal et al., 2010). In an individual patient data (IPD) meta-analysis of all existing trials on preventing relapse/recurrence in recurrent depression (n = 258; Kuyken et al., 2016), only higher severity of depression at baseline was associated with a better treatment effect of MBCT.
In currently depressed patients, a few patient characteristics have been suggested to moderate the effect of MBCT. In terms of reduction of depressive symptoms, Lenz et al. (2016) found that older patients benefited more from MBCT. Another study indicated that female gender and low levels of acceptance (or non-judgment) are associated with greater changes in depressive symptoms over the course of MBCT (van Aalderen et al., 2012). With regard to chronically or treatment-resistant depressed patients, higher baseline levels of rumination appeared to predict a larger decrease in depressive symptoms after MBCT (Cladder-Micus et al., 2018).

Taken together, our current knowledge of moderators in the context of MBCT for depression is still limited and in need of more sophisticated examination. At first, most studies investigated homogeneous populations of depressive patients, limiting the range of depressive symptoms at baseline. Therefore, the current study conducted an IPD analysis based on three multicenter randomized-controlled trials (RCTs), including patients with recurrent depression either in (partial) remission and patients with current or chronic and treatment-resistant depression. Secondly, despite promising results of the effect of MBCT on quality of life (Cladder-Micus et al., 2018; Kuyken et al., 2008, 2015), most research into possible moderators has involved the effect of MBCT on risk of relapse and/or level of depressive symptoms. MDD has a huge impact on quality of life (WHO, 2017) and the initial aim of MBCT is not to change or eliminate unpleasant experiences (e.g., negative thoughts or feelings), but rather to relate to them in a different way. Therefore, the current study includes both the level of depressive symptoms as the primary outcome and quality of life as the secondary outcome.

Another issue we would like to raise concerns the statistical approach to moderator analysis, which is in the context of differential treatment efficacy research often called treatment-subgroup analysis. In all aforementioned studies into the effect of MBCT, no distinction is made between quantitative treatment-subgroup interactions (or treatment-covariate interaction) or qualitative treatment-subgroup interactions. The latter type of interactions indicate that for one or more subgroup(s) of patients one treatment (e.g., MBCT) is better than another treatment (e.g., TAU), while for other subgroup(s) the reverse is true. In contrast, quantitative interactions indicate that one treatment is always better than the other but only the strength of the effect differs for subgroups of patients. For optimal treatment assignment in clinical practice, however, quantitative interactions imply that all patients would still be assigned to one and the same treatment. Therefore, to identify for which type of patients MBCT has added value and for which type of patients MBCT is not recommended, qualitative treatment-subgroup interactions are of utmost importance. In addition, most studies into possible moderators of treatment effect assume linear associations. This assumption is not in line with current thinking that the relationships between psychological and physical processes and outcome may run an inverted
U-curve (non-monotonicity) trajectory (Grant & Schwartz, 2011). For example, it has been suggested that depressive symptoms might have an optimum level in which MBCT is effective, above or below this optimum level the effect might be minimal or undesirable effects might occur (Kuyken et al., 2016; van Dam et al., 2018). Furthermore, most studies only consider two-way interaction effects, while maybe, higher order interaction effects may play a role in explaining the variance in treatment efficacy. As a solution, the current study uses a tree-based method, qualitative interaction trees (QUINT; Dusseldorp & van Mechelen, 2014), which focuses on identifying qualitative treatment-subgroup interactions, allows for non-linear relationships and considers higher order interaction effects. The method identifies subgroups of patients in which one treatment is more beneficial than another. It is especially suited for situations with many potential moderating variables that might interact with the treatment variable without clear a priori hypotheses. The result of an analysis with QUINT is a binary tree from which treatment assignment criteria can be derived, relevant for clinical practice.

The current study sought to answer the following questions: (1) For which subgroup(s) is MBCT + TAU more beneficial than TAU alone?; (2) For which subgroup(s) is MBCT + TAU less beneficial than TAU alone? Based on previously discussed research, a non-linear association between baseline levels of depression severity and outcome is expected, more specifically, we expect that patients with moderate levels of depression benefit more from MBCT than those with relatively low or high values (allowing the possibility of worsening of symptoms for those with highest baseline values). The investigation of additional possible moderators is more exploratory of nature. Next to demographic characteristics (age, gender, educational level, employment, marital status), the following baseline clinical characteristics were investigated as possible moderating variables with the use of the QUINT method: number of prior depressive episodes, age of onset, medication use, mindfulness skills, and rumination.

2. Methods

2.1. Design
Data have been drawn from three (multicenter) RCTs that were conducted in the Netherlands, investigating the effect of MBCT + TAU vs. TAU alone for patients with depression. The respective populations consisted of patients with recurrent depression in (partial) remission (RCT-1; Huijbers et al., 2015), patients either in remission or currently depressed (RCT-2; van Aalderen et al., 2012), and patients with chronic, treatment-resistant depression (RCT-3; Cladder-Micus et al., 2018). By including patients with a wide range of baseline depressive symptoms, the differential treatment effect of baseline depressive symptoms could be
investigated more thoroughly. The RCTs were approved by the Medical Ethics Committee Arnhem-Nijmegen for all participating sites and/or the Medical Ethical Committee of local hospitals in Nijmegen, the Netherlands (RCT-1: nr. 2008/242, RCT-2: nr. 2005/284, RCT-3: nr. 2012/339). Written informed consent from all participants was obtained after complete description of the studies and before eligibility was assessed. Demographic and clinical characteristics were obtained at baseline. Primary and secondary outcome measures were assessed at baseline and after the MBCT + TAU or TAU period (8 - 12 weeks). Participants allocated to the TAU condition were offered participation in the MBCT after the intervention or study period. A full description of the methods and procedures can be found in the respective (protocol) papers (RCT-1: Huijbers et al., 2012; RCT-2: van Aalderen et al., 2012; RCT-3: Cladder-Micus et al., 2015). For the flow chart of the current study, see Figure 1.

2.2. Participants
Participants were on average 48.05 years old (SD = 11.70), mainly female (68.4%), married or cohabiting (56.2%) and highly educated (50.4%). About half were unemployed (51.8%). Most participants had already experienced several prior depressive episodes (M = 6.05, SD = 6.56), and had experienced their first MDD at an average age of 25.65 years old (SD = 12.14). More than half of the participants used antidepressant medication (63.9%). A wide range of depressive symptoms was observed on the (converted) Hamilton Rating Scale for Depression (range: 0 - 37; for conversion see 2.5.1), with an average mean score of 12.43 (SD = 8.08). There were no baseline differences in demographic and clinical characteristics between participants allocated in the MBCT + TAU condition versus TAU alone, see Table 1.

2.3. Interventions
2.3.1. MBCT
The MBCT was largely based on the protocol by Segal et al. (2002) with some adaptations based on the most recent version of the MBCT protocol (Segal et al., 2012). The intervention consisted of 8 weekly sessions of 2.5hrs and one day of silent practice of 6hrs between the 5th and 7th session. It was delivered in groups of 8 - 15 participants. MBCT included both formal (e.g., the body scan, sitting meditation, mindful movement) and informal meditation exercises (e.g., bringing present-moment awareness to daily life activities). Cognitive-behavioral techniques included psycho-education, monitoring and scheduling of activities, identification of negative automatic thoughts, and devising a relapse prevention plan. Participants were encouraged to practice meditation at home for 45 - 60 min a day by using CDs or audio files. Participants of all three RCTs were enrolled in mixed groups comprising patients from the trials as well as regular (remitted) depressed patients. MBCT classes of all three RCTs were taught by
experienced mindfulness teachers who all met the teaching criteria described in the MBCT good practice guidelines (UK Network of Mindfulness-Based Teachers, 2015). In addition to MBCT the participants received TAU, as a concurrent intervention.

Figure 1. Flow chart of the current study. Data were derived from three randomized controlled trials (RCTs) of which participants were assigned to mindfulness-based cognitive therapy (MBCT) as an add-on to treatment-as-usual (TAU) or TAU alone. In the analysis of the primary outcome, the sample size was $n = 292$ for intention-to-treat (ITT) and $n = 271$ per-protocol (PP).
Table 1. Baseline demographic and clinical characteristics of participants allocated to mindfulness-based cognitive therapy (MBCT) in addition to treatment-as-usual (TAU) versus TAU alone: means (SD) and frequencies (%)

<table>
<thead>
<tr>
<th>Variable</th>
<th>MBCT + TAU (n = 193)</th>
<th>TAU (n = 200)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (in years)</td>
<td>48.05 (11.64)</td>
<td>48.05 (11.78)</td>
<td>t(391) &lt; -0.01, p = .99</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>( \chi^2(1) = 0.04, p = .85 )</td>
</tr>
<tr>
<td>Male</td>
<td>60 (31.1%)</td>
<td>64 (32.0%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>133 (68.9%)</td>
<td>136 (68.0%)</td>
<td></td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td>( \chi^2(2) = 4.00, p = .14 )</td>
</tr>
<tr>
<td>Low</td>
<td>24 (12.5%)</td>
<td>30 (15.0%)</td>
<td></td>
</tr>
<tr>
<td>Middle</td>
<td>52 (26.9%)</td>
<td>68 (34.0%)</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>107 (55.4%)</td>
<td>91 (45.5%)</td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td>( \chi^2(2) = 0.14, p = .93 )</td>
</tr>
<tr>
<td>Single</td>
<td>41 (21.2%)</td>
<td>45 (22.5%)</td>
<td></td>
</tr>
<tr>
<td>Married/cohabiting</td>
<td>108 (56.0%)</td>
<td>113 (56.5%)</td>
<td></td>
</tr>
<tr>
<td>Divorced/widowed</td>
<td>29 (15.0%)</td>
<td>28 (14.0%)</td>
<td></td>
</tr>
<tr>
<td>Employment</td>
<td></td>
<td></td>
<td>( \chi^2(1) = 2.67, p = .10 )</td>
</tr>
<tr>
<td>Yes</td>
<td>91 (47.1%)</td>
<td>80 (40.0%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>82 (42.9%)</td>
<td>102 (51.0%)</td>
<td></td>
</tr>
<tr>
<td>Age of onset</td>
<td>25.70 (11.98)</td>
<td>25.61 (12.32)</td>
<td>( t(363) = -0.07, p = .94 )</td>
</tr>
<tr>
<td>Prior depressive episodes</td>
<td>6.29 (7.45)</td>
<td>5.81 (5.58)</td>
<td>( t(367) = -0.71, p = .48 )</td>
</tr>
<tr>
<td>Medication use</td>
<td></td>
<td></td>
<td>( \chi^2(1) = 0.04, p = .84 )</td>
</tr>
<tr>
<td>Yes</td>
<td>125 (64.8%)</td>
<td>126 (63.0%)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>52 (26.9%)</td>
<td>55 (27.5%)</td>
<td></td>
</tr>
<tr>
<td>Depressive symptoms (^a)</td>
<td>12.26 (7.91)</td>
<td>12.59 (8.26)</td>
<td>( t(390) = -0.39, p = .69 )</td>
</tr>
<tr>
<td>Quality of life (^b)</td>
<td>46.56 (16.50)</td>
<td>45.11 (17.98)</td>
<td>( t(346) = -0.79, p = .43 )</td>
</tr>
<tr>
<td>Mindfulness (^c)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Observing</td>
<td>22.34 (5.78)</td>
<td>21.73 (5.79)</td>
<td>( t(377) = -1.03, p = .31 )</td>
</tr>
<tr>
<td>Describing</td>
<td>25.53 (7.76)</td>
<td>25.36 (7.00)</td>
<td>( t(377) = -0.22, p = .83 )</td>
</tr>
<tr>
<td>Non-judging</td>
<td>25.38 (6.91)</td>
<td>224.93 (7.19)</td>
<td>( t(377) = -0.63, p = .53 )</td>
</tr>
<tr>
<td>Rumination (^d)</td>
<td>12.37 (3.01)</td>
<td>12.61 (3.21)</td>
<td>( t(377) = -0.75, p = .46 )</td>
</tr>
</tbody>
</table>

Note. MBCT = mindfulness-based cognitive therapy; TAU = treatment-as-usual. \(^a\) (Transformed) Hamilton rating scale for depression (HRSD-17, Hamilton, 1960; Rush et al., 2003; Trivedi et al., 2004). \(^b\) Psychological domain of the World Health Organization quality of Life, short version (WHOQoL-BREF, The WHOQOL Group, 1998). \(^c\) Five facets mindfulness questionnaire (FFMQ, Baer et al., 2006) or computed from the Kentucky inventory of mindfulness skills with person mean imputation (KIMS, Baer et al., 2004). \(^d\) Brooding scale of the ruminative response scale, extended version (RRS-NL-EXT, Raes et al., 2007) or computed from the ruminative response scale (RRS-NL, Raes et al., 2003) with person mean imputation. Due to missing values the degrees of freedom differ between the analyses.
2.3.2. TAU
Those who were in the TAU condition were encouraged to continue their baseline treatment for the study period. This could include maintenance of antidepressant medication, psychological treatment, support by a psychiatric nurse, or day-hospital treatment.

2.4. Measuring instruments

2.4.1. Primary outcome
Depressive symptoms. In RCT-1 depressive symptoms were assessed by the Hamilton Rating Scale for Depression (HRSD-17; Bech et al., 1986; Hamilton, 1960). The HRSD-17 is a semi-structured 17-item interview designed to assess depressive symptoms over the previous week on a 0 - 52 score range. It has good psychometric properties (Bagby et al., 2004; Morriss et al., 2008). In RCT-2 the Inventory of Depressive Symptomatology - Clinician rated (IDS-C30; Akkerhuis, 1997) was used. The IDS-C30 consists of 30 multiple choice 4-point Likert scale questions assessing depressive symptoms over the last 7 days. The IDSC30 is scored by summing responses of 28 out of 30 items to obtain a total score ranging from 0 to 84 (Rush et al., 1996). The internal consistency and inter-rater reliability of the IDS-C30 have been shown to be adequate, also among individuals with current depression (α range: .76 - .82; Rush et al., 1996; Trivedi et al., 2004). In RCT-3 depressive symptoms were measured with the self-report version of the IDS, which has shown good psychometric properties (IDS-SR; Rush et al., 1996). The HRSD-17, IDS-C and IDS-SR are sensitive to symptom change and highly correlated, indicating high concurrent validity (Geschwind et al., 2012; Rush et al., 1996, 2003; Trivedi et al., 2004).

2.4.2. Secondary outcome
Quality of life. In all three RCTs, perceived quality of life, rated on a 5-point Likert scale in relation to the past two weeks, was assessed using the self-report 26-item World Health Organization Quality of Life scale (WHOQOL-Bref; de Vries & van Heck, 1996). This questionnaire represents four domains: Physical health, Psychological, Social relationships and Environment. The WHOQOL-Bref has good to excellent psychometric properties of reliability and has shown to be a cross-culturally valid assessment of quality of life (Skevington et al., 2004). Psychometric properties tested in a sample of Dutch psychiatric outpatients were good (Trompenaars et al., 2005).

2.4.3. Moderator variables
Mindfulness. In RCT-1, baseline mindfulness was measured with the Kentucky Inventory of Mindfulness (KIMS; Baer et al., 2004). This is a 39-item, 5-point Likert scale, self-report questionnaire, developed to measure mindfulness skills in four domains: Observe (12 items), describe (8 items), Act with Awareness
(10 items), and Accept without Judgment (9 items). The KIMS has good psychometric properties (Baum et al., 2010). In RCT-2 and RCT-3 mindfulness skills were measured with the Five Facet Mindfulness Questionnaire (FFMQ; Baer et al., 2006). This instrument is based on a factor analytic study of five independently developed mindfulness questionnaires (one of which is the KIMS). The FFMQ is a 39-item, 5-point Likert scale, self-report questionnaire, which covers five domains: Observing (8 items), Describing (8 items), Acting with awareness (8 items), Non-judging of inner experience (8 items) and Non-reactivity to inner experience (7 items). The psychometric properties of the Dutch FFMQ are reliable (α range: .73 - .91) and valid for use in adults with clinically relevant symptoms of depression (Bohlmeijer et al., 2011).

**Rumination.** In RCT-2, rumination was measured with the Ruminative Response Scale (RRS-NL; Raes et al., 2003). This questionnaire contains 22 4-point Likert scale items, describing responses to depressed mood that are self-focused, symptom-focused, and focused on the possible causes and consequences of dysphoric mood. In RCT-1 and RCT-3 the extended version was used (RRS-NLEXT; Raes & Hermans, 2007). This questionnaire contains 26 4-point Likert scale items and has an adequate reliability and good validity (Raes et al., 2009). It enables a distinction between ‘reflection’ (5 items) and ‘brooding’ (5 items). The brooding subscale refers to a more maladaptive way of thinking about depression and contains items like “Why do I always react this way?” and “What am I doing to deserve this?” (Schoofs et al., 2010).

### 2.5. Data management

Inconsistencies in measuring instruments were handled as described below.

#### 2.5.1. Primary outcome

**Depressive symptoms.** Per study, total scores on depressive symptoms (HRSD-17, IDS-C, or IDS-SR) were calculated when a patient scored at least 60% of the corresponding items. In case of missing values on the remaining 40% of the items, person mean imputation was applied. Subsequently, scores on the IDS-C and IDS-SR were converted into HRSD-17 values to obtain one measure for depressive symptoms across studies. We refer to this converted measure as HRSD-C. The converter table used can be found in the Inventory of Depressive Symptomatology manual (IDS-QIDS, 2019) and is based on previous psychometric research on these questionnaires in depressed patients by Rush et al. (2003) and Trivedi et al. (2004).

#### 2.5.2. Secondary outcome

**Quality of Life.** The psychological domain of the WHOQOL-Bref was used, which covers the following themes: bodily image and appearance, negative and positive feelings, self-esteem, spiritual/religion/personal beliefs, thinking,
learning, memory and concentration. Scores of the domain were calculated based on the WHOQOL-Bref Manual (The WHOQOL Group, 1996). This includes allowing missing data on 1 item and applying person mean imputation when necessary. We refer to this outcome as QOL-PSY.

2.5.3. Moderator variables
Gender (male/female), age (in years), age of onset (in years), number of prior depressive episodes and medication use at baseline (yes/no) were assessed in the same manner across all participants. For other categorical baseline characteristics the least number of categories used across the three studies was maintained: marital status was brought back to three categories (single/married or cohabiting/divorced or widowed), employment to two categories (yes/no), and level of education to three categories (low/middle/high; Centraal Bureau voor de Statistiek, 2017).

Mindfulness. The FFMQ was used as a starting point, because this instrument is developed more recently. Given the fact that the FFMQ includes the subscale ‘Nonreactivity to inner experiences’, which is not included in the KIMS, it was decided to not use the total score for mindfulness in the current study. Data on three of the remaining FFMQ subscales (‘Observing’, ‘Describing’, and ‘Non-judging of inner experiences’) were calculated when a patient scored at least 60% of the corresponding items. In case of missing values on the remaining 40% of the items, person mean imputation was applied. For patients who scored the items of the KIMS, the same rule was applied (using the overlapping items and treating the non-overlapping items as missing). Only 3 of the 10 items of the FFMQ subscale ‘Acting with awareness’ overlapped with the KIMS, therefore, this subscale was excluded from the analyses in the current study.

Rumination. The brooding scale of the RRS-NL-EXT (Raes & Hermans, 2007) was used to measure rumination in RCT-1 and RCT-3. This subscale contains 5 items. The RRS-NL (Raes et al., 2003), which was used in RCT-2, contains 3 of these 5 items and these were used to calculate the brooding subscale. Again, at least 60% of the brooding scale items (≥ 3 from 5) needed to be present per patient and when necessary, person mean imputation was applied.

2.6. Statistical analysis
Firstly, to compare whether the group of participants included in the analyses was different from the group not included, see Figure 1, with regard to the baseline characteristics and outcome variables, chi-square tests and independent t-tests were performed. Secondly, to test the hypothesis whether MBCT added to TAU was especially beneficial for those with a moderate amount of depressive symptoms, a moderated curvilinear regression analysis was performed. Thirdly, to identify subgroups that differed in the treatment efficacy, QUINT was performed. Below, the details of the latter two analyses are explained.
2.6.1. Confirmatory moderated regression analysis
As outcome variable post-treatment HRSD-C was used. As predictor variables, the condition variable, baseline HRSD-C, and all other baseline characteristics were included. In addition, a quadratic term of baseline HRSD-C was added. Before computing the quadratic term, baseline HRSD-C was centered. Finally, in a second block, the product terms of condition with baseline HRSD-C and of condition with squared baseline HRSD-C were included in the regression analysis. A significant change in multiple R2 indicates whether the curvilinear effect of baseline HRSD-C is different for the two conditions. If so, probing of the interaction terms was used to investigate at which level(s) of baseline HRSD-C the conditions differed. If not, the analysis was performed again without including the interaction terms, as recommended by Hayes (2018).

2.6.2. Exploratory moderator analysis by QUINT
QUINT is a nonparametric tree-based subgroup identification method, appropriate for data from randomized controlled trials involving two experimental conditions. The aim of QUINT is to induce subgroups of patients, defined in terms of baseline characteristics that are involved in qualitative treatment-subgroup interactions. The result of an analysis with QUINT is a binary tree from which treatment assignment criteria can be derived. Therefore, it is recommended that all moderator variables included in the analyses are measured at baseline. QUINT assumes that the outcome variable is measured at interval level and has no further a priori assumptions about the measurement levels of the moderator variables or about the distributions of the variables. Because of the data-driven nature of QUINT, it should be regarded as an exploratory and hypothesis generating method (Breiman, 2001). Examples of applications of QUINT can be found in the field of clinical psychology (Doove et al., 2016), and social and organizational psychology (Formanoy et al., 2016). Before the analysis, the user needs to choose among several options to fit the tree (Dusseldorp et al., 2016). To fit the tree, the effect size criterion or the difference in means criterion may be used. Because the scale of the primary outcome variable, the Hamilton scale, is interpretable (e.g., a 5-points difference between groups has clinical meaning; Leucht et al., 2013), we chose the difference in means criterion. To prune the tree, in order to avoid overfitting, we decided the number of bootstrap samples to be 200 as recommended by (Dusseldorp et al., 2016). Because our total sample size in the analysis was about 300, the absolute value of dmin (i.e., the minimum value of the effect size in one of the green leaves assigned to P1, and in one of the red leaves assigned to P2, see for example Figure 3) was set at a higher value (0.40) than the default (0.30). In this way, the risk of finding spurious subgroups was reduced (i.e., the Type I error rate was acceptable; see Dusseldorp & van Mechelen, 2014). For the remaining options, the default values were used.
QUINT was performed separately for both outcome variables. For depressive symptoms, the change in HRSD-C was used as outcome, that is, the post-treatment HRSD was subtracted from baseline HRSD-C to assure that a higher score means more improvement (i.e., a higher decrease in HRSD-C from baseline to post-treatment). For quality of live, the change in QOL-PSY was computed by subtracting baseline QOL-PSY from post-treatment QOL-PSY. As possible moderators, all baseline characteristics and the baseline levels of outcome measure were included in the analysis.

In the leaves of the pruned tree that resulted from the QUINT analyses, we performed independent t-tests to inspect whether mean differences between the treatment groups were significant. It should be noted that the significance level of these t-tests is somewhat inflated, due to the data-induced subgroups.

2.6.3. Intention to treat and per protocol
In addition to intention-to-treat (ITT) analyses, per-protocol (PP) analyses were performed. Consistent with trials to date (Kuyken et al., 2010; Teasdale et al., 2000), an adequate dose of MBCT was defined as participation in at least 4 MBCT sessions. This minimum of attended MBCT sessions was applied to participants who were randomized to MBCT + TAU. A restriction of 0 MBCT sessions was imposed on participants randomized to TAU alone. See Figure 1 for the number of participants who adhered to the protocol in each condition.

2.6.4. Computational note
As significance level, we used a two-sided alpha level of .050. All analyses were performed in SPSS version 25 (IBM Corporation, 2017), except for the QUINT analyses. The latter were performed using the R package quint version 2.0 (Dusseldorp et al., 2018) in the R software environment.

3. Results
Of the available 393 participants, 101 were excluded from the analyses due to missing values, see Figure 1. The excluded participants did not differ significantly on any of the baseline characteristics and analyses. One hundred forty-two (74%) of the 193 participants in the MBCT + TAU condition remained in the analyses, compared to 150 (75%) of the 200 participants in the TAU condition. This difference was not significant ($\chi^2(1, n = 393) = .10, p = .75$). The average HRSD-C of the participants in the MBCT + TAU condition declined from 11.70 ($SD = 7.96$) at baseline to 9.62 ($SD = 7.57$) at post-treatment ($t(141) = -4.67, p < .001$). In contrast, the HRSD-C of the participants in the TAU condition stayed about the same, 12.87 ($SD = 8.53$) at baseline and 12.70 ($SD = 8.38$) at post-treatment ($t(149) = -0.39, p = .70$). The difference in change of HRSD-C between the
conditions was significant \( t(290) = -3.03, p < .01 \) indicating that overall MBCT + TAU was effective on depressive symptoms. The average QOLPSY of the participants in the MBCT + TAU condition improved from 46.49 (SD = 16.26) at baseline to 53.47 (SD = 16.18) at post-treatment \( t(129) = 6.11, p < .001 \). Also, the average QOL-PSY of the participants in the TAU condition improved from 45.20 (SD = 18.25) at baseline to 49.71 (SD = 19.10) at post-treatment \( t(131) = 3.87, p < .001 \). The difference in increase of QOL-PSY between the conditions was not significant \( t(290) = 1.52, p = .13 \), indicating that overall MBCT + TAU was not effective on quality of life.

3.1. Results confirmatory moderated regression analysis
The addition of the interaction terms of condition*baseline HRSD-C and condition*baseline HRSD-C\(^2\) was not significant in the moderated curvilinear regression analysis of post-treatment HRSD-C \( \Delta R^2 = .003, F(2, 272) = 1.24, p = .29 \). This means that the linear and quadratic effect of baseline HRSD-C did not moderate the effect of condition on post-treatment HRSD-C. Therefore, the regression analysis was repeated without the interaction terms. The result showed that both the linear and quadratic effect of HRSD-C at baseline were significant (respectively, \( b = 0.64, t(274) = 14.48, p < .01 \), and \( b = 0.01, t(274) = 2.82, p < .01 \), see Table 2). This tells us that the curvilinear effect of baseline HRSD-C is present, but it is the same for both conditions. Especially patients with a mild to severe level of baseline HRSD-C (between 9 and 21) show a lower level of post-treatment HRSD-C, see Figure 2. The effect of condition was significant \( (b = - 2.11, t(274) = - 3.61, p < .01) \), which means that on average the MBCT + TAU condition scored - 2.11 lower on post-treatment HRSD-C adjusted for the effects of all other variables. None of the other baseline characteristics showed a significant effect on post-treatment HRSD-C.

3.2. Intention-to-treat results by QUINT
3.2.1. Primary outcome: depressive symptoms
The ITT analysis by QUINT resulted in a pruned tree with seven leaves, see Figure 3. Each leaf indicates a subgroup of patients. In three of these leaves (leaves 2, 4, and 5) MBCT + TAU was effective compared to TAU alone; these subgroups are shown in green. The difference between the conditions in mean improvement was significant in each of these subgroups, see Table 2. Furthermore, the corresponding effect sizes (Cohen’s d) were high (i.e., > 0.80). QUINT also identified subgroups for which TAU alone was effective compared to MBCT + TAU; these are shown in red, see Figure 3. However, in each of these subgroups the difference between the conditions in mean improvement was not significant, see Table 2. The branches of the tree identify the characteristics of the patients in the subgroups. We focus here on the subgroups that showed a significant treatment outcome difference. Patients with a lower age of onset (≤ 30.5) and higher baseline
levels of brooding at baseline (RRS-brooding > 14.5) who received MBCT + TAU showed a larger improvement in HRSD-C (6.2 points larger) than the same type of patients who received TAU alone (leaf 5). In addition, patients with a “medium” age of onset (between 15 and 30), a lower level of brooding (≤ 14.5), and a higher level of depressive symptoms at baseline (HRSD-C > 12.5) who received MBCT + TAU showed a larger improvement in HRSD-C (5.1 points larger) than the same type of patients who received TAU alone (leaf 4). Finally, patients with a medium age of onset (between 15 and 30), lower levels of both brooding (≤ 14.5), and depressive symptoms at baseline (HRSD-C < 4.5) showed less deterioration in HRDS-C after MBCT + TAU (- 0.1 points) than after TAU alone (- 3.9 points; leaf 2, see Table 2).

### 3.2.2. Secondary outcome: psychological subscale of quality of life

The ITT QUINT analysis for QOL-PSY resulted in a pruned tree with seven subgroups, see Figure 4. In two of these subgroups (leaves 2 and 7), MBCT + TAU was effective compared to TAU alone whereas in two subgroups the reverse was true: TAU alone was more effective than MBCT + TAU (leaves 1 and 3). In the subgroups of patients for whom MBCT + TAU was more beneficial, the difference in mean change score was significant, see Table 3. The corresponding effect sizes were high (> 0.80). One of the subgroups of patients for whom TAU alone was better than MBCT + TAU, showed a significant difference in mean change score (leaf 3). The corresponding effect size was high (> |0.80|). In the

<table>
<thead>
<tr>
<th>MBCT + TAU</th>
<th>TAU</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Leaf 1</td>
<td>25</td>
<td>1.18</td>
</tr>
<tr>
<td>Leaf 2</td>
<td>15</td>
<td>-0.13</td>
</tr>
<tr>
<td>Leaf 3</td>
<td>15</td>
<td>1.73</td>
</tr>
<tr>
<td>Leaf 4</td>
<td>18</td>
<td>4.97</td>
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<tr>
<td>Leaf 5</td>
<td>30</td>
<td>4.57</td>
</tr>
<tr>
<td>Leaf 6</td>
<td>22</td>
<td>1.77</td>
</tr>
<tr>
<td>Leaf 7</td>
<td>17</td>
<td>-1.35</td>
</tr>
</tbody>
</table>

Note. Dif. = difference in mean change scores (baseline HRSD-C minus post-treatment HRSD-C) between conditions; CI = confidence interval; LB = lower bound; UB = upper bound; d = Cohen’s d. * p < .05. ** p < .01 *** p < .001.
remaining subgroups (leaves 4, 5, and 6), there was no difference in response to the two interventions. Patients with a lower baseline QOL-PSY ($\leq 27.08$) who received MBCT + TAU showed a larger improvement in QOL-PSY (15.9 points) than the same type of patients who received TAU alone (leaf 2, Table 3). The characterization of the other two subgroups with a significant difference in treatment outcome (leaves 3 and 7) is more complex: they consist of combinations of splits on four different splitting variables (i.e., age of onset, baseline QOL-PSY, age, and either FFMQ-non-judging or FFMQ-observing).

Figure 2. Curvilinear effect of baseline depressive symptoms on post-treatment depressive symptoms, fitted separately for mindfulness-based cognitive therapy as an add-on to treatment-as-usual (MBCT + TAU, red solid line) and for TAU alone (grey solid line). As reference, the linear effects are displayed as dotted lines. The lines for MBCT + TAU are lower than those of TAU, suggesting a treatment main effect. The curves are about parallel, suggesting no interaction effect.
Figure 3. Result of QUINT analysis with improvement in depressive symptoms (baseline HRSD-C minus post-treatment HRSD-C) as outcome using the intention-to-treat sample. In the green leaves (P1), MBCT + TAU is more beneficial than TAU alone; for the red leaves (P2) the reverse is true. In the grey leaves (P3), there is no difference between the interventions.
Figure 4. Result of QUINT analysis with improvement in quality-of-life (post-treatment QOL-PSY minus baseline QOL-PSY) as outcome using the intention-to-treat sample. In the green leaves (P1), MBCT + TAU is more beneficial than TAU alone; for the red leaves (P2) the reverse is true. In the grey leaves (P3), there is no difference between the interventions.
3.3. Per-protocol results by QUINT

3.3.1. Primary outcome: depressive symptoms

The PP analysis by QUINT resulted in a pruned tree with 6 leaves (see Appendix A, Figure A1). The first, third and fourth split of this tree (i.e., on the variables age of onset, RRS-brooding, and again on age of onset) were exactly the same as in the ITT tree, see Figure 3. In the subgroups of patients for whom MBCT + TAU was more beneficial (leaves 3 and 4, see Figure A1), the difference in mean change score was significant, see Table A1. In the other four subgroups the difference in mean change score between the conditions was not significant, see Table A1. The characteristics of the patients in leaf 4 were the same as those in leaf 5 of the ITT analysis: patients with an earlier onset (≤ 30.5) and a higher level of brooding at baseline (RRS-brooding > 14.5) who received MBCT + TAU showed a larger improvement in HRSD-C (6.5 points) than the same type of patients who received TAU alone.

3.3.2. Secondary outcome: psychological subscale of quality of life

The PP analysis by QUINT for the secondary outcome resulted in a pruned tree with 6 leaves, see Appendix A, Figure A2. The first and second split of this tree (i.e., on the variables baseline QOL-PSY and age) corresponded to the second and third split of the ITT tree, see Figure 4. In the subgroups of patients for whom MBCT + TAU was more beneficial (leaves 1 and 6; see Figure A2), the difference in mean change score was significant, see Table A2. Also, in the

**Table 3.** Descriptive statistics in the leaves of the QUINT results (Figure 4) for QOL-PSY using the intention-to-treat sample. The mean values and standard deviations (SD) on improvement in QOL-PSY are displayed. A higher score means more improvement.

<table>
<thead>
<tr>
<th></th>
<th>MBCT + TAU</th>
<th>TAU</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Leaf 1</td>
<td>18</td>
<td>4.54</td>
<td>14.56</td>
</tr>
<tr>
<td>Leaf 2</td>
<td>16</td>
<td>19.53</td>
<td>17.66</td>
</tr>
<tr>
<td>Leaf 3</td>
<td>19</td>
<td>4.65</td>
<td>10.59</td>
</tr>
<tr>
<td>Leaf 4</td>
<td>20</td>
<td>5.63</td>
<td>9.77</td>
</tr>
<tr>
<td>Leaf 5</td>
<td>21</td>
<td>4.96</td>
<td>12.26</td>
</tr>
<tr>
<td>Leaf 6</td>
<td>19</td>
<td>3.95</td>
<td>10.80</td>
</tr>
<tr>
<td>Leaf 7</td>
<td>18</td>
<td>7.18</td>
<td>10.09</td>
</tr>
</tbody>
</table>

Note. Dif. = difference in mean change scores (post-treatment QOL-PSY minus baseline QOL-PSY) between conditions; CI = confidence interval; LB = lower bound; UB = upper bound; d = Cohen’s d. *p < .05. **p < .01.
subgroup of patients for whom TAU alone was more beneficial (leaf 3), the difference in mean change score was significant, see Table A2. The characteristics of the patients in leaf 1 were the same as those in leaf 2 of the ITT analysis: patients with a lower baseline QOL-PSY (≤ 27.1) who received MBCT + TAU showed a larger improvement in QOL-PSY (17.5 points) than the same type of patients who received TAU alone (Table A2).

4. Discussion

The current study aimed to identify moderators of treatment effect for MBCT + TAU versus TAU alone, in patients with depression. An IPD analysis was performed (n = 292), including patients with recurrent depression in (partial) remission, currently depressed and chronically or treatment-resistant depressed. Overall efficacy results showed that MBCT + TAU outperformed TAU alone in decreasing depressive symptoms from baseline to post-treatment. Furthermore, all patients (irrespective of condition) with mild to severe baseline levels of depressive symptoms, showed a stronger decrease in depressive symptoms compared to patients with none to very mild or very severe baseline levels of depressive symptoms. Qualitative interaction sub-group analyses revealed that MBCT + TAU might be more beneficial than TAU alone for patients with earlier onset and higher baseline levels of rumination and for patients with a lower baseline quality of life.

4.1. Depression

Overall, MBCT + TAU outperformed TAU alone, which is in line with literature to date for recurrently depressed patients in (partial) remission (Kuyken et al., 2016), those who are currently depressed (Goldberg et al., 2018; Hedman-Lagerlof et al., 2018; Lenz et al., 2016), and patients with chronic or treatment-resistant depression (Barnhofer et al., 2009). To our knowledge, this is the first study that examined a possible curvilinear association of baseline depressive symptoms on post-treatment depressive symptoms. As expected, patients with very mild and very severe baseline depressive symptoms appeared to have a smaller reduction of depressive symptoms than patients with mild to severe levels of baseline depressive symptoms (inverted U-curve). This is in line with recent suggestions that psychological processes and outcome may run an inverted U-curve trajectory (Grant & Schwartz, 2011).

However, baseline depressive symptoms did not moderate the intervention effect. This contradicts the idea that adding MBCT to TAU could cause harm in patients with severe depression as lately has been proposed (van Dam et al., 2018). Although the current study included patients with a wide range of baseline depressive symptoms, it should be noted that extremely severe
depressed patients (≥ 37 points on the HRSD), were not included in the current study. For this specific patient group, no statements can be made about whether MBCT for depression can be of added value or has a possible counterproductive effect. The current findings also seem to be in contrast with the results of the IPD meta-analysis by Kuyken et al. (2016), who found that severity of baseline depressive symptoms predicted a better response to MBCT in terms of prevention of relapse. In their study, only recurrently depressed patients (partial) in remission were included, restricting the range of baseline depression severity, which might be in line with the upward slope of the inverted U-curve (Britton, 2019). Besides, Kuyken et al. (2016) performed linear regression analyses including condition, baseline depressive symptoms and their interaction, while not allowing a possible non-linear trajectory of baseline depression severity which could have led to finding a spurious moderating effect (Lubinski & Humphreys, 1990).

Results from the qualitative interaction trees (QUINT) analysis on depression outcome revealed that for several subgroups MBCT + TAU appeared to be more beneficial than TAU alone. Especially for those with an earlier onset (≤ 30.5 years) and higher baseline levels of rumination (> 14.5). This subgroup was found in both the ITT and PP analysis. This is in line with the theoretical underpinnings of MBCT. In MBCT, patients learn to recognize automatic activation of their habitual dysfunctional cognitive processes that lead to depression, e.g., rumination, and decenter and disengage from these dysfunctional processes. The underlying theoretical model is called the ‘differential activation hypothesis’ (Teasdale, 1988) which assumes that vulnerability to depression increases with each depressive episode, because previous patterns of negative thoughts become easier accessible when feeling low. In line with the current finding, Ma and Teasdale (2004) found in recurrently depressed patients in remission that patients with an earlier onset had stronger benefits of MBCT in terms of preventing depressive relapse/recurrence. However, this was not confirmed by the research by Kuyken et al. (2016).

The QUINT analysis did not reveal clear evidence of subgroups for whom TAU alone was more beneficial than additional MBCT. This points into the direction that, in general, the addition of MBCT to TAU does not lead to worsening of depressive symptoms. No clear moderating effects were found for age, gender, educational level and marital status, employment, number of prior depressive episodes, and medication use.

### 4.2. Quality of life

To our knowledge, this is the first study that investigated qualitative treatment-subgroup interactions with an increase in quality of life as outcome measure. Results from the QUINT analysis showed that for patients with relatively lower scores on quality of life at baseline (≤ 27.08), the addition of MBCT to TAU is more beneficial than TAU alone. This effect was found in both
the ITT and PP analysis. In addition, MBCT + TAU was also more beneficial than TAU alone for patients with an age of onset of 13.5 years or older, relatively higher baseline quality of life (> 27.08), who were > 53.5 years old, and scored relatively high on the mindfulness skill ‘Observing’ (> 23.5). One very specific subgroup of patients was identified in which TAU seemed to outperform MBCT + TAU, namely patients with an age of onset during adolescence (between 13.5 and 22.5 years), with relatively higher baseline levels of quality of life (> 27.08), age of 53.5 years or younger, who score 27.21 or lower on the mindfulness skill ‘Non-judging of inner experience’. This seems less practical to implement in clinical practice but nevertheless gives a clear direction of which variables to further investigate in future research. These results encourage similar research in different populations to further investigate age of onset, baseline quality of life, age, and separate facets of mindfulness as possible moderating variables in terms of treatment effect on quality of life in MBCT for depression. No moderating effects were found for gender, educational level, marital status, employment, number of prior depressive episodes, medication use, and baseline levels rumination.

4.3. Strengths
The analytical technique used in the current study is clearly an advantage to investigate which subgroups benefit more from which type of intervention, which is very important in optimizing treatment assignment. Being a data-driven subgroup identification method, there is a risk of overfitting the data (i.e., fitting a tree that is too large and in this way finding spurious subgroups). However, by applying a pruning procedure based on bias-corrected bootstrapping QUINT controls this risk (Lipkovich et al., 2017). This procedure uses resampling with replacement of patients in the original sample and estimates the amount of optimism in the partitioning criterion using the bootstrap samples as training data and the original sample as test data. In this way, bootstrapping is combined with cross-validation, which is recommended as a model validation method not only in tree-based models (LeBlanc & Crowley, 1993) but in any multivariable prognostic model (Harrell et al., 1996). In addition, QUINT allows the user to control the Type I error rate by specifying the minimum value of the effect size in a leaf. QUINT yields output with possible treatment assignment criteria, which makes it highly suitable for generating hypotheses about which patient characteristics to consider in future research and which patient characteristics possibly matter for clinical practice.

Second, the current study is highly ecologically valid, which contributes to the generalization to secondary and tertiary care in depressed patients. Data were derived from three multicenter RCTs with few exclusion criteria. In addition, patients were treated in routine clinical care where they received MBCT in mixed groups comprising both research participants and clinical patients.
Third, the current study analyzed data from a wide range of depressed patients, from fully remitted to chronic and treatment-resistant depression. This led to a more adequately powered investigation of the possible moderating effect of baseline depressive symptoms on treatment outcome.

Fourth, different facets of mindfulness were included as possible moderators for treatment outcome, which is in line with recent suggestions that each mindfulness skill might influence treatment outcome in its own way (Eisenlohr-Moul et al., 2012).

4.4. Limitations

Of course, the current study is not without limitations. First, the three RCTs used different measurement instruments to assess depressive symptoms. The three resulting scales had to be converted to a common metric using a converter table. As a conversion table always introduces some error, we would ideally have used the same measurement instrument in each study. However, the converter table used is based on previous psychometric research on the same three scales in large samples \((n = 596 - 946)\) in patients with depressive disorders (Rush et al., 2003; Trivedi et al., 2004). It was found that these scales were equally sensitive to symptom change indicating high concurrent validity.

Second, it is important to acknowledge that the effects in the subgroups found by a data-driven method are overestimated (Lipkovich et al., 2017). Therefore, the current study used a particularly conservative approach by also performing independent \(t\)-tests within the subgroups to inspect whether mean differences between the treatment groups were significant. However, the significance level of such a test is somewhat inflated due to the data-induced subgroups. QUINT has a double bootstrapping method to obtain honest estimates for the effect sizes in the subgroups, but this procedure is yet restricted to the two extreme leaves only (Dusseldorp & van Mechelen, 2014, Supplementary Material). A better option for inference in the leaves of the tree would be to estimate confidence intervals around the treatment outcome difference using a bootstrap procedure such as Loh et al. (2015) but this procedure still needs to be developed for QUINT.

Third, a problem not specific to this study, is that most tree-based algorithms have the (slight) tendency to prefer variables with more possible split points (e.g., continuous variables and categorical variables with many categories; Hothorn et al., 2006). Even though it is likely that the categorical variables included in the current study did not moderate the intervention effect (i.e., gender, employment, medication use, educational level, and marital status), this cannot be ruled out entirely.

Finally, due to missing data on at least one of the investigated variables, the analyses were finally conducted among 292 patients, while the recommended sample size for QUINT is higher \((n \geq 400;\) Dusseldorp & van Mechelen, 2014).
However, this problem was highly diminished by a priori adjustment of a control parameter used in the analysis (i.e., increasing the minimum required value of the effect size in a leaf dmin).

4.5. Conclusions and implications
This study aimed to identify moderators of treatment effect for MBCT versus TAU in depressed patients by using the QUINT method. Particularly patients with an earlier onset and higher rumination levels and patients with a lower quality of life seemed to benefit more from the addition of MBCT to TAU than TAU alone. This is a first step to improve personalized assignment of MBCT for depressed patients. Before definite treatment assignment criteria can be formulated and implemented in clinical practice, the current findings should be replicated, treatment outcome of the leaf nodes of the trees should be estimated in an independent test dataset and, preferably, also long-term outcomes should be included in future research.
References


cognitive therapy compared with maintenance antidepressant treatment in the prevention of depressive relapse or recurrence (PREVENT): A randomised controlled trial. The Lancet, 386(9988), 63-73. https://doi.org/10.1016/S0140-6736(14)62222-4


**Supplementary Material – Appendix A**

*Per-protocol (PP) QUINT analyses*

### Table A.1. Descriptive statistics in the leaves of the QUINT results for HRSD-C (Figure A.1) using the per-protocol sample. The mean values and standard deviations (SD) on improvement in HRSD-C are displayed. A higher score means more improvement.

<table>
<thead>
<tr>
<th>MBCT + TAU</th>
<th>TAU</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Leaf 1</td>
<td>22</td>
<td>1.16</td>
</tr>
<tr>
<td>Leaf 2</td>
<td>15</td>
<td>0.23</td>
</tr>
<tr>
<td>Leaf 3</td>
<td>29</td>
<td>3.59</td>
</tr>
<tr>
<td>Leaf 4</td>
<td>25</td>
<td>4.88</td>
</tr>
<tr>
<td>Leaf 5</td>
<td>18</td>
<td>- 1.06</td>
</tr>
<tr>
<td>Leaf 6</td>
<td>14</td>
<td>1.82</td>
</tr>
</tbody>
</table>

*Note. Dif. = difference in mean change scores (baseline HRSD-C minus post-treatment HRSD-C) between conditions; CI = confidence interval; LB = lower bound; UB = upper bound; \(d\) = Cohen’s \(d\). * \(p < .05\). ** \(p < .01\).*

### Table A.2. Descriptive statistics in the leaves of the QUINT results for QOL-PSY (Figure A.2) using the per-protocol sample. The mean values and standard deviations (SD) on improvement in QOL-PSY are displayed. A higher score means more improvement.

<table>
<thead>
<tr>
<th>MBCT + TAU</th>
<th>TAU</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Leaf 1</td>
<td>14</td>
<td>21.13</td>
</tr>
<tr>
<td>Leaf 2</td>
<td>23</td>
<td>6.16</td>
</tr>
<tr>
<td>Leaf 3</td>
<td>11</td>
<td>- 1.52</td>
</tr>
<tr>
<td>Leaf 4</td>
<td>24</td>
<td>4.03</td>
</tr>
<tr>
<td>Leaf 5</td>
<td>20</td>
<td>4.50</td>
</tr>
<tr>
<td>Leaf 6</td>
<td>20</td>
<td>6.46</td>
</tr>
</tbody>
</table>

*Note. Dif. = difference in mean change scores (post-treatment QOL-PSY minus baseline QOL-PSY) between conditions; CI = confidence interval; LB = lower bound; UB = upper bound; \(d\) = Cohen’s \(d\). * \(p < .05\). ** \(p < .01\).*
Figure A.1. Result of QUINT analysis with improvement in depressive symptoms (baseline HRSD-C minus post-treatment HRSD-C) as outcome using the per-protocol sample. In the green leaves (P1), MBCT + TAU is more beneficial than TAU alone; for the red leaves (P2) the reverse is true. In the grey leaves (P3), there is no difference between the interventions.
Figure A.2. Result of QUINT analysis with improvement in quality-of-life (post-treatment QOL-PSY minus baseline QOL-PSY) as outcome using the per-protocol sample. In the green leaves (P1), MBCT + TAU is more beneficial than TAU alone; for the red leaves (P2) the reverse is true. In the grey leaves (P3), there is no difference between the interventions.
# Import from SPSS data:
library(foreign)
mbct <- read.spss(file = “MODdatasetsmergedWORKING.sav”, use.value.labels = FALSE, to.data.frame = TRUE)
dim(mbct)

# Make sure that categorical variables are factor variables:
mbct$edu <- as.factor(mbct$edu)
mbct$mst <- as.factor(mbct$mst)

# R code for the QUINT analysis of depressive symptoms:
mbct$con2 <- (-1*mbct$con) + 1 # to recode condition, T=1 is now MBCT + TAU
library(quint)
formula1 <- I(dep.hrsd17.t0.c - dep.hrsd17.t1.c) ~ con2 | dep.hrsd17.t0.c + age + sex + mst + edu + mst + emp + med + pde + amo + rrs.b.t0 + ffmq.o.t0 + ffmq.d.t0 + ffmq.j.t0
contr2 <- quint.control(crit = "dm", B = 200, dmin = 0.40 )

# Fix the seed to ensure that the bootstrap results are the same (when repeated):
set.seed(52)
quint_dep < quint(formula1, data = mbct, control = contr2)

# Prune the tree:
Quintdeppr <- prune(quint_dep)

# Inspect the final result (split and leaf information):
summary(Quintdeppr)

# Plot the tree:
plot(Quintdeppr)
Course and interplay of Self-compassion and Affect during Mindfulness-Based Compassionate Living for Recurrent Depression: an Autoregressive Latent Trajectory Analysis

Abstract

Background. The current study aimed to investigate the course of and possible interplay between self-compassion and affect during mindfulness-based compassionate living (MBCL) in recurrently depressed individuals.

Methods. Data was used from a subsample of a parallel-group randomized controlled trial investigating the efficacy of MBCL in recurrently depressed adults ($n = 104$). Self-reports of self-compassion and positive/negative affect were obtained at the start of each of the eight MBCL sessions.

Results. Autoregressive latent trajectory (ALT) modeling showed that, when looking at the course of each variable via univariate ALT models separately, self-compassion increased ($\mu_{SC} = 0.095$, $s.e. = 0.018$, $p < .001$), while positive affect stayed stable (i.e., the final model did not contain a slope factor nor a slope variance) and negative affect decreased ($\mu_{NA} = -0.068$, $s.e. = 0.029$, $p = .018$) over the duration of the MBCL intervention. When looking at the interplay between self-compassion and positive/negative affect on a session-to-session basis with the use of bivariate ALT modeling, no significant reciprocal cross-lagged effects between self-compassion and positive affect were found. Although there were no cross-lagged effects from negative affect to self-compassion, higher levels of self-compassion at each session did predict lower levels of negative affect at the subsequent session ($b_{SC(t-1),NA(t)} = -0.182$, $s.e. = 0.076$, $p = .017$).

Conclusions. The current study shows that self-compassion increases during MBCL for recurrent depression. Moreover, negative affect decreases, which is preceded by increases in self-compassion.
1. Introduction

Major depressive disorder (MDD) is one of the most prevalent and impairing mental disorders (Wittchen et al., 2011; World Health Organization, 2017). MDD is recognized as having a chronic and recurrent course, whereby the risk of relapse increases with each successive episode (Richards, 2011; Solomon et al., 2000). Next to antidepressant medication, various psychological interventions are available for individuals with recurrent depression, such as mindfulness-based cognitive therapy (MBCT; Segal et al., 2012). MBCT has been shown effective in reducing relapse and/or recurrence in recurrently depressive individuals (Kuyken et al., 2016; Strauss et al., 2014). Unfortunately, many individuals still experience residual depressive symptoms after MBCT, which are a predictor for relapse to depression (Buckman et al., 2018; Piet & Hougaard, 2011).

Self-compassion has been shown to mediate the effect of MBCT for recurrent MDD (Kuyken et al., 2010). It may reduce low self-esteem or self-denigration which are possible underlying mechanisms for the chronic and recurrent nature of depressive symptoms (Gilbert & Procter, 2006). Individuals with MDD have been found to report less self-compassion when suffering from negative emotions than healthy controls (Krieger et al., 2013). In addition, higher levels of self-compassion have been shown to predict lower levels of depressive symptoms and reduced risk of relapse/recurrence depression (Krieger et al., 2016).

Although compassion is implicitly conveyed in MBCT, explicit cultivation of self-compassion might be a fruitful approach to further improve outcome of MBCT in this population. Van den Brink and Koster (2015) developed mindfulness-based compassionate living (MBCL) as a follow-up intervention to MBCT or mindfulness-based stress reduction (MBSR; Kabat-Zinn, 1990), with the intention to offer (self-)compassion building on already established mindfulness skills. In MBCL, (self-)compassion encompasses, the capacity to be sensitive to the suffering of self and others, and the commitment to alleviate and prevent this suffering (Gilbert & Choden, 2013). MBCL shares content with other compassion-based interventions (CBIs), such as compassion-focused therapy (CFT; Gilbert, 2010) and the mindful self-compassion program (MSC; Neff & Germer, 2013). It has been structured in a similar way as MBCT/MBSR (van den Brink & Koster, 2015): it is a group-based intervention consisting of eight (bi)weekly sessions of 2.5h, a silent (half)day, and daily home-practices of 45-60 minutes. The practices are explicitly focused on cultivating compassion and kindness towards self and others, including informal practices (e.g., breathing space with kindness or compassion) and formal practices (e.g., kindness meditation and compassionate breathing).

Research to date shows promising evidence for MBCL in individuals with recurrent depression. In a pilot study among recurrently depressed individuals who previously participated in MBCT (n = 17), MBCL was shown to be feasible and acceptable (Schuling et al., 2018). A recent randomized controlled trial (RCT)
of recurrently depressed individuals who previously attended MBCT \((n = 122)\), showed that MBCL resulted in a greater reduction of depressive symptoms and improvement of quality of life than treatment-as-usual (TAU). Further reduction of depressive symptoms and improvement of quality of life, relative to TAU, took place during the 6 months follow-up (Schuling et al., 2020). In addition, self-compassion appeared to mediate the post-intervention effect of MBCL. However, the mediation analyses only used pre-post measurements, therefore inferences about possible causality cannot be made. More research is needed into the (dynamic) process of self-compassion in MBCL for recurrently depressed individuals.

Affect regulation of both positive and negative emotions is an additional working mechanism proposed for CBIs. Three basic types of emotion regulation systems are distinguished in MBCL (van den Brink and Koster, 2015; Gilbert, 2009): 1. the threat system, activated when there is threat/danger and aimed at self-protection; 2. the drive system, triggered by desire and aimed at satisfaction; 3. the soothing system, activated when the threat and drive system are inactive. It is aimed at social connectedness, care and safeness. A disbalance may arise in case of an easily activated threat system (e.g., history of trauma) or drive system (e.g., tendency to compete), or in the presence of an insufficiently developed soothing system (e.g., history of emotional neglect). During MBCL, one is invited to explore the soothing system as a source of resilience, especially in the face of unpleasant events. This may simultaneously increase the ability to tolerate and regulate negative affect (van den Brink & Koster, 2015; Sommers-Spijkerman et al., 2018).

Changes in self-compassion have also been associated with changes in affect during CBIs. An intervention study in individuals vulnerable to depression \((n = 63)\) found that practicing self-compassion resulted in subsequent increases in happiness and decreases in depression (Shapira & Mongrain, 2010). In addition, several experimental studies seem to show that self-compassion increases positive affect (e.g., Engen & Singer, 2015) and decreases in negative affect (e.g., Arimitsu & Hofmann, 2017; Leary, et al., 2007). Only one experimental study has been conducted among individuals with MDD \((n = 48;\) Diedrich et al., 2014). Depressed mood was induced at 4 points in time. After each mood induction, participants were instructed to either wait, reappraise the situation, accept their negative emotions, or employ self-compassion to regulate their depressed mood. Self-ratings of depressed mood were assessed before and after each mood induction and regulation phase. Results showed that the reduction of depressed mood was significantly greater in the self-compassion condition than in the waiting condition. In addition, the self-compassion condition was most effective for individuals who reported higher baseline levels of depressed mood. Reverse effects of positive/negative affect on self-compassion have not yet been scientifically researched.
The current study expands previous literature by investigating the course and interplay between self-compassion and positive/negative affect in individuals with recurrent depression participating in MBCL as a follow-up to MBCT. Measurements of self-compassion and positive/negative affect took place prior to each of the eight MBCL sessions. Autoregressive latent trajectory (ALT) modeling was used to model changes in the course of variables over the whole duration of the intervention, and in addition, changes in variables on a session-to-session basis. We hypothesized that self-compassion and positive affect increase, while negative affect decreases over the whole duration of the intervention. Additionally, we hypothesized that higher levels of self-compassion result in subsequent higher levels of positive affect and lower levels of negative affect. No hypotheses were formulated for the reciprocal relations between levels of positive/negative affect and subsequent levels of self-compassion.

2. Methods

2.1. Design

Data was used from a parallel-group RCT (Schuling et al., 2016), comparing MBCL + TAU to TAU alone. The RCT was carried out between July 2013 and April 2015 at the Radboudumc center for mindfulness, the Netherlands. Prior to randomization, additional demographic and clinical characteristics were collected. Sixty-one participants were randomly allocated to MBCL + TAU and 61 to TAU alone. Participants in the TAU group were invited to take part in MBCL after the TAU period and 57 of them did participate. Data on self-compassion and positive/negative affect were collected prior to each session in all 118 participants who eventually participated in MBCL. The protocol of the RCT was approved by the ethical review board CMO Arnhem-Nijmegen (2013/220). For further study details and outcomes of the RCT and follow-up study, see the respective paper (Schuling et al., 2020).

2.2. Participants

Individuals with recurrent depression who had previously participated in MBCT at the Radboudumc center for mindfulness were invited to take part in the RCT. Those interested were invited for a research interview to assess eligibility. Inclusion criteria were: recurrent depression according to the Diagnostic and Statistical Manual of Mental Disorders IV (American Psychiatric Association [APA], 1994), with or without a current depressive episode assessed with the Structured Clinical Interview for DSM disorders I (SCID-I; First et al., 1996); previous participation (≥ one year ago) in MBCT at the Radboudumc center for mindfulness (≥ 4 sessions); and ≥ 18 years. Exclusion criteria were:
≥ 1 previous (hypo)manic episodes according to the DSM-IV (APA, 1994); primary psychotic disorder; neurological/somatic conditions possibly related to the depression; current alcohol and/or drug dependence; electro convulsive therapy < 3 months; and inability to complete interviews and/or self-report questionnaires. If eligible, individuals were included only after written informed consent had been obtained. Of all 118 participants who eventually participated in MBCL, 104 attended at least four sessions of MBCL and were therefore included in the current study. No differences were found in demographic and clinical characteristics between participants who were randomized to the MBCL + TAU condition and those who were initially randomized to the TAU condition and received MBCL + TAU afterwards. Demographic and clinical characteristics of the included participants can be found in Table 1. Participants participated, on average, 7.12 MBCL sessions (range: 4 - 8, $SD = 1.01$).

2.3. Interventions
The MBCL intervention was based on the original protocol of van den Brink and Koster (2015). Participants received 8 biweekly 2.5-hour sessions in groups of 8-10 participants. Daily home practice took about 30 minutes and was guided by CDs. In addition, participants received a folder containing background information on each session and accompanying practices. One of the primary practices of the MBCL program is the practice of befriending self and others (van den Brink & Koster, 2015). During MBCL, this quality of befriending is gradually developed from self to a close, neutral, and difficult person. For a detailed description of the MBCL sessions, see Schuling et al. (2016). The MBCL intervention was taught by two teachers who met the good practice guidelines (UK Network of Mindfulness-Based Teachers, 2015) and were trained by the developers of the intervention. An independent MBSR/MBCT teacher assessed treatment integrity and therapist competence using the Mindfulness Based Interventions Teaching Assessment Criteria (MBI:TAC; Crane et al., 2013) based on two randomly selected videotapes of each teacher. Both teachers of the current study were rated as ‘competent’. In addition to MBCL, participants were allowed to receive TAU (i.e., any medical, psychiatric and/or psychological treatment, with the exception of compassion focused interventions).

2.4. Measuring instruments
2.4.1. Self-compassion
Of each of the 6 subscales of the Dutch version of the Self-Compassion Scale-Short Form (SCS-SF; Raes et al., 2011), the item with the largest factor loading was used to assess self-compassion. These were as follows: self-kindness (“When I'm going through a very hard time, I give myself the caring and tenderness I need”), self-judgment (“I'm disapproving and judgmental about my own flaws and inadequacies”, common humanity “I try to see my failings as part of the human
Table 1. Baseline demographic and clinical characteristics of participants with recurrent depression receiving mindfulness-based compassionate living (n = 104)

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>78 (75.0%)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>22 (21.2%)</td>
</tr>
<tr>
<td>Married or Cohabiting</td>
<td>65 (62.5%)</td>
</tr>
<tr>
<td>Divorced or Widowed</td>
<td>13 (12.5%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>Level of education</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>7 (6.7%)</td>
</tr>
<tr>
<td>Middle</td>
<td>74 (71.2%)</td>
</tr>
<tr>
<td>High</td>
<td>19 (18.3%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>Employed</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>59 (56.7%)</td>
</tr>
<tr>
<td>No</td>
<td>41 (39.4%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>ADM use</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>48 (46.2%)</td>
</tr>
<tr>
<td>No</td>
<td>52 (50.0%)</td>
</tr>
<tr>
<td>Missing</td>
<td>4 (3.8%)</td>
</tr>
<tr>
<td>Prior MDEs ≥ 3 b</td>
<td>91 (87.5%)</td>
</tr>
<tr>
<td>Current MDD c</td>
<td>32 (30.8%)</td>
</tr>
<tr>
<td>Childhood trauma d</td>
<td>45 (43.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.74 (10.69)</td>
</tr>
<tr>
<td>Depressive symptoms e</td>
<td>16.87 (10.17)</td>
</tr>
<tr>
<td>Age at MDD onset (years)</td>
<td>24.47 (11.68)</td>
</tr>
<tr>
<td>Time since MBCT (years) f</td>
<td>3.90 (1.74)</td>
</tr>
</tbody>
</table>

Note. ADM = antidepressant medication; MDE = major depressive episode; MDD = major depressive disorder; MBCT = mindfulness-based cognitive therapy. a Low = No education, Primary school, LBO, VMBO, KMBO, and MAO; Middle = MBO, HAVO, VWO, and HBO; High = WO. Abbreviations refer to the Dutch education system. b Based on self-report. c Assessed with the Structured Clinical Interview for DSM-IV Axis I disorders part I (SCID-I; First et al., 1996). d Assigned ‘yes’ when ≥ 1 item was being answered positively on the physical or sexual abuse subscales of the childhood trauma questionnaire (Bernstein & Fink, 1998). e Assessed with the Beck-Depression Index-II (BDI-II; van der Does, 2002) and based on n = 103. f Based on n = 70.
condition”), isolation (“When I’m feeling down, I tend to feel like most other people are probably happier than I am”), mindfulness (“When something painful happens I try to take a balanced view of the situation”), and over-identification (“When I’m feeling down I tend to obsess and fixate on everything that’s wrong”). Items were rated on a 10-point Likert scale ranging from ‘Totally untrue’ to ‘Totally true’ relating to the time period between sessions. The internal consistency in the current study was calculated for every session and ranged from acceptable to good (α range: .73 - .83).

2.4.2. Affect
Positive and negative affect were assessed with the two items with the largest factor loadings on each subscale (i.e., positive and negative) of the Dutch version of the Positive and Negative Affect Schedule (PANAS; Watson et al., 1988). Items assessing negative affect were ‘Upset’ and ‘Scared’, and items assessing positive affect were ‘Active’ and ‘Excited’. All items were rated on a 10-point Likert scale ranging from ‘Totally untrue’ to ‘Totally true’ with regard to the time period between sessions. The internal consistency was calculated at every session and appeared to be acceptable to good for positive affect (α range: .72 - .85) and poor to acceptable for negative affect (α range: .52 - .76).

2.5. Statistical analysis
2.5.1. Self-compassion
To compute a total self-compassion score, first the negative subscale items (i.e., self-judgment, isolation, and over-identification) were reverse scored. Then a mean score of the 6 items was calculated and used in the current study. In case of a missing value on one item, person mean imputation was applied for that missing value. If data on more than 1 item was missing, the self-compassion score was not calculated and indicated as missing.

2.5.2. Affect
For positive affect and negative affect, both items needed to be available to calculate the mean score. If data on at least one item was missing, this was considered as missing data.

2.5.3. ALT modeling technique
The current study used the ALT modeling technique based on the recommendations of Bollen and Curran (2004), which combines a bivariate autoregressive (AR) and a bivariate latent trajectory model (LTM) into a bivariate ALT model. A bivariate AR model captures reciprocal session-to-session associations between variables, so called cross-lagged (CL) effects, while controlling each measurement point for its prior value (AR effects). However, when not accounting for the overall trajectories (courses) of both variables over the duration of the MBCL intervention,
spurious CL effects might appear (Voelkle, 2008). A bivariate LTM does allow a
different overall course for each individual (i.e., a different intercept and slope
factor), however, but it does not capture CL and AR effects. Hence, the combination
of a bivariate AR with a bivariate LTM makes it possible to study reciprocal CL
effects (i.e., interplay) while controlling for overall courses and AR effects. This
makes statements about the processes of stability and change during MBCL
for recurrent depression more reliable. A predetermined model specification
was adopted to prevent parameter bias from being introduced by not accounting
for prior, unassessed levels of the variables (Bollen & Curran, 2004). As a
consequence, the intercept factor no longer represents the initial baseline value,
but resembles the value of the second measurement point which is not yet
explained by the first measurement point. To improve readability, in the
remainder, we refer to the intercept as the general level of a variable.

Firstly, several univariate ALT models were fitted for each variable separately
(i.e., self-compassion, positive affect, and negative affect) and compared to
identify which model best represented the course of each variable separately
during MBCL. Secondly, several bivariate ALT models were fitted for self-
compassion and positive affect, and self-compassion and negative affect. These
models were compared in order to find the most parsimonious bivariate ALT
model that best represented the possible interplay between self-compassion and
positive/negative affect from session to session during MBCL. This analysis
controls for the course of self-compassion and positive/negative affect over the
full MBCL period and AR effects of each variable separately. For a detailed
description of the univariate and bivariate ALT models that were fitted, see
Supplementary Material A.

2.5.4. Model fit
Several fit indices were used to evaluate model fit: (1) chi-square ($\chi^2$) to degrees
of freedom ($df$) ratio, values close to 1 were considered good, values between 2
and 3 as acceptable and less than 2 as preferable fit (Carmines & McIver, 1981;
Marsh & Hocevar, 1985); (2) the Tucker-Lewis index (TLI; Tucker & Lewis, 1973)
and comparative fit index (CFI; Bentler, 1990) of which values higher than 0.90
were considered an adequate and higher than 0.95 a very good fit (Bollen, 1989;
Hu & Bentler, 1999); (3) the root-mean-square error of approximation (RMSEA;
Steiger, 1998) of which values below 0.07 were indicative of good fit and (4) the
standardized root-mean-square residual values (SRMR; Hooper et al., 2008) of
which values below 0.08 were adequate and below 0.05 were considered good.

Nested models were compared with the chi-square difference test. If two
models were significantly different, the more complex model (i.e., the model
with more estimated parameters) was retained, otherwise the simpler model
was maintained. Non-nested models were compared based on differences in the
Akaike information criterion (AIC; Akaike, 1973) and the Bayesian information
criterion (BIC; Raftery, 1995) values, in which the model with the lowest AIC and BIC was favored. Differences between 2-6 points were considered as small, 6-10 points as medium strong, and > 10 points as very strong evidence of differences in model fit. Differences of 2 or less suggested that both models fitted the data equally well and the simplest model was favored in that case (Raftery, 1995).

2.5.5. Computational note
Descriptive analyses and normality tests were performed with SPSS version 25 (IBM Corporation, 2017). The ALT modeling technique was carried out with Mplus version 6.11 (Muthén & Muthén, 1998-2011). Full information maximum likelihood (FIML) was employed in order to account for missing data (i.e., ranging from 2.9% to 21.2% for each variable at each time point). The FIML estimator takes all available measurement values into account when estimating model parameters and is suitable for the comparison of multiple structural equation models (Enders & Bandalos, 2001). For all analyses, a two-sided alpha level of .050 was considered significant.

3. Results
The descriptive statistics of and correlations between all studied variables can be found in Tables 2 and 3.

3.1. Univariate models
For the model fit indices of all univariate ALT models that were fitted, see Supplementary Material B. The final univariate ALT models showed that self-compassion increased ($\mu_{\beta_{SC}} = 0.095$, s.e. = 0.018, $p < .001$), while positive affect showed a stable course (i.e., the final model did not contain a slope factor nor a slope variance), and negative affect decreased ($\mu_{\beta_{NA}} = -0.068$, s.e. = 0.029, $p = .018$) over the full MBCL intervention. A detailed description of the results of the final univariate ALT models can be found in Supplementary Material B.

3.2. Bivariate models
The model fit indices of the bivariate ALT models that were fitted in order to find the final bivariate ALT models can be found in Supplementary Material B, Table B.3. For sake of clarity, only the results of the final bivariate ALT models are described in detail below. The variances, covariances and correlations of the final bivariate ALT models can be found in Table 4.

3.2.1. Self-compassion and positive affect
The final bivariate ALT model of self-compassion and positive affect that demonstrated the best fit to the data had no slope for positive affect, and no slope
Table 2. Correlations between and univariate statistics of self-compassion and positive affect during 8 sessions of mindfulness-based compassionate living

<table>
<thead>
<tr>
<th></th>
<th>Self-compassion</th>
<th>Positive affect</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>S1</td>
<td>S2</td>
<td>S3</td>
</tr>
<tr>
<td>SC S1</td>
<td>.651**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC S2</td>
<td></td>
<td>.631**</td>
<td>.672**</td>
</tr>
<tr>
<td>SC S3</td>
<td></td>
<td></td>
<td>.627**</td>
</tr>
<tr>
<td>SC S4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC S5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC S6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC S7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SC S8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PA S1</td>
<td>.209*</td>
<td>.521**</td>
<td>.487**</td>
</tr>
<tr>
<td>PA S2</td>
<td>.175</td>
<td>.277**</td>
<td>.530**</td>
</tr>
<tr>
<td>PA S3</td>
<td>.312**</td>
<td>.363**</td>
<td>.582**</td>
</tr>
<tr>
<td>PA S4</td>
<td>.283**</td>
<td>.376**</td>
<td>.446**</td>
</tr>
<tr>
<td>PA S5</td>
<td>.078</td>
<td>.332**</td>
<td>.286*</td>
</tr>
<tr>
<td>PA S6</td>
<td>.225*</td>
<td>.290*</td>
<td>.420**</td>
</tr>
<tr>
<td>PA S7</td>
<td>.295**</td>
<td>.289**</td>
<td>.387**</td>
</tr>
<tr>
<td>M</td>
<td>5.01</td>
<td>5.19</td>
<td>5.51</td>
</tr>
<tr>
<td>SD</td>
<td>1.51</td>
<td>1.49</td>
<td>1.61</td>
</tr>
<tr>
<td>γ₁</td>
<td>0.56</td>
<td>0.31</td>
<td>0.42</td>
</tr>
<tr>
<td>γ₂</td>
<td>0.76</td>
<td>0.14</td>
<td>-0.06</td>
</tr>
</tbody>
</table>

Note. SC = self-compassion; PA = positive affect; S1-8 = session 1-8; M = mean; SD = standard deviation; γ₁ = skewness; γ₂ = kurtosis. Level of significance is indicated for the correlations only. a Available n varies from 82 to 101 across S1-8. b Available n varies from 82 to 100 across S1-8. *p ≥ .050, *p < .050, **p < .010.
This final bivariate ALT model had an adequate model fit ($\chi^2 = 179.037, df = 112; p < .001; CFI = 0.928; TLI = 0.924; RMSEA = 0.076; SRMR = 0.104$). The significant standardized parameter estimates are depicted in Figure 1.

When looking at the course of self-compassion, an increase was found over the duration of the MBCL intervention ($\mu_{SC} = 0.094, s.e. = 0.018, p < .001$), with this increase being the same for all participants (i.e., the slope variance of self-compassion could be removed from the model without significantly decreasing the model fit). Participants differed in both their general level of self-compassion ($\mu_{aSC} = 4.254, s.e. = 0.313, p < .001$; $\sigma_{aSC} = 0.838, s.e. = 0.180$).
Table 4. Variances, covariances and correlations between the first measurements (session 1) and the intercepts of self-compassion and positive affect (upper part), and of self-compassion and negative affect (lower part) based on the final bivariate autoregressive latent trajectory (ALT) models

<table>
<thead>
<tr>
<th>SC S1</th>
<th>PA S1</th>
<th>SC Intercept</th>
<th>PA Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC S1</td>
<td>2.244 (.314)***</td>
<td>.366</td>
<td>.695</td>
</tr>
<tr>
<td>PA S1</td>
<td>.915 (.263)***</td>
<td>2.776 (.392)***</td>
<td>.476</td>
</tr>
<tr>
<td>SC Intercept</td>
<td>.953 (.186)***</td>
<td>0.726 (.186)***</td>
<td>.838 (.180)***</td>
</tr>
<tr>
<td>PA Intercept</td>
<td>0.584 (.208)**</td>
<td>1.111 (.239)***</td>
<td>.666 (.180)***</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SC S1</th>
<th>NA S1</th>
<th>SC Intercept</th>
<th>NA Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC S1</td>
<td>2.247 (.314)***</td>
<td>-.597</td>
<td>.699</td>
</tr>
<tr>
<td>NA S1</td>
<td>-1.785 (.345)***</td>
<td>3.976 (.559)***</td>
<td>-.537</td>
</tr>
<tr>
<td>SC Intercept</td>
<td>.930 (.183)***</td>
<td>-0.950 (.224)***</td>
<td>.788 (.173)***</td>
</tr>
<tr>
<td>NA Intercept</td>
<td>-0.523 (.238)*</td>
<td>1.336 (.328)***</td>
<td>-.479 (.190)*</td>
</tr>
</tbody>
</table>

Note. SC = self-compassion; PA = positive affect; NA = negative affect; S1 = Observed variable of the first session. Variances are depicted on the diagonal, covariances below and correlations above the diagonal. Standard errors are shown between parenthesis. The slope is omitted from this table, given that no slope variances were fitted in the final bivariate ALT models. Level of significance is indicated for the covariances and variances only. * p < .050, ** p < .010, *** p < .001.

$p < .001$, and their baseline level of self-compassion ($\mu_{SC1} = 4.991$, s.e. = 0.148, $p < .001$; $\sigma_{SC(t1)} = 2.244$, s.e. = 0.314, $p < .001$). Self-compassion at session 1 covaried positively with its intercept factor ($\psi_{SC(t1),asc} = 0.953$, s.e. = 0.186, $p < .001$).

Positive affect showed a stable course over the duration of the MBCL intervention; i.e., the final model did not contain a slope factor for positive affect. Participants differed in their general level of positive affect ($\mu_{PA} = 5.029$, s.e. = 0.435, $p < .001$; $\sigma_{PA(t1)} = 1.093$, s.e. = 0.253, $p < .001$). In addition, participants differed in their baseline level of positive affect ($\mu_{PA(t1)} = 5.465$, s.e. = 0.166, $p < .001$; $\sigma_{PA(t1)} = 2.776$, s.e. = 0.392, $p < .001$). Positive affect at session 1 covaried positively with the intercept of positive affect ($\psi_{PA,PA(t1)} = 1.111$, s.e. = 0.239, $p < .001$).

In general, self-compassion and positive affect were positively associated with each other. This is represented by the positive covariance between the intercept factors of both variables ($\psi_{PA,asc} = 0.666$, s.e. = 0.180, $p < .001$), the positive covariance between both variables at the first sessions ($\psi_{PA(t1),SC(t1)} = 0.915$, s.e. = 0.263, $p < .001$), the positive covariance between self-compassion at the first session and the intercept of positive affect ($\psi_{PA,t1,SC(t1)} = 0.584$, s.e. = 0.208, $p < .001$), the positive covariance between positive affect at the first session and the intercept factor of self-compassion ($\psi_{PA(t1),SC(t1)} = 0.726$, s.e. = 0.186, $p < .001$), and the positive time-specific residual covariances for each session, which were equal over time ($\psi_{PA(tx),SC(tx)} = 0.402$, s.e. = 0.053, $p < .001$).
When looking at additional session-to-session effects, both self-compassion and positive affect showed stable but rather small AR effects ($\rho_{\text{AR}(1)_{\text{SC}}} = 0.217$, s.e. = 0.055, $p < .001$; $\rho_{\text{AR}(1)_{\text{PA}}} = 0.207$, s.e. = 0.052, $p < .001$). CL effects from self-compassion to positive affect were not found ($0.082 < p < .597$), nor vice versa ($p = .741$), indicating that the level of self-compassion at a certain session did not predict the level of positive affect at the next session nor vice versa (no interplay).

3.2.2. Self-compassion and negative affect

The final bivariate ALT model of self-compassion and negative affect included no slope for negative affect, and no slope variance for self-compassion, equal time-specific, AR, and CL effects over time for both self-compassion and negative affect. This final bivariate ALT model provided an adequate to good model fit ($\chi^2 = 152.078; df = 118, p = .019; \text{CFI} = 0.959; \text{TLI} = 0.958; \text{RMSEA} = 0.053; \text{SRMR} = 0.091$). Figure 2 shows the significant standardized parameter estimates of the final bivariate ALT model between self-compassion and negative affect.

Self-compassion increased over the full duration of the MBCL intervention ($\mu_{\text{SC}} = 0.087$, s.e. = 0.018, $p < .001$). The strength of this increase was the same for all participants (i.e., the final model did contain a slope factor but no slope variance). Participants differed both in their general levels of self-compassion ($\mu_{\alpha\text{SC}} = 4.407$, s.e. = 0.362, $p < .001$; $\sigma_{\alpha\text{SC}} = 0.788$, s.e. = 0.173, $p < .001$), and their baseline levels of self-compassion ($\mu_{\text{SC}_1} = 4.994$, s.e. = 0.148, $p < .001$; $\sigma_{\text{SC}_1} = 2.247$, s.e. = 0.314, $p < .001$). Self-compassion at session 1 covaried positively with the intercept of self-compassion ($\psi_{\alpha\text{SC},\text{SC}_1} = 0.930$, s.e. = 0.183, $p < .001$).

Negative affect showed a stable course over the duration of the MBCL intervention (i.e., the final model did not contain a slope factor nor a slope variance). Participants showed differences in both their general levels of negative affect ($\mu_{\alpha\text{NA}} = 5.198$, s.e. = 0.542, $p < .001$; $\sigma_{\alpha\text{NA}} = 1.553$, s.e. = 0.341, $p < .001$), and their baseline levels of negative affect ($\mu_{\text{NA}_1} = 4.419$, s.e. = 0.198, $p < .001$; $\sigma_{\text{NA}_1} = 3.976$, s.e. = 0.559, $p < .001$). Finally, negative affect at session 1 covaried positively with the intercept of negative affect ($\psi_{\alpha\text{NA},\text{NA}_1} = 1.336$, s.e. = 0.328, $p < .001$).

In general, self-compassion and negative affect were negatively associated with each other. This is shown by the negative covariance between the first measurements of both variables ($\psi_{\text{NA}_1,\text{SC}_1} = -1.785$, s.e. = 0.345, $p < .001$) and both intercept factors ($\psi_{\alpha\text{NA},\alpha\text{SC}} = -0.479$, s.e. = 0.190, $p = .012$). Moreover, a negative covariance was found between self-compassion at session 1 and the intercept of negative affect ($\psi_{\alpha\text{NA},\text{SC}_1} = -0.523$, s.e. = 0.238, $p = .028$), and between negative affect at session 1 and the intercept of self-compassion ($\psi_{\alpha\text{SC},\text{NA}_1} = -0.950$, s.e. = 0.224, $p < .001$). Finally, residual covariances between both variables at each session were all negative and stable over time (i.e., time-specific covariances: $\psi_{\varepsilon\text{NA}_x,\varepsilon\text{SC}_x} = -0.410$, s.e. = 0.062, $p < .001$).

Additional session-to-session effects showed positive AR effects of self-compassion which were stable over time ($\rho_{\text{AR}(1)_{\text{SC}}} = 0.203$, s.e. = 0.055, $p < .001$).
Figure 1. Standardized parameter estimates of the final bivariate ALT model of self-compassion (SC) and positive affect (PA). Note that when having set (unstandardized) parameters to be equal over time, the standardized effects may still slightly differ over time. Only significant estimates of (error) correlations, autoregressive and cross-lagged parameters are shown. Double-headed arrows represent correlations.
Figure 2. Standardized parameter estimates of the final bivariate ALT model of self-compassion (SC) and negative affect (NA). Note that when having set (unstandardized) parameters to be equal over time, the standardized effects may still slightly differ over time. Only significant estimates of (error) correlations, autoregressive and cross-lagged parameters are shown. Double-headed arrows represent correlations.
This indicates that the level of self-compassion at a specific session predicted the level of self-compassion at a subsequent session, which was equal over time. AR effects were absent for negative affect ($p = .627$), meaning that the level of negative affect at a certain session did not predict the level of negative affect at a subsequent session. When looking at the interplay between self-compassion and negative affect, negative CL effects from self-compassion to negative affect were found ($b_{SC(t-1),NA(t)} = -0.182$, s.e. = 0.076, $p = .017$). This indicates that higher levels of self-compassion at a certain session predicted lower levels of negative affect at the subsequent session. CL effects from negative affect towards self-compassion were not found ($p = .375$).

4. Discussion

The aim of the current study was to investigate the course of and possible interplay between self-compassion and positive/negative affect in MBCL in recurrently depressed individuals ($n = 104$) using autoregressive latent trajectory (ALT) modeling. When looking at the course of each variable separately, it was found that self-compassion increased, while positive affect showed a stable course and negative affect decreased over the duration of the MBCL intervention. Results from investigating the interplay between self-compassion and positive/negative affect on a session-to-session basis showed no cross-lagged (CL) effects from self-compassion at one session to positive affect at the subsequent session nor vice versa. Higher levels of self-compassion at each session did however predict lower levels of negative affect at the subsequent session, but not vice versa.

4.1. Univariate ALT modeling: course of self-compassion and affect

As hypothesized, self-compassion showed an increase over the duration of the MBCL intervention. This supports the notion that, even after an initial increase in self-compassion through MBCT, MBCL can further develop self-compassion in recurrently depressed individuals. Contrary to expectations, positive affect did not increase over the duration of the intervention. A reason for this might be that the two items assessing positive affect in the current study (i.e., ‘Active’ and ‘Excited’) represent quite aroused, energetic forms of positive affect. However, during MBCL one is invited to soothe oneself in difficult times, promoting feelings of relaxation, connectedness, safety, and wellbeing. It might be that a different course would have been found if these more subtle positive emotions had been included. Finally, as expected, negative affect did decrease over the duration of the MBCL intervention.
4.2. Bivariate ALT modeling: self-compassion and positive affect
Against expectations, no reciprocal session-to-session CL effects between self-compassion and positive affect were found. This is in contrast with previous literature that supports higher baseline levels of self-compassion to be associated with subsequent higher levels of positive affect (Krieger et al., 2015), and that self-compassion interventions lead to higher levels of positive affect (e.g., Shapira & Mongrain, 2010; Sommers-Spijkerman et al., 2018). Even neurobiological changes associated with positive affect seem to support this (Engen & Singer, 2015). As mentioned before, one reason for these non-significant session-to-session effects might be the items used to assess positive affect in the current study. Another reason could be the differences in analytical strategies used. For example, Krieger et al. (2015) used multilevel modeling, which does not account for the overall course and previous values over time of each variable. However, when not accounting for the overall courses of both variables over the duration of the MBCL intervention, spurious CL effects might appear (Voelkle, 2008). The current study used ALT modeling, which investigates CL effects, while accounting for both the baseline value, overall course, and previous value of each variable over time. This analyzing technique enables a more reliable and conservative interpretation of the processes of stability and change.

4.3. Bivariate ALT modeling: self-compassion and negative affect
In contrast to the univariate ALT model for negative affect, no slope was modeled for negative affect in the bivariate ALT model for self-compassion and negative affect. This suggests that, after accounting for the influence of self-compassion on negative affect, negative affect did not decrease over the duration of the MBCL intervention. As such, it seemed that the observed decrease of negative affect over time was fully accounted for by the negative CL effects from self-compassion towards negative affect. As hypothesized, higher levels of self-compassion at a certain session predicted lower levels of negative affect at the subsequent session. This is in line with previous experimental research into individuals with MDD, which found a decrease in experimentally induced depressed mood after self-compassion was employed (n = 48; Diedrich et al., 2014).

4.4. Strengths and limitations
The current study is the first study to investigate the course of and possible interplay between self-compassion and positive/negative affect during MBCL in recurrently depressed individuals. The inclusion of multiple measurements and the use of the ALT modeling technique, which allows to investigate CL effects while controlling for a variables’ previous value and overall course of each variable (i.e., intercepts and slopes), is of great value to infer possible causation. However, it cannot be ruled out that other variables that currently were not
modeled also play a role. A second strength is that only a few exclusion criteria were applied and both individuals with and without a current depression were allowed to participate, which increases the generalizability of the current findings. Finally, the assessments and high quality of mindfulness teacher competency is another strength of this study. Indeed, both teachers had long-standing experience in teaching MBCT and were trained by the MBCL developers themselves. This supports the quality of the intervention and its effects on outcome.

There were also some limitations. First of all, the current study did not include process data of a control group. Therefore, it cannot be ruled out that the associations found in the current study, might not also have been found without MBCL or during another active control condition. In future research, multiple measurements should ideally be conducted both during MBCL and during an active control condition to infer specificity of findings to MBCL. Another limitation is that in order to reduce participants’ burden in completing biweekly assessments shorter versions of the original questionnaires for self-compassion and positive/negative affect were used. For the Self-Compassion Scale this resulted in a still adequate to good internal consistency. For affect, however, this resulted in a poorer content validity and internal consistency compared to the original Positive and Negative Affect Scale (PANAS; Watson et al., 1988). The use of self-report measures only is another limitation of the current study. As commonly known, self-report measures are more prone to certain biases (e.g., social desirability). The (additional) use of more objective measures during MBCL for depression might be of interest for future research. Lastly, there is a debate whether the negative subscale of the SCS (i.e., self-judgment, isolation, and over-identification; reverse-scored items) “contaminates” the total self-compassion score, given that this negative subscale has been found to be responsible for the association between self-compassion and psychopathological symptoms such as negative affect (e.g., López et al., 2015; Muris et al., 2018). However, others support the notion that both subscales represent the relative balance of compassionate and uncompassionate responses to suffering, and that both are important contributors to the overall concept of self-compassion (e.g., Krieger et al., 2016; Neff, 2016), which is why we used both subscales to obtain a total score in our study.

4.5. Conclusions and implications
The current study shows that MBCL for recurrently depressed individuals result in increases of self-compassion, and that higher levels of self-compassion at each session predicts lower levels of negative affect at the subsequent session. This seems to be in line with the hypothesis that during MBCL negative affect is alleviated through increasing the ability to tolerate and regulate negative emotions. These changes might not be specific to MBCL, and might be found in
other interventions as well (e.g., exposure therapy, schema therapy). Further research into possible mediators, predictors and moderators of MBCL compared to other interventions should be conducted to give us more insight into how MBCL works and for whom it works best. This might help the optimal integration of MBCL for recurrently depressed individuals.
References


Supplementary Material A – Method section
Model building steps of the univariate and bivariate models

1. Univariate model building steps
Various univariate autoregressive latent trajectory (ALT) models were fitted for each variable separately (i.e. self-compassion, positive affect, and negative affect) to investigate their course over the duration of the MBCL intervention. These models were compared to find the most parsimonious model that fitted the data adequately (without a significant decrease in model fit when compared to the best fitting model).

First, a predetermined ALT-full model was fitted. This model contained the eight measurement points (t1-8), an intercept factor (with factor loadings of t2-8 set to 1), a linear slope factor (with factor loadings of t2-8 set to 0-6), and autoregressive (AR) effects. Note that because of the predetermined model specification, the first measurement point was considered as a separate variable in the model. As a consequence, the intercept factor no longer represents the initial baseline value, but resembles the value of the second measurement point which is not yet explained by the first measurement point. The first measurement point, intercept and slope factor were allowed to covary. In the remainder, we refer to the intercept as the general level of a variable.

Subsequently, several (cumulative) restrictions were applied to the ALT-full model in order to further simplify the model without significantly decreasing model fit. When a restriction did decrease model fit significantly, the restriction was removed from the model before the next restriction was applied. However, when a restriction of the model appeared suited (i.e., no significant decrease in model fit), the next restriction was applied on top of that restriction. The following restrictions were subsequently tested: (1) excluding the AR parameters (ALT-LTM), (2) excluding the slope factor variance (ALT-no slope variance), (3) excluding the slope factor (ALT-no slope), and (4) constraining the AR parameters to be equal to each other over time (ALT-AR constraints).

2. Bivariate model building steps
To examine how self-compassion and positive/negative affect influence one another over time during MBCL for recurrent depression, several bivariate ALT models were estimated and compared to determine which model fitted the data well and, at the same time, provided a parsimonious representation of the data. Below, the bivariate model steps of self-compassion and positive affect are described. The same model building steps were used for the bivariate models of self-compassion and negative affect.

At first, a predetermined ALT-full model was fitted. This model contained the eight measurement points of both self-compassion (t1-8) and positive affect.
(t1-8). For both variables, an intercept factor (with factor loadings of t2-8 set to 1), a linear slope factor (with factor loadings of t2-8 set to 0-6), AR effects, and cross-lagged (CL) effects were included. The first measurement point of both self-compassion and positive affect were considered as separate variables in the model (i.e., a predetermined model specification). Moreover, these first measurement points, as well as all intercept and slope factors were allowed to covary (within and between both variables). Lastly, residual correlations between the (residuals of) measurement points of self-compassion and positive affect at the same time were estimated and allowed to vary across time (i.e., time-specific correlations).

Again, several restrictions were applied to the bivariate ALT-full model in order to further simplify the model without significantly decreasing model fit. When a restriction appeared to decrease the model fit, this restriction was removed from the model before the following restriction was applied. However, when a restriction did fit the data (i.e., no significant decrease in model fit), the following restriction was applied on top of this restriction. Subsequently, the following restrictions were imposed on the bivariate ALT-full model: (1) exclude AR and CL effects (ALT-LTM), (2) exclude the variance of the slope (ALT-no slope variance), (3) exclude the slope (ALT-no slope), (4) exclude the time-specific correlations (ALT-no time-specific correlations), (5) set the time-specific correlations equal to each other over time (ALT-time-specific correlation constrains), (6) set the AR effects to equality over time (ALT-AR constraints), and (7) set the CL effects equal to each other over time (ALT-CL constraints). Constraints 2, 3, 6, and 7 were applied to each variable (self-compassion and positive affect) separately, in which the order was defined based on the results of the previous model. Constraint 1 was applied to both variables simultaneously (see Supplementary Material B for the order of restrictions that was ultimately applied).
Supplementary Material B – Result section

Description of the univariate and bivariate models that were fitted and results of the final univariate ALT models

1. Univariate models

The model fit indices of the estimated univariate autoregressive latent trajectory (ALT) models for self-compassion, positive affect, and negative affect are shown in Table B.1. The estimated variances, covariances and correlations of the final univariate ALT models are presented in Table B.2. Only the parameters of the final univariate ALT models are discussed below.

1.1. Self-compassion

The univariate ALT-LTM model (model 2) fitted significantly worse than the univariate ALT-full model (model 1). When further simplifying the univariate ALT-full model, the variance of the slope could be removed (model 3) without decreasing model fit, meaning that there was no difference in rate of change (i.e., slope) of self-compassion between participants over the duration of the MBCL intervention. The model fit significantly worsened when removing the slope entirely (model 4), indicating that participants did change in their level of self-compassion over time. Lastly, in addition to removing the slope variance, the autoregressive (AR) effects could be set equal to each other over time (model 5), which yielded a more parsimonious model without decreasing model fit. Therefore, the univariate model without slope variance and including AR constraints was considered as the final model for self-compassion; it had a good fit to the data ($\chi^2 = 52.418, df = 30, p = .007; CFI = 0.955; TLI = 0.958; RMSEA = 0.085; SRMR = 0.122$).

When looking at the overall course of self-compassion, the results of the final univariate ALT model showed that participant’s self-compassion increased over the duration of the MBCL intervention ($\mu_{\text{SC}} = 0.095, s.e. = 0.018, p < .001$). Removing the slope variance yielded a similar model fit as the model including the variance of the slope factor, meaning that participants did not differ in their overall increase in self-compassion. Furthermore, a mean intercept factor of 4.211 with a significant variance ($\sigma_{\alpha_{\text{SC}}} = 0.825, s.e. = 0.177, p < .001$), and a mean of the first measurement point (i.e., session 1) of 4.993 with a significant variance ($\sigma_{\alpha_{\text{SC}(t1)}} = 2.246, s.e. = 0.314, p < .001$) was found. This indicates that participants differed in their general level and baseline level of self-compassion. Lastly, self-compassion at session 1 covaried positively with the intercept factor of self-compassion ($\psi_{\alpha_{\text{SC(SC(t1)}}} = 0.953, s.e. = 0.186, p < .001$).

In addition to the overall course of self-compassion, session-to-session effects were found. Results showed small AR effects ($\rho_{\text{AR}(1)_{\text{SC}}} = 0.214, s.e. = 0.053, p < .001$), meaning that the level of self-compassion at a specific session slightly predicted the level of self-compassion at the next session.
1.2. Positive affect

For positive affect, the univariate ALT-LTM model (model 2) fitted clearly worse than the univariate ALT-full model (model 1). Both, the slope variance (model 3) as well as the slope factor (model 4) could be removed without significantly decreasing model fit. However, constraining the AR (model 5) effects yielded a model that fitted significantly worse. Hence, the final univariate model for positive affect included an ALT model including an intercept factor and freely estimated AR effects. This final univariate ALT model had a very good fit to the data ($\chi^2 = 29.194, df = 25, p = .256; \text{CFI} = 0.985; \text{TLI} = 0.984; \text{RMSEA} = 0.040; \text{SRMR} = 0.084$).

The overall course of positive affect showed that positive affect did not decrease nor increase over the full MBCL period and this for all participants (i.e., the final model did not contain a slope factor nor a slope variance). Participants differed in both their general level of positive affect ($\mu_{\alpha_{\text{PA}}} = 4.633, \text{s.e.} = 0.302, p < .001; \sigma_{\alpha_{\text{PA}}} = 0.984, \text{s.e.} = 0.226, p < .001$), and their baseline levels of positive affect ($\mu_{\text{PA}(t_1)} = 5.465, \text{s.e.} = 0.166, p < .001; \sigma_{\text{PA}(t_1)} = 5.465, \text{s.e.} = 0.166, p < .001$). Finally, a positive covariance was found between positive affect at session 1 and the intercept of positive affect ($\psi_{\alpha_{\text{PA}},\text{PA}(t_1)} = 1.064, \text{s.e.} = 0.228, p < .001$).

Additionally, session-to-session AR effects were observed which varied slightly over time ($0.148 < \rho_{\text{AR}(1)_{\text{PA}}} < 0.246, 0.052 < \text{s.e.} < 0.057, .0001 < p < .007$). In general, higher levels of positive affect at one session predicted higher levels of positive affect at the following session.

1.3. Negative Affect

As the ALT-full model (model 1) did not fit the data significantly better than the ALT-LTM model (model 2) the AR effects could be removed from the ALT-full model (model 1). The ALT-LTM model (model 2) could further be constraint by removing the slope variance (model 3), however, removing the slope factor entirely (model 4) yielded a model that fitted the data significantly worse. The final model for negative affect therefore included an ALT model without slope variance and AR effects and had a good fit to the data ($\chi^2 = 38.050, df = 31, p = .179; \text{CFI} = 0.972; \text{TLI} = 0.975; \text{RMSEA} = 0.047; \text{SRMR} = 0.084$).

The overall course of negative affect showed a decrease over the duration of the MBCL intervention ($\mu_{\text{NA}} = - 0.068, \text{s.e.} = 0.029, p = .018$) that was constant across participants (i.e., the final model did not contain a slope variance). Participants differed in their general levels of negative affect ($\mu_{\alpha_{\text{NA}}} = 4.501, \text{s.e.} = 0.172, p < .001; \sigma_{\alpha_{\text{NA}}} = 1.963, \text{s.e.} = 0.324, p < .001$), and their baseline levels of negative affect ($\mu_{\text{NA}(t_1)} = 4.419, \text{s.e.} = 0.199, p < .001; \sigma_{\text{NA}(t_1)} = 4.002, \text{s.e.} = 0.565, p < .001$). Lastly, negative affect at session 1 covaried positively with the intercept factor of negative affect ($\psi_{\alpha_{\text{NA}},\text{NA}(t_1)} = 1.642, \text{s.e.} = 0.344, p < .001$).

Additional session-to-session effects for negative affect (i.e., AR effects) were not found.
2. Bivariate models
For the model fit indices of the consecutive bivariate AR, bivariate LTM, and bivariate ALT models that were fitted for both self-compassion and positive affect, as well as self-compassion and negative affect, see Table B.3.

2.1. Self-compassion and positive affect
The bivariate ALT-LTM model (model 2) fitted significantly worse than the bivariate ALT-full model based on the chi-square difference test (model 1). When further simplifying the bivariate ALT-full model by removing the slope variance of positive affect (model 3), the model fit significantly decreased, this model, however, yielded a small negative (non-significant) variance of the slope of positive affect, indicating a model convergence problem. As a consequence, the model fit values of this model cannot be fully trusted and therefore the slope variance of PA was removed. Excluding the slope of positive affect entirely (model 4) and the slope variance of self-compassion (model 5) yielded simpler models that fitted the data as good. However, removing the slope of self-compassion entirely (model 6) resulted in a model that fitted significantly worse. Therefore, the slope of self-compassion was retained in the model. The time-specific correlations could not be removed from the model (model 7), however setting the time-specific correlations equal to each other (model 8) was possible without decreasing model fit. Finally, constraining the AR effects over time for both self-compassion (model 9) and positive affect (model 10), and constraining the cross-lagged (CL) effects from positive affect (PA) to self-compassion (SC) over time (model 11), yielded simpler models without decreasing model fit. However, the CL effects from SC to PA (model 12) could not be set equal across time. As such, the bivariate ALT model that demonstrated the best fit to the data had no slope for positive affect, and no slope variance for self-compassion, equal time-specific correlations, equal AR effects over time for both SC and PA, and equal CL effects over time for PA to SC. This final bivariate ALT model provided an adequate model fit ($\chi^2 = 179.037$, $df = 112$, $p < .001$; CFI = 0.928; TLI = 0.924; RMSEA = 0.076; SRMR = 0.104).

2.2. Self-compassion and negative affect
The bivariate ALT-LTM model (model 2) fitted clearly worse than the bivariate ALT-full model (model 1). Removing the slope variance (model 3) and slope (model 4) of negative affect and the slope variance of self-compassion (model 5) was possible without decreasing model fit. However, removing the slope of self-compassion entirely resulted in a model that fitted significantly worse (model 6). Excluding the time-specific correlations clearly led to a significant decrease in model fit (model 7), however, constraining the time-specific correlations to equal each other led to a simpler model that fitted the data equally well (model 8). Further constraining the AR effects of both variables (model 9-10)
and constraining the CL effects from negative affect to self-compassion (model 11) and vice versa (model 12) yielded in more parsimonious models without significantly decreasing model fit. Therefore, the final bivariate ALT model that included no slope for negative affect, and no slope variance for self-compassion, equal time-specific, AR, and CL effects over time for both self-compassion and negative affect. This final bivariate ALT model provided a good model fit \( \chi^2 = 152.078, \hspace{1em} df = 118, \hspace{1em} p = .019; \hspace{1em} CFI = 0.959; \hspace{1em} TLI = 0.958; \hspace{1em} RMSEA = 0.053; \hspace{1em} SRMR = 0.091 \).
Table B.1. Model fit indices for the unconditional univariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for self-compassion, positive affect and negative affect

<table>
<thead>
<tr>
<th></th>
<th>$\chi^2$ (df)</th>
<th>CM</th>
<th>$\Delta\chi^2$ (df)</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>SRMR</th>
<th>AIC</th>
<th>BIC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-compassion</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>ALT - full model</td>
<td>40.855 (21)**</td>
<td>0.960</td>
<td>0.947</td>
<td>0.095</td>
<td>0.090</td>
<td>2146.848</td>
<td>2207.669</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>ALT - LTM model</td>
<td>56.917 (28)**</td>
<td>1</td>
<td>16.062 (7)*</td>
<td>0.942</td>
<td>0.942</td>
<td>0.100</td>
<td>0.087</td>
<td>2148.910</td>
</tr>
<tr>
<td>3</td>
<td>ALT - no slope variance</td>
<td>41.517 (24)*</td>
<td>1</td>
<td>0.662 (3) ns</td>
<td>0.965</td>
<td>0.959</td>
<td>0.084</td>
<td>0.093</td>
<td>2141.510</td>
</tr>
<tr>
<td>4</td>
<td>ALT - no slope</td>
<td>50.095 (25)**</td>
<td>3</td>
<td>8.578 (1)**</td>
<td>0.950</td>
<td>0.944</td>
<td>0.098</td>
<td>0.155</td>
<td>2148.087</td>
</tr>
<tr>
<td>5</td>
<td>ALT3 - AR constraints</td>
<td>52.418 (30)**</td>
<td>3</td>
<td>10.901 (6) ns</td>
<td>0.955</td>
<td>0.958</td>
<td>0.085</td>
<td>0.122</td>
<td>2140.410</td>
</tr>
<tr>
<td><strong>Positive affect</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>ALT - full model</td>
<td>24.005 (21) ns</td>
<td>-</td>
<td>0.990</td>
<td>0.986</td>
<td>0.037</td>
<td>0.064</td>
<td>2596.736</td>
<td>2657.557</td>
</tr>
<tr>
<td>2</td>
<td>ALT - LTM model</td>
<td>52.001 (28)**</td>
<td>1</td>
<td>27.996 (7)***</td>
<td>0.917</td>
<td>0.917</td>
<td>0.091</td>
<td>0.098</td>
<td>2610.732</td>
</tr>
<tr>
<td>3</td>
<td>ALT - no slope variance</td>
<td>28.914 (24) ns</td>
<td>1</td>
<td>4.909 (3) ns</td>
<td>0.983</td>
<td>0.980</td>
<td>0.044</td>
<td>0.079</td>
<td>2595.644</td>
</tr>
<tr>
<td>4</td>
<td>ALT - no slope</td>
<td>29.194 (25) ns</td>
<td>3</td>
<td>0.280 (1) ns</td>
<td>0.985</td>
<td>0.984</td>
<td>0.040</td>
<td>0.084</td>
<td>2593.924</td>
</tr>
<tr>
<td>5</td>
<td>ALT4 - AR constraints</td>
<td>43.411 (31) ns</td>
<td>4</td>
<td>14.217 (6)*</td>
<td>0.957</td>
<td>0.961</td>
<td>0.062</td>
<td>0.098</td>
<td>2596.141</td>
</tr>
<tr>
<td><strong>Negative affect</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>ALT - full model</td>
<td>26.861 (21) ns</td>
<td>-</td>
<td>0.977</td>
<td>0.969</td>
<td>0.052</td>
<td>0.076</td>
<td>2815.619</td>
<td>2876.440</td>
</tr>
<tr>
<td>2</td>
<td>ALT - LTM model</td>
<td>36.553 (28) ns</td>
<td>1</td>
<td>9.692 (7) ns</td>
<td>0.966</td>
<td>0.966</td>
<td>0.054</td>
<td>0.079</td>
<td>2811.311</td>
</tr>
<tr>
<td>3</td>
<td>ALT2 - no slope variance</td>
<td>38.050 (31) ns</td>
<td>2</td>
<td>1.497 (3) ns</td>
<td>0.972</td>
<td>0.975</td>
<td>0.047</td>
<td>0.084</td>
<td>2806.808</td>
</tr>
<tr>
<td>4</td>
<td>ALT2 - no slope</td>
<td>43.519 (32) ns</td>
<td>3</td>
<td>5.469 (1)*</td>
<td>0.954</td>
<td>0.960</td>
<td>0.059</td>
<td>0.091</td>
<td>2810.277</td>
</tr>
<tr>
<td>5</td>
<td>ALT3 - AR constraints</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Note. $\chi^2$ = chi-square test of model fit; df = degrees of freedom; $\Delta\chi^2$ = chi-square difference test; CM = comparison model in the $\Delta\chi^2$; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean-square residual; AIC = Akaike information criterion; BIC = Bayesian information criterion. The final ALT model is shown in bold. Note that constraining the AR effects of the univariate ALT model of negative affect has not been carried out, because the LTM model (which does not contain AR effects) was previously preferred over the ALT-full model. $^*$ $p \leq .050$, $^*$ $p < .050$, $^{**} p < .010$, $^{***} p < .001$. 
Table B.1. Model fit indices for the unconditional univariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for self-compassion, positive affect and negative affect

<table>
<thead>
<tr>
<th></th>
<th>Session 1</th>
<th>Intercept</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Self-compassion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>2.246*** (0.314)</td>
<td>.700</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.953*** (0.186)</td>
<td>0.825*** (0.177)</td>
</tr>
<tr>
<td><strong>Positive affect</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>2.784*** (0.394)</td>
<td>.643</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.064*** (0.228)</td>
<td>0.984*** (0.226)</td>
</tr>
<tr>
<td><strong>Negative affect</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>4.002*** (0.565)</td>
<td>.586</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.642*** (0.344)</td>
<td>1.963*** (0.324)</td>
</tr>
</tbody>
</table>

Note. χ² = chi-square test of model fit; df = degrees of freedom; Δχ² = chi-square difference test; CM = comparison model in the Δχ²; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean-square residual; AIC = Akaike information criterion; BIC = Bayesian information criterion. The final ALT model is shown in bold. Note that constraining the AR effects of the univariate ALT model of negative affect has not been carried out, because the LTM model (which does not contain AR effects) was previously preferred over the ALT-full model. 

Table B.2. Variances, covariances and correlations between session 1 and the intercept factor for self-compassion, positive affect and negative affect based on each final univariate autoregressive latent trajectory (ALT) model

<table>
<thead>
<tr>
<th></th>
<th>Session 1 Intercept</th>
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<tbody>
<tr>
<td><strong>Self-compassion</strong></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>2.246*** (0.314)</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.953*** (0.186)</td>
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<tr>
<td><strong>Positive affect</strong></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>2.784*** (0.394)</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.064*** (0.228)</td>
</tr>
<tr>
<td><strong>Negative affect</strong></td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>4.002*** (0.565)</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.642*** (0.344)</td>
</tr>
</tbody>
</table>

Note. Variances are depicted on the diagonal, covariances below and correlations above the diagonal for each variable separately. Standard errors are shown between parenthesis. The slope factor is omitted from this table, given that no slope variances were fitted in the final univariate ALT models. Level of significance is indicated for the covariances and variances only. ns p ≥ .050, * p < .050, ** p < .010, *** p < .001.
Table B.3. Model fit indices for the unconditional bivariate autoregressive (AR), latent trajectory models (LTM) and autoregressive latent trajectory (ALT) models for self-compassion (SC), positive affect (PA) and negative affect (NA)

<table>
<thead>
<tr>
<th>Model</th>
<th>$\chi^2$ (df)</th>
<th>CM</th>
<th>$\Delta\chi^2$ (df)</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>SRMR</th>
<th>AIC</th>
<th>BIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALT - full model</td>
<td>129.403 (76)**</td>
<td>0.943</td>
<td>0.911</td>
<td>0.082</td>
<td>0.073</td>
<td>4641.275</td>
<td>4842.249</td>
<td></td>
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</tr>
<tr>
<td>ALT - LTM model</td>
<td>257.785 (111)**</td>
<td>1</td>
<td>128.382 (35)**</td>
<td>0.846</td>
<td>0.833</td>
<td>0.113</td>
<td>0.095</td>
<td>4699.657</td>
<td>4808.077</td>
</tr>
<tr>
<td>ALT - no slope variance PA</td>
<td>143.749 (82)**</td>
<td>1</td>
<td>14.346 (6)*</td>
<td>0.934</td>
<td>0.904</td>
<td>0.085</td>
<td>0.075</td>
<td>4643.621</td>
<td>4828.728</td>
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<tr>
<td>ALT - no slope on PA</td>
<td>144.215 (83)**</td>
<td>3</td>
<td>0.466 (1) ns</td>
<td>0.935</td>
<td>0.906</td>
<td>0.084</td>
<td>0.078</td>
<td>4642.087</td>
<td>4824.550</td>
</tr>
<tr>
<td>ALT4 - no slope variance SC</td>
<td>149.219 (88)**</td>
<td>4</td>
<td>5.004 (5) ns</td>
<td>0.935</td>
<td>0.912</td>
<td>0.082</td>
<td>0.080</td>
<td>4637.091</td>
<td>4806.332</td>
</tr>
<tr>
<td>ALT4 - no slope on SC</td>
<td>160.075 (89)**</td>
<td>5</td>
<td>10.856 (1)*</td>
<td>0.924</td>
<td>0.899</td>
<td>0.088</td>
<td>0.105</td>
<td>4645.947</td>
<td>4812.544</td>
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<tr>
<td>ALT5 - no time-specific correlations</td>
<td>226.177 (95)**</td>
<td>5</td>
<td>76.958 (7)*</td>
<td>0.860</td>
<td>0.825</td>
<td>0.115</td>
<td>0.092</td>
<td>4700.049</td>
<td>4850.779</td>
</tr>
<tr>
<td>ALT5 - time-specific correlation constrains</td>
<td>155.827 (94)**</td>
<td>5</td>
<td>6.608 (6) ns</td>
<td>0.934</td>
<td>0.916</td>
<td>0.080</td>
<td>0.085</td>
<td>4631.699</td>
<td>4785.073</td>
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<tr>
<td>ALT8 - AR constraints SC</td>
<td>164.151 (100)**</td>
<td>8</td>
<td>8.324 (6) ns</td>
<td>0.932</td>
<td>0.919</td>
<td>0.079</td>
<td>0.096</td>
<td>4628.023</td>
<td>4765.531</td>
</tr>
<tr>
<td>ALT9 - AR constraints PA</td>
<td>170.002 (106)**</td>
<td>9</td>
<td>5.851 (6) ns</td>
<td>0.932</td>
<td>0.923</td>
<td>0.076</td>
<td>0.098</td>
<td>4621.874</td>
<td>4743.516</td>
</tr>
<tr>
<td>ALT10 - CL constraints from PA to SC</td>
<td>179.037 (112)**</td>
<td>10</td>
<td>9.035 (6) ns</td>
<td>0.928</td>
<td>0.924</td>
<td>0.076</td>
<td>0.104</td>
<td>4618.909</td>
<td>4724.684</td>
</tr>
<tr>
<td>ALT11 - CL constraints from SC to PA</td>
<td>191.835 (118)**</td>
<td>11</td>
<td>12.798 (6) *</td>
<td>0.921</td>
<td>0.921</td>
<td>0.078</td>
<td>0.108</td>
<td>4619.707</td>
<td>4709.616</td>
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</tbody>
</table>

Note. $\chi^2$ = chi-square test of model fit; df = degrees of freedom; $\Delta\chi^2$ = chi-square difference test; CM = comparison model in the $\Delta\chi^2$; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean-square residual; AIC = Akaike information criterion; BIC = Bayesian information criterion. The final ALT models are shown in bold.

*a* model retained given that the ALT-full model yielded a small negative non-significant variance of the slope of positive affect.

Ns. $p \geq .050$, *$p < .050$, ***$p < .001$. 

<table>
<thead>
<tr>
<th>Model</th>
<th>$\chi^2$ (df)</th>
<th>CM</th>
<th>$\Delta\chi^2$ (df)</th>
<th>CFI</th>
<th>TLI</th>
<th>RMSEA</th>
<th>SRMR</th>
<th>AIC</th>
<th>BIC</th>
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<tbody>
<tr>
<td>ALT - full model</td>
<td>129.403 (76)**</td>
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<td>0.911</td>
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<td>14.346 (6)*</td>
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<tr>
<td>ALT - no slope on PA</td>
<td>144.215 (83)**</td>
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<td>0.466 (1) ns</td>
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<td>0.906</td>
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<tr>
<td>ALT4 - no slope variance SC</td>
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<td>5.004 (5) ns</td>
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<td>ALT5 - no time-specific correlations</td>
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<td>76.958 (7)*</td>
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<tr>
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<td>8</td>
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<td>0.079</td>
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<td>ALT9 - AR constraints PA</td>
<td>170.002 (106)**</td>
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<td>5.851 (6) ns</td>
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<td>ALT10 - CL constraints from PA to SC</td>
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<td>0.924</td>
<td>0.076</td>
<td>0.104</td>
<td>4618.909</td>
<td>4724.684</td>
</tr>
<tr>
<td>ALT11 - CL constraints from SC to PA</td>
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<td>1</td>
<td>ALT - full model</td>
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<td>ALT - LTM model</td>
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<td>7</td>
<td>ALT5 - no time-specific correlations</td>
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<td>5</td>
<td>55.951 (7)***</td>
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<td>0.960</td>
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<tr>
<td>12</td>
<td>ALT11 - CL constraints from SC to NA</td>
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<td>11</td>
<td>8.969 (6) ns</td>
<td>0.959</td>
<td>0.958</td>
<td>0.053</td>
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</tr>
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Note. χ² = chi-square test of model fit; df = degrees of freedom; Δχ² = chi-square difference test; CM = comparison model in the Δχ²; CFI = comparative fit index; TLI = Tucker-Lewis index; RMSEA = root-mean-square error of approximation; SRMR = standardized root-mean-square residual; AIC = Akaike information criterion; BIC = Bayesian information criterion. The final ALT models are shown in bold. * model retained given that the ALT-full model yielded a small negative non-significant variance of the slope of positive affect. ns p ≥ .050, * p < .050, *** p < .001.
Summary and general discussion
This chapter contains a short background and an overview of the findings from the current thesis, which will then be elaborated upon in relation to the existing literature. In addition, strengths and limitations are identified and directions for future research and clinical implications are given.

1. Summary

Major depressive disorder (MDD) is a common psychiatric disorder in which emotion regulation plays an important role (Joormann & Stanton, 2016; World Health Organization, 2017). Along with the diminished experience of positive emotions, the frequent experience of negative emotions is a key characteristic of depressive symptomatology (American Psychiatric Association, 2013). Currently, MDD is a leading cause of disease burden worldwide (World Health Organization, 2017). The most commonly used treatment to prevent new episodes of depression is the use of antidepressant medication (Spijker et al., 2013). However, the use of antidepressant medication also has disadvantages (i.a. long-term use and side effects) and many patients prefer psychological interventions (Biesheuvel-Leliefeld et al., 2015). Fortunately, numerous psychological interventions have been developed for MDD which appear a good alternative to antidepressants (Biesheuvel-Leliefeld et al., 2015; Breedvelt et al., 2021), including mindfulness-based cognitive therapy (MBCT; Segal et al., 2002, 2012). MBCT is an eight-week group training, which aims to develop a decentered perspective from currently arising thoughts, emotions, physical sensations and automatic behavioral patterns, and teaches individuals to approach these in an open, curious, accepting and non-judgmental way (Baer et al., 2019; Kabat-Zinn, 1994; Segal et al., 2012). Accumulating evidence suggests that MBCT is effective in both reducing risk of relapse/recurrence as well as reducing depressive symptoms in depressed patients (Thimm & Johnson, 2020). However, many people still experience residual depressive symptoms after MBCT, which are a predictor for relapse into depression (Buckman et al., 2018).

In order to further improve outcomes in individuals with recurrent depression, further knowledge is needed on how to best adapt and apply MBCT to maximize its benefits. Research into how MBCT for depression works and for whom MBCT might be particularly beneficial, is developing. In parallel, mindfulness-based compassionate living (MBCL; van den Brink & Koster, 2015) has been developed as a follow-up training to mindfulness-based interventions (MBIs), with the intention to offer (self-)compassion building on already established mindfulness skills. (Self-)compassion encompasses the capacity to be sensitive to the suffering of self and others, and the commitment to alleviate or prevent this suffering (Gilbert & Choden, 2013). Although there is promising evidence
that MBCL reduces depressive symptoms in individuals with recurrent depression (Schuling, Huijbers, van Ravesteijn, Donders et al., 2020), research into its working mechanisms is still in its infancy. The current thesis aimed to shed more light on how MBCT and MBCL work in individuals with recurrent depression.

Previous evidence supports the notion that increases in mindfulness are associated with increases in positive affect and decreases in negative affect. However, knowledge of the dynamic processes and temporal order of these changes in recurrently depressed individuals during MBCT is still limited. To this end, Chapter 2 expanded previous literature by investigating the course and mutual associations of mindfulness and both positive and negative affect in patients with recurrent depression in (partial) remission participating in MBCT ($n = 235$). Assessments of mindfulness, positive affect, and negative affect took place prior to each MBCT session. Autoregressive latent trajectory (ALT) modeling showed that mindfulness and positive affect increased over the course of MBCT, while levels of negative affect showed a more irregular course. Individuals with larger increases in mindfulness showed significantly larger increases in positive affect. Moreover, individuals with higher general levels of negative affect showed less increase in their levels of mindfulness during MBCT. Against expectations, no robust evidence was found for reciprocal cross-lagged effects between mindfulness and positive or negative affect between each successive session.

An improvement in mindfulness skills is hypothesized to be related to mindfulness practice, which is considered a key element in increasing treatment effectiveness of MBCT for depression (Segal et al., 2012). Although there is evidence to support this hypothesis (Parsons et al., 2017), more fine-grained studies are needed into both short- and long-term effects of formal mindfulness practice in MBCT for clinical populations. Chapter 3 therefore presented the results of investigating prospective associations between the extent of formal mindfulness practice and depression severity, and vice versa, during 15 months of follow-up in individuals with recurrent depression in (partial) remission ($n = 200$). Formal home practice frequency was calculated for each 3-month period. Depressive symptoms were assessed at 3-month intervals: 0 (baseline), 3 (post-treatment), 6, 9, 12, and 15 months. Participants appeared to practice formal mindfulness exercises with a mean of 4 days per week during MBCT, but the frequency of practice declined rapidly thereafter. The level of depressive symptoms did not change over the full study period. Against expectations, no clear evidence was found that the amount of formal mindfulness practice during each 3-month period influences subsequent depressive symptom severity. In contrast, severity of depression did seem to be associated with practicing less frequently during the subsequent 3-month period, suggesting that depressive symptoms might indeed act as a barrier for practice.
Looking at participant characteristics to see who benefits most from MBCT is another way to potentially maximize treatment effect. As described in the general introduction, evidence suggests stronger treatment effects of MBCT for depression in those with increased vulnerability, particularly those with more pronounced residual symptoms at baseline (Kuyken et al., 2016). However, studies to date have methodological limitations, including a limited range of baseline depression levels, a focus on ‘negative’ outcomes, a restriction to two-way interactions, and no distinction between quantitative and qualitative treatment-subgroup interactions. For optimal treatment assignment in clinical practice, however, knowledge about for which subgroup treatment A outperforms treatment B, and for whom the reverse holds true, qualitative treatment-subgroup interactions are needed. Hence, Chapter 4 aimed to bring the field further by applying the qualitative interaction trees method (QUINT; Dusseldorp & van Mechelen, 2014), which identifies qualitative treatment-subgroup interactions, allowing for non-linear relationships and considering higher order interaction effects. This method was applied on individual patient data based on three RCTs investigating the effect of MBCT + TAU versus TAU alone ($n = 292$). Individuals were either in (partial) remission, currently depressed or had chronic, treatment-resistant depression. Outcomes were depressive symptoms and quality of life. Results showed that MBCT + TAU outperformed TAU alone in reducing depressive symptoms. For both conditions, the effect of baseline depressive symptoms on post-treatment depressive symptoms was curvilinear. This indicates that in both, MBCT + TAU and TAU alone, individuals who fall into the ‘high’ and ‘low ends’ of depression severity were less likely to benefit from either treatment. For individuals with an earlier onset of depression and higher levels of rumination, MBCT + TAU was more beneficial than TAU alone in terms of depressive symptom reduction. For patients with a lower quality of life, MBCT + TAU was more beneficial than TAU alone in terms of improving quality of life.

In parallel to investigating the interplay between mindfulness and affect during MBCT for depression, the possible interplay between self-compassion and affect was investigated during MBCL as follow-up intervention after MBCT. Again, multiple assessments over time were analyzed with the ALT modeling technique. Chapter 5 expanded previous literature by investigating the interplay between self-compassion and positive and negative affect during MBCL as a follow-up intervention to MBCT in individuals in remission or currently depressed ($n = 104$). Results from the ALT modeling analyses showed that self-compassion increased, while positive affect remained stable and negative affect decreased over time. In addition, no reciprocal effects were found between self-compassion and subsequent positive affect, nor vice versa, between each successive session. Although there were no effects from negative affect at one session to self-
compassion at the next session, we did find evidence for the reverse: higher levels of self-compassion at one session did predict lower levels of negative affect at the next session.

2. General discussion

2.1. “How does MBCT for depression work?”

Theory suggests that mindfulness should increase following MBCT (Segal et al., 2012). This was indeed confirmed in the results from Chapter 2 of this thesis, as for individuals with recurrent depression, levels of mindfulness increased during MBCT. This finding is also consistent with the literature to date (van der Velden et al., 2015). In addition to the increase of mindfulness, the current thesis found increases in levels of positive affect during MBCT for depression. Moreover, greater increases in levels of mindfulness were associated with greater increases in positive affect during MBCT for depression. This is in line with the mindfulness-to-meaning theory (MMT; Garland et al., 2015), which states that mindfulness is a central mechanism for energizing upward spirals of positive psychological processes (e.g., resilience). As Segal et al. (2012) suggested that practicing (self-)compassion without a foundation in mindfulness may trigger vulnerability in clinically depressed individuals, this may be a supportive starting point for exposing oneself to more difficult emotions during MBCL for depression.

Unexpectedly, negative affect did not significantly decrease over the MBCT course (Chapter 2). This is contrary to findings of previous studies, for example Batink et al. (2013), who found that negative affect significantly mediated the efficacy of MBCT for depression. An explanation could be the absence of a clear main effect of MBCT on depression severity found in the clinical trials from which the current data were derived (Huijbers et al., 2015, 2016), which may have been due to the overall lower teacher competency in these studies compared to previous studies (Kuyken et al., 2008; Kuyken et al., 2015; Segal et al., 2010), and the inclusion of individuals in remission at baseline, leaving less room for improvement in terms of depression severity. Another explanation could be that participants became more able to observe negative affect rather than engaging in elaboration or rumination, which can, but does not necessarily, lead to a reduction of negative affect. According to the MMT (Garland et al., 2015), mindfulness helps to decenter from dysphoric schemas which result in attentional biases towards negative life events, and broadens the attentional field to encompass an expanded set of positive and negative life events (i.e., a more balanced view of what is occurring). This touches upon a paradox within mindfulness research. Negative mental health outcomes, such as reduction of depressive symptoms are commonly used, although these may not be the most
suitable outcome for mindfulness research. When developing mindfulness, one learns to approach experiences in a non-judgmental, kind and accepting way rather than striving to change the experiences themselves. Therefore, outcome measures encompassing attitude, resilience, and more positive health outcomes such as well-being or life-satisfaction might be more suitable.

The current thesis revealed that negative affect might act as a barrier to develop mindfulness during MBCT for depression (Chapter 2). While most studies have investigated the association between mindfulness and subsequent levels of negative affect, reverse associations between negative affect and subsequent levels of mindfulness have been studied less and show mixed results (e.g., Gotink et al., 2016; Snippe et al., 2015). An advantage of the analyses used in the current thesis is that the interrelationship between mindfulness and affect was modeled in both directions within a single model (i.e., between mindfulness and negative affect, as well as reversed associations), while controlling for overall trajectories of both variables over time, decreasing the chance to find spurious effects (Voelkle, 2008). However, the possible inhibiting role of negative affect on developing mindfulness needs to be further examined and replicated before clinical implications can be formulated. Preferably with the use of multiple assessments of both constructs over time, also after the intervention period, and the use of advanced statistical techniques (e.g., ALT modeling).

In sum, positive affect plays a prominent role in MBCT for depression in which negative affect might act as a barrier to develop mindfulness. However, results are preliminary and should be replicated first before recommendations for clinical practice can be formulated.

Against expectations, the current thesis found no support for the effect of formal mindfulness practice frequency on depressive symptoms (Chapter 3). This is in contrast to a systematic review and meta-analysis by Parsons et al. (2017), who found a small but significant association between the extent of formal mindfulness home practice and improvements after MBCT and MBSR for a wide range of clinical and non-clinical populations. When taking a closer look at studies that investigated the association between formal mindfulness practice and both short- and long-term outcomes of MBCT in depression, most studies yielded positive effects (i.e., Crane et al., 2014; Hawley et al., 2014, van Aalderen et al., 2012, Geschwind et al., 2012), but some also reported non-significant findings (i.e., Bondolfi et al., 2010; Shallcross et al., 2015).

An explanation for the differences in results found may include differences in the amount of formal mindfulness practice reported, and the rapid decline of engagement in formal mindfulness practice over time. Non-compliance of home practice during and after psychological interventions remains a common problem in clinical practice (Bondolfi et al., 2010; Gaynor et al., 2006). Segal et al. (2019), suggested that improved outcome in individuals with recurrent
depression requires sustained skills utilization beyond the end of MBCT. However, we cannot preclude generalization of adaptive coping skills over time. It might be that individuals tend to engage less in formal but more in informal mindfulness practice over time (e.g., Bondolfi et al., 2010). In addition, non-monotonicity of effects (i.e., an inverted U-curve) of mindfulness practice could provide an overarching explanatory framework for the mix of positive and null findings in mindfulness research (Britton, 2019). For example, it has been suggested that MBCT is less effective for those at the lowest or highest end of the spectrum of depression levels (Kuyken et al., 2016; van Dam et al., 2018). For future research it would be a step forward to examine the effects of adherence prospectively and randomized controlled rather than through secondary analyses (Dimidjian & Segal, 2015). For example, direct comparisons of effectiveness between groups containing different amounts of mindfulness practice, including no mindfulness practice at all, could be considered. Similar research in cognitive behavioral therapy (CBT; Beck et al., 1979), showed that study conditions including homework as a main component produce superior treatment effects to those that do not (Kazantzis et al., 2010). Moreover, next to quantity of practice, quality of practice may also impact outcome (Kazantzis et al., 2016). As discussed before, mindfulness does not only involve self-regulation of attention to the present moment experience (i.e., the ‘what’) but it also involves an open, curious, accepting and non-judgmental attitude towards one’s experience (i.e., the ‘how’; Baer et al., 2019). Recent developments focusing on practice quality show an additive (or even stronger) effect of practice quality on trait mindfulness (Hassed et al., 2020) and outcome (Del Re et al., 2013; Goldberg et al., 2014, 2020) compared to practice quantity. Thus, it is recommended to include both amount of time spent engaged in practice (i.e., quantity) and the acquired skills in meaningful attentional focus and non-judgmental acceptance (i.e., quality) in future research studying the impact of mindfulness practice on outcome.

The current thesis did not find effects of formal mindfulness practice on outcome, but reverse effects were found: higher levels of depressive symptoms at each measurement point (0, 3, 6, 9, 12, and 15 months of follow-up) were followed by less frequent formal mindfulness practice during the subsequent 3-month periods in individuals with recurrent depression following MBCT (Chapter 3). This is a remarkable finding, given that previously found negative associations were based on correlational designs (Parsons et al., 2017) and usually interpreted as improved outcomes due to more mindfulness practice. To date, a reverse effect has not yet been investigated in MBCT for depression, and this might shed a new light on the association between formal home practice and depressive symptoms in MBCT for recurrent depression. The current finding that depressive symptomatology may hinder engaging in mindfulness practices is in line with the previous finding from Chapter 2 that negative affect
might act as a barrier to develop mindfulness during MBCT for depression and with findings by Banerjee et al. (2018) that rumination and worry may increase risk of disengagement which may in turn hinder cultivating mindfulness. Qualitative research into barriers and facilitators associated with engagement in mindfulness practices could provide more insight in the underlying processes. To date, qualitative studies have reported that a lack of group support, physical discomfort, feeling exhausted or disoriented, self-doubt and long practices may hinder engaging in meditation practice, while prior knowledge on mindfulness, positive beliefs, motivation, perceptions of consequences (e.g., improved well-being, change in self-compassion, and increased sense of agency of thoughts) and long-term connection (e.g., refresher sessions, post-course retreats) may facilitate meditation practice (Banerjee et al., 2017; Dobkin et al., 2012; Langdon et al., 2011; Lomas et al., 2015). According to a grounded-theory study on mindfulness practice after MBCT by Langdon et al. (2011), individuals felt they needed to bypass cognitions and feelings that could act as obstacles to practice by “just doing it”. This fits the the well-known advice about practicing “You don’t have to like it, you just have to do it” (Kabat-Zinn, 1990).

To conclude, the interplay between mindfulness practice and outcome might not be as straightforward as assumed. This underlines the importance of replication studies and publishing of negative study results. In addition, preliminary results suggest that depressive symptoms might act as a barrier to carrying out mindfulness practices, which is in accordance with the preliminary evidence found in the current thesis that negative affect might acts as a barrier to develop mindfulness in MBCT for depression.

2.2. “For whom does MBCT for depression work?”
In MBCT, one learns to recognize automatic activation of their habitual dysfunctional cognitive processes that lead to depression (e.g., rumination), and decenter and disengage from these dysfunctional processes. The current thesis suggests that MBCT + TAU is more beneficial than TAU alone for those individuals with an earlier age of onset of MDD and higher baseline levels of rumination, and for those with a lower baseline quality of life (Chapter 4). This is in line with the underlying theoretical model, called the ‘differential activation hypothesis’ (Teasdale, 1988), which assumes that vulnerability to depression increases with each depressive episode, because previous patterns of negative thinking become more easily accessible when feeling low. In addition, current findings are in line with previous studies suggesting that effects of MBCT for depression may be moderated by vulnerability factors such as individuals with three or more previous major depressive episodes, earlier onset of MDD (Ma & Teasdale, 2004; Teasdale et al., 2000), a history of early adversity (Kuyken et al., 2015; Williams et al., 2014) and more fluctuation in depressive symptoms (Segal et al., 2010). Although the current research included patients with a wide range
of baseline depressive symptoms, it should be noted that very severely depressed patients (≥ 37 points on the HRSD-17; Hamilton, 1960), were not included. For this specific patient group, no statements can be made about whether MBCT for depression can be of added value or has a possible countereffect (e.g., less effective or causing harm).

The current thesis did not find support for the hypothesis that baseline depressive symptoms would moderate the intervention effect (Chapter 4). This is seemingly in contrast with the results of the individual patient data (IPD) meta-analysis by Kuyken et al. (2016), which found that severity of baseline depressive symptoms predicted a better response to MBCT in terms of prevention of relapse. It also seems to contrast with the preliminary evidence found in the current thesis that depressive symptoms possibly impede engagement in mindfulness practice (Chapter 3) and that negative affect might act as a barrier to develop mindfulness in recurrently depressed individuals (Chapter 2). However, the IPD meta-analysis was restricted to individuals with recurrent depression in (partial) remission, limiting the range of baseline depression severity, which might be in line with the upward slope of the inverted U-curve (Britton, 2019; ter Avest et al., 2019). In addition, differences in statistical approaches may account for the differences in results found. Most studies into possible moderators of treatment effect assumed linear associations and considered two-way interaction effects (e.g., Kuyken et al., 2016), whereby no distinction could be made between quantitative and qualitative treatment-subgroup interactions. The current thesis used the QUINT method, which focuses on identifying qualitative treatment-subgroup interactions, allows for non-linear relationships and considers higher order interactions effects. Other moderator variables found (e.g., rumination levels, age of onset, quality of life) had a stronger impact on intervention outcome than baseline depressive symptoms, which did not emerge as a clear moderator.

In conclusion, the current thesis found the strongest support for vulnerability factors age of MDD onset and rumination to moderate treatment effect of MBCT for depression, in which individuals with an earlier age of onset and higher levels of rumination were more likely to benefit from MBCT.

2.3. “How does MBCL for depression work?”

Theory suggests that self-compassion should increase following MBCL (van den Brink & Koster, 2015; Segal et al., 2012). This was indeed confirmed in a trial of MBCL for individuals with recurrent depression (Schuling, Huijbers, van Ravesteijn, Donders, et al., 2020) and secondary analyses of these data showing week-to-week improvements in self-compassion as reported in this thesis. These findings are also consistent with the literature to date (Ferrari et al., 2019).

As expected, negative affect decreased during MBCL for depression, which was preceded by increases in self-compassion (Chapter 5). This is in line with
previous (experimental) studies (e.g., Diedrich et al., 2014). In MBCT, one develops a non-judgmental stance towards the self and others and becomes more aware of both positive and negative emotions, thoughts, and bodily sensations, and their accompanied automatic reactions. However, according to a recent qualitative study into the added value of MBCL in recurrently depressed individuals (Schuling, Huijbers, van Ravesteijn, Kuyken, & Speckens, 2020), participants stated that, during MBCT, they had been able to remain in a more ‘neutral’ observing stance towards difficult emotions, thoughts and bodily sensations. As MBCT lacked the active invitation to approach these difficulties, it was possible to continue not engaging with strongly-rooted avoidance patterns. It may be that individuals with recurrent depression need more explicit instructions and practice to develop a compassionate attitude to both self and others, especially during negative experiences, as they are often highly self-critical and suffer from feelings of shame, guilt and inferiority (Gilbert et al., 2012; Gilbert et al., 2008; Gilbert & Procter, 2006). MBCL explicitly focuses on developing (self-)compassion by deliberately exposing oneself to unpleasant feelings, thoughts and bodily sensations, while learning new ways to alleviate and soothe oneself in the midst of this in a non-judgmental and friendly way (van den Brink & Koster, 2015).

Clear differences were found between MBCT and MBCL in the trajectories of positive and negative affect (Chapter 2 and 5), which suggests that different affective processes are taking place in MBCT as compared to MBCL for depression. It might be that positive affect plays a more prominent role in MBCT for depression, which seem to tie in nicely with existing therapies for MDD, such as antidepressants and cognitive therapy, since these therapies are suggested to repair negative affect more effectively than positive affect (Dunn et al., 2020). As previous studies show that repair of positive affect is perceived at least as important as reduction in negative affect in individuals recovering from depression (Demyttenaere et al., 2015; Zimmerman et al., 2006), and existing mainstream treatments fail to normalize levels of positive affect (Dunn et al., 2020), this indicates that there is still room for improvement. Besides MBCT, various drugs (e.g., Jamerson et al., 2003; Lally et al., 2015; Tomarken et al, 2004) and modified psychotherapies targeting positive affect and wellbeing are emerging (e.g., Geschwind et al., 2019, Craske et al., 2019; Ruini & Fava, 2012; Dunn et al., 2019; Chaves et al., 2017). It may be that further normalizing levels of positive affect leads to a more equanimous state of mind.

Whereas positive affect plays a more prominent role in MBCT, cultivating (self-)compassion during MBCL may more explicitly target negative affect. However, results are preliminary and should be replicated first before recommendations for clinical practice can be formulated. In addition, as MBCL was not directly compared to another active control condition as follow-up to MBCT, this leaves little information about the specificity of MBCL. Lastly, as the
sequential treatment design was pragmatic in nature (i.e., participation was offered to all former MBCT participants who met the in- and exclusion criteria), little is known about the characteristics of those who responded versus those who did not. Consequently, possible selection bias cannot be ruled out (e.g., selection of participants for whom MBCT might have been less effective).

2.4. Strengths, limitations and future directions
2.4.1. Statistical approaches
A major strength of the current thesis is the use of advanced statistical methodology. With the inclusion of multiple measurements over time and the use of the ALT modeling technique, a clear distinction could be made between the overall course of each variable over time and the reciprocal effects between the variables on a session-to-session basis. This made it possible to study processes between mindfulness, self-compassion and positive and negative affect over time in much more detail compared to pre-post study designs. As a result, this design increased the opportunity to infer possible causation (Voelkle, 2008).

In addition to the ALT modeling technique, the QUINT method was applied. This method identifies subgroups of individuals in which one treatment is more beneficial than another, which makes it especially suited for situations in which many potential moderating variables might be interacting with the treatment variable without clear a priori hypotheses. The result of an analysis with QUINT is a binary tree from which (new) hypotheses on treatment assignment criteria can be derived, relevant for clinical practice. The current thesis found support that MBCT in addition to TAU is more beneficial than TAU alone for those with higher rumination levels and an earlier age of MDD onset, and for those with a lower quality of life. However, before definite treatment assignment criteria can be formulated and implemented in clinical practice, the current findings should be replicated, treatment outcome of the cut-off scores should be estimated in an independent test dataset and, preferably, also long-term outcomes should be included in future research. Currently, the field of personalized psychological treatment is expanding rapidly and new approaches, such as network estimation techniques (Boschloo et al., 2019), machine learning (Lutz et al., 2019), and the use of large observational data from routine practice (Kessler et al., 2019) are promising developments, which is setting in a shift from a nomothetic to a more idiographic approach (Hofmann & Hayes, 2019). While new statistical approaches may add to the knowledge for whom existing therapies could be most beneficial, they could also lead to further knowledge about the underlying mechanisms of change, which may lead to combining elements from different interventions in order to target the underlying process more effectively (Hofmann & Hayes, 2019; Rosen and Davison, 2003).
2.4.2. Design and population

The findings of this thesis advance previous and mostly cross-sectional correlation research, by using prospective study designs including multiple measurements over both short- and long-term periods. In addition, most studies were based on multicenter RCTs which were embedded in standard clinical practice with few exclusion criteria. This real-life setting increases the generalizability of the current findings to (recurrently) depressed individuals in both secondary and tertiary care. There were also some limitations.

First of all, when investigating processes of change, the current studies did not include process data of the control groups. Therefore, it cannot be ruled out that the associations found in the current studies are not specific to MBCT and MBCL. Future research should collect process data from both an intervention and a -preferably active- control condition to determine specificity of change. In addition, it is encouraged to use state-of-the art experience sampling methods (ESM; Larson & Csikszentmihalyi, 1983) that use a high sampling frequency and app-based measurements to investigate the processes of change during MBCT and MBCL on a smaller time scale and with enhanced accuracy. Moreover, it would be valuable to include outcome measures (e.g., depressive symptoms, quality of life) to further determine changes in process measures (e.g., mindfulness, self-compassion, affect) as possible mechanisms of change in MBCT and/or MBCL for depression (Kazdin, 2007).

Secondly, the current thesis only investigated the influence of mindfulness practice in terms of its quantity, lacking data on its quality. To shed further light on the relationship between mindfulness practice and outcome, future research should routinely assess quality as addition to quantity. Ideally, this would be consistently operationalized and in the same way across studies to facilitate comparison. For example, practice quality could be assessed with the 7-item Practice Quality-Mindfulness (PQM; Del Re et al., 2013) or with the single-item PQM (Goldberg et al., 2020) to reduce participant burden and increase response rates. More recently, the Mindfulness Adherence Questionnaire (MAQ; Hassed et al., 2020) has been developed, which makes a clear distinction between formal and informal mindfulness practice in addition to practice quality and quantity.

Thirdly, research into the working mechanisms of MBCT and MBCL in acute and chronically, treatment-resistant depressed individuals should further be explored. Lastly, MBCL was provided as a follow-up to MBCT in the current thesis. It is suggested that individuals who suffer from relatively severe depressive symptoms might especially benefit from a sequential approach (Cuijpers et al., 2020). However, future studies must be performed to confirm this. For example, by directly comparing the effectiveness and possible working mechanisms of MBCT and MBCL in depression. To further make a distinction if the sequence of interventions matter, both interventions could be presented in a counter-balanced order. Though Segal et al. (2012) suggested that practicing
self-compassion without a foundation in mindfulness may trigger vulnerability in depressed individuals, offering MBCL at an earlier stage or as a stand-alone treatment might significantly reduce the treatment trajectory for individuals with high levels of self-criticism or avoidance tendencies (Schuling, Huijbers, van Ravesteijn, Donders, et al., 2020). In addition, this may lead to further reductions in healthcare costs, as Schuling, Huijbers, van Ravesteijn, Donders, et al. (2020) found that MBCL participants made less use of health care services than those in the control group, except for attending the general practitioner.

2.4.3. Measures
The current thesis used self-report questionnaires which are at risk for recall and response bias. Although moderate support has been found for the differential sensitivity to change of mindfulness questionnaires in mindfulness-based programs (Goldberg et al., 2018), establishing a consensus about a more precise definition of mindfulness has been difficult (Baer et al., 2019) and the validity of mindfulness questionnaires are still disputed (Bergomi et al., 2013; Grossman & van Dam, 2011; van Dam et al., 2018). For example, some researchers suggest that the meaning of items comprising self-report mindfulness questionnaires tend to be interpreted differently based on one's level of mindfulness (Grossman & van Dam, 2011; van Dam et al., 2009). In addition, the Self-Compassion Scale (SCS) is under debate. Some state that the negative domain of the SCS, containing the subscales self-judgment, isolation, and over-identification, “contaminates” the total self-compassion score, given that this negative domain has been found to correlate moderately to strongly to psychopathological constructs such as negative affect, depressive symptoms and rumination (e.g., López et al., 2015; Muris et al., 2018). However, others support the notion that both the negative and positive domains represent the relative balance of compassionate and uncompassionate responses to suffering, and that both are important contributors to the overall concept of self-compassion (e.g., Krieger et al., 2016; Neff, 2016). For future research, it is recommended to concomitantly collect self-report measures as well as more objective behavioral measures (Hadash & Bernstein, 2019) and physical, biological and neuroscientific data (van Dam et al., 2018) in order to further establish their validity. Lastly, with regard to affect measures, it seems important to include more subtle emotions too in future research (e.g., calm, relaxed), considering that particularly these emotions are assumed to increase during meditation (Jones et al., 2018).

Given that the roots of MBIs can be found in Buddhist psychology, it may be interesting to further build upon these ancient pieces of wisdom. For example, modern interventions might benefit from integrating practices that, next to compassion and kindness, more explicitly cultivate sympathetic joy and equanimity, which may have additive value in individuals with recurrent depression. Furthermore, in the context of studying adherence to practice, it
could be interesting to consider the five hindrances that can be found in Buddhist teachings, which are mental factors that hinder progress in meditation practice. Outcome measures such as sensory desire, aversion, restlessness and worry, fatigue or lack of energy, and doubt or a lack of trust can be targets of future investigation to understand better why people adhere to the practice or not. For example, it could be that the tendency to seek for pleasurable experiences might make it more challenging to allow difficult or uncomfortable feelings or sensations when they arise during practice.

2.5. Clinical implications
There are several clinical implications that could be derived from the current thesis. First, a clear role for positive affect in MBCT for depression was found, which suggests that a further refinement of MBCT for depression might be possible by placing more emphasis on exercises that cultivate positive affect, or even adjusting the program by expanding the section on pleasurable experiences. For example, by adding exercises from positive psychology. Secondly, current findings emphasize that depressive symptomatology may have a potentially hindering effect on engaging in mindfulness practice and developing mindfulness. It might be of added value to discuss this issue in clinical practice at an early stage, and regularly address it to provide proper guidance. Perhaps, for those who experience high levels of depressive symptomatology, more intense monitoring may be of benefit (e.g., with the use of apps). Thirdly, although replication is still warranted, individuals with high levels of rumination and early onset of MDD might especially benefit from MBCT as addition to TAU (e.g., antidepressants). Lastly, MBCL may particularly target negative affect via (further) increases in self-compassion. Residual depressive symptoms (e.g., negative affect) are an important predictor of depressive relapse and recurrence, therefore this finding supports the potential clinical relevance of MBCL, and its possible influence on relapse rates. Future research hopefully will reveal whom might especially benefit from MBCL, and whether MBCL is preferably offered as an additional treatment to MBCT for depression (or vice versa), or that MBCL can be offered as a stand-alone intervention. Moreover, it would be interesting to investigate whether integrating self-compassion in a more explicit way in MBCT may improve its effectiveness.

2.6. Conclusion
This thesis included studies investigating the dynamic interplay between mindfulness and affect in MBCT and between self-compassion and affect in MBCL for depression, the effect of formal mindfulness practice in MBCT for depression and the differential treatment effect of MBCT in individuals with depression. Preliminary evidence suggests that increases in positive affect play a more prominent role in MBCT for depression, while this is the case for
decreases in negative affect in MBCL for depression. In addition, the effect of formal mindfulness practice might not be as straightforward as expected, and reverse effects might also play a role. Lastly, MBCT in addition to TAU may be more beneficial for those who ruminate more and had their first depressive episode at an earlier age. These findings may lead to further refinement of MBCT for depression and targeting of MBCT in this population.
References


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Appendix

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1. Inleiding

1.1. Depressie

Momenteel is depressie de belangrijkste oorzaak van ziektelast wereldwijd (WHO, 2017). Bovendien heeft het ziektebeeld vaak een chronisch en recidiverend karakter en ervaren veel mensen restklachten nadat zij eerder een depressieve periode hebben doorgemaakt (Verduijn et al., 2017; Richards, 2011). De meest gebruikelijke vorm van terugvalpreventie is het gebruik van antidepressieve medicatie (Spijker et al., 2013). Het gebruik van antidepressieve medicatie heeft echter ook nadelen (o.a. langdurig gebruik en bijwerkingen) en veel mensen hebben de voorkeur voor psychologische interventies (Biesheuvel-Leliefeld et al., 2015). Gelukkig zijn er tal van psychologische interventies ontwikkeld voor depressie welke een goed alternatief blijken voor antidepressiva (Biesheuvel-Leliefeld et al., 2015; Breedvelt et al., 2021), waaronder mindfulness-based cognitive therapy (MBCT; Segal et al., 2002, 2012).

1.2. Mindfulness-Based Cognitieve Therapie
Van origine is MBCT ontwikkeld als groepstherapie door Segal et al. (2002) om de kans op het ontwikkelen van een nieuwe depressieve periode te verkleinen. Het onderliggende theoretische model heet de ‘differentiële activatie hypothese’ (Lau et al., 2004; Teasdale, 1988), wat beschrijft dat bij iedere ervaren depressieve periode, disfunctionele gedachtpatronen gemakkelijker en sterker worden geactiveerd, wat vervolgens het risico op een terugval vergroot (Segal et al., 2006). Tijdens MBCT leert men eigen patronen te herkennen en zichzelf los te koppelen van disfunctionele gedachtpatronen die mogelijk tot depressie
zouden kunnen leiden door het aannemen van een niet-oordelende houding ten opzichte van negatieve gedachten (Segal et al., 2012). Oorspronkelijk definieerde Jon Kabat-Zinn (1994) de term mindfulness als “het schenken van aandacht op een bepaalde manier: bewust, in het huidige moment en zonder te oordelen” (p.4). Vervolgens is de conceptualisatie van mindfulness verder ontwikkeld tot een twee-componenten model. Enerzijds gericht op wat er plaatsvindt: zelfregulatie van aandacht voor de ervaring op dit moment. Anderzijds op hoe dit wordt bewerkstelligd: door een open, nieuwsgierige, accepterende en niet-oordelende houding aan te nemen in relatie tot de huidige ervaring (Baer et al., 2019).

Het MBCT programma combineert elementen uit het mindfulness-based stress reductie programma (MBSR; Kabat-Zinn, 1990) met elementen uit de cognitieve therapie voor depressie (Beck et al., 1979). Het bestaat uit 8 wekelijkse bijeenkomsten van 2-2,5 uur en 1 stilte dag (Segal et al., 2012). Tijdens de training worden deelnemers aangemoedigd om dagelijks ongeveer 45 minuten thuis te oefenen om hun mindfulness vaardigheden verder te ontwikkelen. Mindfulness oefeningen worden ondervindeeld in formele oefeningen, zoals bijvoorbeeld de bodyscan en zitmeditatie, en informele oefeningen, waarbij mindfulness wordt ontwikkeld door regelmatig dagelijkse activiteiten in aandacht uit te voeren (Segal et al., 2012).

1.2.1. Effectiviteit
Toenemend bewijs toont aan dat MBCT effectief is bij mensen met recidiverende depressie in het verminderen van het risico op terugval (Thimm & Johnson, 2020). Tegenwoordig wordt MBCT dan ook aanbevolen in (inter)nationale richtlijnen als terugvalpreventie interventie bij depressie (American Psychological Association, 2019; National Institute for Health and Care Excellence, 2009; Spijker et al., 2013).

Aanvankelijk werd MBCT niet geschikt geacht voor mensen met een huidige depressie, omdat men verwachtte dat het brengen van de aandacht naar gedachten, gevoelens en fysieke sensaties tijdens een depressie extra lastig zou zijn. Zo zou men in beslag genomen kunnen worden door ervaren negatieve gedachten en zouden concentratieproblemen mogelijk het effect van de interventie kunnen verminderen (Baer et al., 2019; Segal et al., 2012; Strauss et al., 2014). In de loop van de tijd zijn ook mensen met een huidige depressie geïncludeerd bij onderzoek naar de effectiviteit van mindfulness-based interventies (MBI’s). Hieruit blijkt dat MBCT in deze doelgroep ook haalbaar en effectief is (Goldberg et al., 2018; Hedman-Lagerlof et al., 2018; Lenz et al., 2016; Strauss et al., 2014; Wang et al., 2018). Er zijn enkele onderzoeken uitgevoerd naar de mogelijke effectiviteit van MBCT bij personen met chronische of therapiere sistente depressie. Sommige hiervan lieten zien dat MBCT effectief kan zijn (Barnhofer et al., 2009; Cladder-Micus et al., 2018; Eisendrath et al., 2016; Kenny
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& Williams, 2007), terwijl Michalak et al. (2015) ontdekten dat MBCT niet effectiever was dan gebruikelijke zorg in het verminderen van depressieve symptomen bij deze populatie.

Concluderend kan worden gesteld dat MBCT voor depressie effectief is gebleken. Echter, veel mensen die aan MBCT hebben deelgenomen ervaren nog steeds restklachten die een voorspeller zijn voor een terugval in depressie (Buckman et al., 2018). Om de werkzaamheid van MBCT en het doelgericht inzetten van deze interventie bij mensen met (recidiverende) depressie verder te verbeteren, is meer kennis nodig over de werkingsmechanismen ervan.

1.2.2. Werkingsmechanismen

1.2.2.1. Mediatie “Hoe werkt het?”

Om de effectiviteit van MBCT voor recidiverende depressie te verbeteren, is het van belang om meer kennis te vergaren over de processen die verandering bewerkstelligen (Dimidjian & Segal, 2015; Kazdin, 2007). Bij onderzoek naar mogelijke werkingsmechanismen wordt vaak gebruik gemaakt van verschillende concepten. Volgens Kazdin (2007) is een mechanisme de basis voor een effect, dat wil zeggen, de processen of gebeurtenissen die verantwoordelijk zijn voor de verandering; de redenen waarom verandering is opgetreden of hoe verandering tot stand is gekomen. Eén manier om een mogelijk mechanisme van verandering te onderzoeken is door mogelijke mediatoren te onderzoeken. Zo kan het zijn dat een interventie (bijvoorbeeld MBCT) kan zorgen voor vermindering van klachten (bijvoorbeeld depressieve symptomen) via een bepaalde verandering in een andere variabele (bijvoorbeeld mindfulness), ook wel de mediator genoemd (Kazdin, 2007). Het is van belang te realiseren dat een mediator niet noodzakelijkerwijs het gehele proces van hoe verandering tot stand komt verklaart (Kazdin, 2007). Zo kan het zijn dat verandering in een mediator leidt tot verandering in een volgende mediator, waarna het pas resulteert in de uiteindelijke verandering in de uitkomstmaat. Ook kan het zijn dat er meerdere veranderingsprocessen naast elkaar bestaan.

Onderzoek tot op heden suggereert verschillende mediatoren die mogelijk het effect van MBCT bij personen met recidiverende depressie (deels) verklaren. Uit een systematische review die 23 studies incl. de waarbij MBCT bij mensen met recidiverende depressie werd onderzocht, waaronder 20 gerandomiseerde gecontroleerde onderzoeken (RCTs), kwam daarbij een toename in mindfulness, zelfcompassie en metabewustzijn en een afname in rumineren en piekeren naar voren (van der Velden et al., 2015). Met rumineren wordt bedoeld: het herhaaldelijk nadenken over de betekenis en oorzaken van problemen, gevoelens en klachten, vaak gericht op nare gebeurtenissen die men eerder heeft meegemaakt. Piekeren heeft betrekking op het herhaaldelijk negatief denken rond en oplossingen zoeken voor zaken die nog moeten gebeuren. Voorlopig bewijs werd gevonden voor veranderingen in aandacht, geheugenspecificiteit,
zelfdiscrepantie (verschil tussen hoe men zichzelf ziet en zichzelf wil zien), emotionele reactiviteit en positief en negatief affect (stemming/emotie). Een belangrijke beperking van onderzoek naar mogelijke mediatoren is echter dat zowel de verandering in de mediator als de uitkomstmaat over hetzelfde tijdsbestek is gemeten (voor en na de interventie), waardoor uitspraken over de volgorde van verandering niet kunnen worden gedaan (Kazdin, 2007). Om met meer zekerheid vast te stellen of verandering in de mediator daadwerkelijk voorafgaat aan verandering in de uittkomstvariabele, dienen zowel de mediator als de uittkomstmaat gedurende de behandelperiode op verscheidene maar gelijktijdige momenten te worden gemeten.

1.2.2.1.1. Mindfulness en affect
Emotieregulatie speelt een belangrijke rol bij depressie (Joormann & Stanton, 2016). Samen met een vermindering van positieve emoties, is het frequent aanwezig zijn van negatieve emoties een belangrijk kenmerk van depressie (American Psychiatric Association, 2013). De mindfulness-to-meaning theorie (MMT; Garland et al., 2015) suggereert dat mindfulness een positieve wederkerige relatie heeft met positief affect (meer mindfulness leidt tot meer ervaren positief affect, wat weer leidt tot meer mindfulness, etc.) en een negatieve wederkerige relatie met negatief affect (meer mindfulness leidt tot minder ervaren negatief affect, wat weer leidt tot meer mindfulness, etc.). Er wordt verondersteld dat positief affect het welbevinden verbetert en depressieve klachten en het risico op het terugkeren van een depressie vermindert (Bolier et al., 2013; Khazanov & Ruscio, 2016; Sin & Lyubomirsky, 2009). Het verder ontwikkelen van mindfulness zou dus kunnen leiden tot een toename in positief affect en een afname van negatief affect, wat weer zou kunnen leiden tot een verdere toename van mindfulness, wat uiteindelijk zou kunnen leiden tot een verbetering in klachten en een kleinere kans op terugval bij mensen met (recidiverende) depressie.

1.2.2.1.2. Mindfulness beoefening
Er wordt verondersteld dat mindfulness beoefening een essentieel element is van MBCT (Kabat-Zinn, 1990; Segal et al., 2012). Het wordt gezien als een vorm van mentale training (Tang et al., 2015), waarbij meer oefenen gepaard gaat met betere uitkomsten. Volgens een systematische review en meta-analyse van Parsons et al. (2017), lijkt er een kleine maar significante samenhang te bestaan tussen de mate van het doen van formele mindfulness oefeningen en positieve resultaten na MBCT of MBSR bij een breed scala aan patiënten. De sterkte van deze samenhang was vergelijkbaar met die gerapporteerd in meta-analyses over de samenhang tussen huiswerkbeoefening tijdens cognitieve gedagtherapie (CGT) en uitkomsten (Kazantzis et al., 2010). Deze bevinding suggereert dat het inderdaad waardevol kan zijn om deelnemers te ondersteunen en aan te moedigen om formele mindfulness oefeningen te doen tijdens MBCT en MBSR.
De meeste studies zijn echter tot nog toe uitgevoerd onder mensen waarbij geen psychiatrische diagnose was vastgesteld, die grotendeels MBSR ontvingen en waarbij uitkomsten met name op korte termijn waren gemeten waardoor het lastig was om de volgorde van verandering daarbij vast te stellen (Lloyd et al., 2018; Parsons et al., 2017). Daarnaast bleek er een grote variatie te bestaan in de mate van mindfulness beoefening tussen de verschillende studies, waarbij er mogelijk sprake is geweest van publicatiebias; dat studies waarbij minder werd geofend mogelijk minder vaak zijn gepubliceerd (Parsons et al., 2017).

Slechts enkele studies onderzochten de samenhang tussen formele mindfulness beoefening en behandeluitkomsten van MBCT bij mensen met recidiverende depressie op de korte termijn. Sommige studies vonden geen relatie (i.e., Hawley et al., 2014; van Aalderen et al., 2012; Geschwind et al., 2012), terwijl anderen een positieve relatie rapporteerden waarbij meer beoefening gepaard ging met betere uitkomsten (i.e., Crane et al., 2014; Shallcross et al., 2015). Slechts twee studies onderzochten de samenhang tussen mindfulness beoefening tijdens MBCT en het risico op terugval bij personen met recidiverende depressie over een langere periode na de interventie, wat gemengde resultaten opleverde. Zo vonden Crane et al. (2014) dat de duur van dagelijkse formele mindfulness beoefening het risico op terugval 1 jaar na MBCT voorspelde, waarbij langere beoefening samenhang met een vermindere kans op terugval (HR: .97, CI: .947 - .995). Bovendien hadden diegenen die ten minste 3 dagen per week formele mindfulness oefeningen uitvoerden tijdens MBCT bijna de helft minder kans op een terugval 1 jaar na de interventie ten opzichte van diegenen die minder vaak oefenden (HR: .53, CI: .30 - .94). De tweede studie daarentegen, vond geen samenhang tussen de frequentie van formele mindfulness beoefening gedurende 12 maanden na MBCT en het risico op terugval bij personen met recidiverende depressie (Bondolfi et al., 2010). In die studie werd mindfulness beoefening meer algemeen gemeten. Zo werd de deelnemers achteraf gevraagd om hun mate van beoefening te rapporteren zoals die was tijdens MBCT, gedurende 6 maanden na MBCT, en tijdens de 7e tot en met de 12e maand na de interventie. Gezien de nadruk die wordt gelegd op dagelijkse mindfulness beoefening tijdens MBCT, waarbij er van deelnemers een aanzienlijke inspanning en tijdsinvestering wordt gevraagd, zijn methodologisch sterke (replicatie) studies nodig naar de langetermijneffecten van formele mindfulness beoefening bij MBCT in klinische populaties.

Verder is er weinig bekend over het mogelijk bestaan van een omgekeerd effect: dat meer depressieve klachten mogelijk een barrière zouden kunnen zijn voor het uitvoeren van mindfulness oefeningen. Zo kan het zijn dat men eerder in beslag wordt genomen door lastige of negatieve gedachten en gevoelens tijdens beoefening (Beck & Clark, 1997) of dat men eerder geneigd is te focussen op negatieve ervaringen (aandachtsbias; Mogg et al., 1995) en te rumineren (Whitmer & Gotlib, 2013). Aangezien veel mensen de neiging hebben om
Samenvatting (Dutch summary)

Onaangename ervaringen te vermijden of te onderdrukken (Aldao et al., 2010) en dat er tijdens een depressie nog motivatie- en concentratieproblemen bij kunnen komen (Keller et al., 2019; Ravizza & Delgado, 2014), lijkt het plausibel om een negatieve invloed van depressieve klachten op de beoefening te verwachten. Om het verloop en mogelijke wederkerige relaties tussen mindfulness beoefening en uitkomsten te onderzoeken bij mensen met recidiverende depressie, zijn meerdere meetmomenten van zowel mindfulness beoefening als depressieve klachten in de tijd nodig, bij voorkeur zowel tijdens als na MBCT, en moet deze data worden geanalyseerd met geavanceerde statistische technieken. De autoregressive latent trajectory (ALT) modelleringstechniek (Bollen & Curran, 2004), zoals gebruikt in het huidige proefschrift, is geschikt om dynamische processen en de volgorde van verandering tussen variabelen over tijd te ontrafelen.

1.2.2.2. Moderatie “Voor wie werkt het?”
Een andere manier om mogelijke werkingsmechanismen te onderzoeken is via onderzoek naar mogelijke moderators, dat wil zeggen variabelen die de grootte en/of richting van de relatie tussen twee variabelen beïnvloeden (Kazdin, 2007). Bijvoorbeeld, als het effect van MBCT op het verminderen van depressieve symptomen sterker is voor vrouwen in vergelijking tot mannen, dan is geslacht een moderator (Kuyken et al., 2010). Moderatoren zijn gerelateerd aan mediatoren en mechanismen, omdat ze suggereren dat er verschillende processen spelen afhankelijk van de waarde van de moderator (Kazdin, 2007), zoals in het voorbeeld verschillende processen bij mannen en vrouwen.

Gezien de diversiteit aan mensen met een depressie, zou meer kennis over welke persoonskenmerken het effect van MBCT positief of juist negatief beïnvloeden bij kunnen dragen aan het doelgerichter toewijzen van MBCT aan die personen die er het meest baat bij hebben (van der Velden et al. 2015). Verschillende studies die de effectiviteit van MBCT op terugval percentages hebben onderzocht, hebben ook naar mogelijke moderatoren gekeken. Daarbij werden aanwijzingen gevonden dat MBCT mogelijk meer effect had voor mensen met een verhoogde kwetsbaarheid, waaronder minimaal drie eerder doorgemaakte depressieve perioden in de voorgeschiedenis, een eerste depressieve periode op jongere leeftijd (Ma & Teasdale, 2004; Teasdale et al., 2000), trauma opgelopen op jonge leeftijd (Kuyken et al., 2015; Williams et al., 2014) en meer schommelingen in depressieve klachten (Segal et al., 2010). In een meta-analyse gebaseerd op individuele patiëntgegevens (IPD) van alle bestaande onderzoeken naar de effectiviteit van MBCT op het voorkomen van terugval bij recidiverende depressie ($n = 1258$; Kuyken et al., 2016), bleek dat MBCT effectiever was onder mensen die meer depressieve klachten vlak voor de interventie rapporteerden. Voor mensen die een huidige depressie hebben is gesuggereerd dat MBCT meer effect heeft in het verminderen van depressieve symptomen.
onder oudere mensen (Lenz et al., 2016). Bij mensen met chronische of behandelingresistente depressie, bleek een hogere mate van rumineren samen te hangen met een sterkere afname in depressieve klachten na MBCT (Cladder-Micus et al., 2018).

Er zijn enkele kwesties die van belang zijn om te bespreken met betrekking tot moderatie analyses in de context van MBCT voor depressie. Allereerst onderzochten de meeste studies populaties van mensen met een depressie met een beperkt scala aan depressieve klachten bij aanvang (bijvoorbeeld alleen mensen die hersteld waren van een depressie, of alleen mensen met een huidige depressie). Daarnaast heeft het meeste onderzoek naar mogelijke moderatoren betrekking gehad op het effect van MBCT op het risico op terugval en/of de mate van depressieve klachten. Depressie heeft echter een enorme impact op de kwaliteit van leven (WHO, 2017) en het doel van MBCT is niet zozeer om onprettige ervaringen (zoals sombere gedachten of gevoelens) te veranderen of weg te nemen, maar om je er op een andere manier toe te verhouden. Tot op heden zijn er veelbelovende resultaten van het effect van MBCT op kwaliteit van leven (Cladder-Micus et al., 2018; Kuyken et al., 2008, 2015). Onderzoek naar mogelijke moderatoren met kwaliteit van leven als uitkomstmaat zijn echter nog schaars.

Andere kwesties betreffen de statistische benadering die meestal wordt toegepast om moderatoren te onderzoeken, ook wel behandeling-subgroep analyses genoemd. De meeste studies naar mogelijke moderatoren van het effect van MBCT gaan uit van lineaire relaties (hoe hoger men scoort op een bepaalde moderator hoe sterker of minder sterk het effect van MBCT is op de uitkomstmaat). Deze aanname strookt echter niet met het huidige denken dat er mogelijk ook sprake kan zijn van een omgekeerde U-curve (Grant & Schwartz, 2011): zo is gesuggereerd dat MBCT effectiever is onder hen met meer depressieve klachten, maar dat er op een gegeven moment een omslagpunt komt waarna MBCT mogelijk minder effectief of zelfs ongewenste effecten zou kunnen bewerkstelligen (Kuyken et al., 2016; van Dam et al., 2018). Daarnaast werd in onderzoek tot op heden geen onderscheid gemaakt tussen kwantitatieve en kwalitatieve behandeling-subgroep interacties. Kwantitatieve behandeling-subgroep interacties geven aan dat de ene behandeling altijd beter is dan de andere, maar dat alleen de grootte van het effect verschilt tussen subgroepen. Deze interacties impliceren dat alle mensen nog steeds aan één en dezelfde behandeling zouden worden toegewezen. Daarentegen kunnen kwalitatieve behandeling-subgroep interacties erop wijzen dat voor één of meer subgroep(en) de ene behandeling (bijvoorbeeld MBCT) beter is dan de andere (bijvoorbeeld medicatie), terwijl voor andere subgroep(en) het omgekeerde geldt. Om te bepalen voor wie MBCT toegevoegde waarde heeft en voor wie een andere interventie mogelijk geschikter is, zijn dus kwalitatieve behandeling-subgroep interacties nodig. Bovendien kijken de meeste studies alleen naar tweeweg interactie-effecten, terwijl ook hogere-orde
Interactie-effecten kunnen een rol spelen in het verklaren van de variantie in effectiviteit. Onze huidige kennis van moderatoren in de context van MBCT voor depressie is dus nog beperkt. Meer geavanceerdere statistische analysemethoden, zoals bijvoorbeeld de in dit proefschrift gebruikte qualitative interaction trees methode (QUINT; Dusseldorp & van Mechelen, 2014), zijn hiervoor nodig.

1.3. Mindfulness-Based Compassievol Leven
Naast het verkrijgen van kennis over hoe MBCT voor mensen met recidiverende depressie werkt, kan het onderzoeken van werkingsmechanismen van veelbelovende vervolg interventies verder bijdragen aan het verbeteren van uitkomsten in deze populatie. Van den Brink en Koster (2015) ontwikkelden mindfulness-based compassionate living (MBCL) als vervolginterventie op MBCT of MBSR. In MBCL ontwikkelt men expliciet zelfcompassie, wat meer impliciet wordt overgebracht in MBCT en een mogelijke mediator is van het effect van MBCT bij mensen met recidiverende depressie (Kuyken et al., 2010). In MBCL omvat (zelf)compassie het vermogen om gevoelig te zijn voor het lijden van zichzelf en anderen, en de intentie om dit lijden te verlichten of te voorkomen (Gilbert & Choden, 2013). MBCL is gebaseerd op andere compassie-based interventies (CBI’s), zoals compassion-focused therapy (CFT; Gilbert, 2010) en het mindful self-compassion program (MSC; Neff & Germer, 2013). Het is op een vergelijkbare manier gestructureerd als de MBCT en MBSR (van den Brink & Koster, 2015): het is een groepsinterventie bestaande uit acht sessies van 2,5 uur, een stilte dag en dagelijkse oefeningen van 45-60 minuten. De oefeningen zijn expliciet gericht op het cultiveren van compassie en vriendelijkheid naar jezelf en anderen, waaronder informele oefeningen (zoals de ademruimte met vriendelijkheid of compassie) en formele oefeningen (zoals de mildheidsmeditatie en compassioneel ademen). Een recent gerandomiseerd gecontroleerd onderzoek toonde aan dat MBCL, als vervolg interventie op MBCT bij mensen met recidiverende depressie, resulteerde in een sterkere vermindering van depressieve klachten en verbetering in kwaliteit van leven ten opzichte van gebruikelijke zorg (Schuling, Huijbers, van Ravesteijn, Donders, et al., 2020). Daarnaast leek zelfcompassie een mediator van het effect van MBCL op korte termijn uitkomsten. De mediatie analyses maakten echter gebruik van metingen voor en na de interventie, waardoor niets over een mogelijk oorzakelijk verband kan worden geconcludeerd. Meer onderzoek is nodig naar het (dynamische) proces van zelfcompassie in MBCL bij mensen met recidiverende depressie.

Veranderingen in (zelf)compassie zijn, naast de samenhang met depressieve klachten, eerder ook geassocieerd met veranderingen in affect tijdens CBI’s. Een interventiestudie bij personen met een kwetsbaarheid voor depressie (n = 63) vond dat het beoefenen van zelfcompassie resulteerde in een toename in geluk (Shapira & Mongrain, 2010). Daarnaast suggereren verschillende experimentele
studies dat zelfcompassie resulteert in meer positief affect (e.g., Engen & Singer, 2015) en minder negatief affect (e.g., Arimitsu & Hofmann, 2017; Leary, et al., 2007). Slechts één experimentele studie is uitgevoerd onder personen met depressie (n = 48; Diedrich et al., 2014). Hierbij werd de mate van depressieve stemming op vier momenten gemeten. Nadat een negatieve stemming werd opgewekt, kregen de deelnemers de instructie om: 1. niets te doen en te wachten, 2. de situatie opnieuw te beoordelen, 3. negatieve emoties te accepteren, of 4. zelfcompassie in te zetten om hun depressieve stemming te reguleren. Het toepassen van zelfcompassie bleek daarbij effectiever dan niets doen en wachten. Effecten van zelfcompassie op positief/negatief affect of omgekeerde effecten van positief/negatief affect op zelfcompassie tijdens MBCL voor depressie zijn nog niet eerder onderzocht.

2. Proefschrift

2.1. Doelstellingen
Het algemene doel van dit proefschrift was om te onderzoeken hoe MBI’s werken bij mensen met recidiverende depressie. Aangezien het meeste eerdere onderzoek naar de mogelijke werkingsmechanismen gebaseerd is op onderzoek waarbij zowel mogelijke mediatoren als uitkomstmaten voor en na de interventie zijn gemeten, tracht het huidige proefschrift dit veld verder te brengen door zowel korte als lange termijn uitkomsten mee te nemen en door meer geavanceerde statistische technieken toe te passen, zoals de ALT methode. De ALT methode combineert een autoregressief (AR) model met een latent traject model (LTM). Hierbij worden wederkerige effecten onderzocht, waarbij er gecontroleerd wordt voor algemene trajecten, zodat voorkomen wordt dat onterecht wederkerige effecten worden gevonden terwijl deze er in wezen niet zijn (Voelkle, 2008). Met behulp van de ALT methode kunnen dus meer betrouwbare uitspraken worden gedaan over processen van verandering tijdens MBCT bij mensen met recidiverende depressie.

Als onderdeel van het bestuderen van mogelijke werkingsmechanismen, werpt dit proefschrift licht op de diversiteit van mensen met een depressie. Dit wordt bereikt door inzicht te verschaffen in welke persoonskenmerken het effect van MBCT beïnvloeden, wat behulpzaam kan zijn in het verbeteren van het gericht toewijzen van deze interventie bij mensen met (recidiverende) depressie. Het huidige proefschrift beoogt te voorzien in de behoefte aan meer verfijnd onderzoek naar mogelijke moderatoren door de QUINT methode toe te passen. In tegenstelling tot eerder onderzoek, dat meestal gebaseerd is op tweeweg behandeling-subgroep interacties en lineaire relaties, richt QUINT zich op het identificeren van kwalitatieve behandeling-subgroep interacties, waarbij mogelijke hogere-orde interactie-effecten en niet-lineaire relaties
worden toegestaan. Deze methode identificeert subgroep(en) van personen bij wie de ene behandeling een gunstiger effect heeft dan de andere, en voor wie het omgekeerde geldt. De methode is bijzonder geschikt voor situaties met veel mogelijke modererende variabelen zonder dat er vooraf duidelijke hypotheses zijn gesteld. Het resultaat van een analyse met QUINT is een beslisboom waaruit criteria voor toewijzing van behandeling kan worden afgeleid, hetgeen zeer relevant is voor de klinische praktijk.

Samenvattend worden in dit proefschrift de volgende onderzoeksvragen behandeld:
1. Hoe werkt MBCT bij depressie?
2. Voor wie werkt MBCT bij depressie?
3. Hoe werkt MBCL bij depressie?

2.2. Resultaten
Allereerst werd in Hoofdstuk 2 het beloop en de mogelijk wederkerige relaties tussen mindfulness en zowel positief als negatief affect onderzocht gedurende MBCT bij mensen met recidiverende depressie (n = 235). Voorafgaand aan elke MBCT sessie werden zowel mindfulness, positief affect als negatief affect gemeten door middel van zelfrapportage vragenlijsten. De data werd geanalyseerd door middel van de ALT methode, welke onderscheid maakt tussen algemene veranderingen over de gehele interventie heen en specifieke veranderingen die van week tot week plaatsvonden. De algemene veranderingen lieten zien dat mindfulness en positief affect toenamen gedurende de MBCT, terwijl het verloop van negatief affect een meer onregelmatig beloop vertoonde. Personen met sterkere toenames in mindfulness vertoonden significant sterker toenames in positief affect. Bovendien lieten mensen die meer kampten met negatief affect een minder sterke toename in mindfulness zien. Tegen de verwachting in werd er geen robuust bewijs gevonden voor de meer specifieke wederkerige week-to-week effecten tussen mindfulness en positief/negatief affect.

In Hoofdstuk 3 werden de mogelijke wederkerige relaties tussen de mate van formele mindfulness beoefening en de ernst van depressieve klachten, gedurende 15 maanden onderzocht bij personen met recidiverende depressie (n = 200). De frequentie van de formele mindfulness oefeningen werd berekend voor elke periode van 3 maanden. De mate van depressieve klachten werd op iedere drie maanden vastgesteld: bij 0 (voor MBCT), 3 (na MBCT), 6, 9, 12 en 15 maanden. Deelnemers bleken gemiddeld 4 dagen per week formele mindfulness oefeningen te verrichten tijdens de MBCT (tussen 0 en 3 maanden), maar de frequentie van het oefenen nam daarna sterk af. De mate van depressieve symptomen veranderde niet gedurende de volledige onderzoeksperiode. Tegen de verwachting in werd er geen duidelijk bewijs gevonden voor de hypothese dat de mate van formele mindfulness beoefening gedurende elke periode van
drie maanden de ernst van de daaropvolgende depressieve klachten beïnvloedt. De ernst van de depressieve klachten leek daarentegen wel verband te houden met het minder vaak oefenen tijdens de daaropvolgende periode van drie maanden. Dit suggereert dat depressieve symptomen mogelijk een belemmering kunnen vormen voor het uitvoeren van formele mindfulness oefeningen.

In **Hoofdstuk 4** werd de QUINT methode toegepast op individuele persoonsgegevens op basis van drie RCT’s die het effect van MBCT + gebruikelijke zorg versus gebruikelijke zorg alleen onderzochten (n = 292). De onderzoekspopulatie bevatte mensen die (gedeeltelijk) waren hersteld van depressie, mensen die depressief waren, maar ook mensen met chronische, therapieresistente depressie. De uitkomstmaten waren depressieve klachten en kwaliteit van leven. De resultaten toonden aan dat MBCT + gebruikelijke zorg betere resultaten lieten zien dan gebruikelijke zorg alleen in het verminderen van depressieve klachten. Personen die in de ‘hoge en lage uiteinden’ van ernst van de depressie vielen hadden minder baat bij beide interventie groepen. Voor mensen waarbij depressie voor het eerst werd vastgesteld op jongere leeftijd en mensen met een sterkere mate van rumineren bleek MBCT ter aanvulling op gebruikelijke zorg gunstiger dan gebruikelijke zorg alleen in relatie tot het verminderen van depressieve klachten. Voor mensen met een lagere kwaliteit van leven bleek MBCT + gebruikelijke zorg gunstiger dan gebruikelijke zorg alleen in het verbeteren van de kwaliteit van leven.

Parallel aan het onderzoek naar de wisselwerking tussen mindfulness en positief/negatief affect tijdens MBCT voor depressie, werd in **Hoofdstuk 5** de mogelijke wisselwerking tussen zelfcompassie en positief/negatief affect onderzocht tijdens MBCL. De MBCL werd toegepast als vervolginterventie na MBCT bij mensen die waren hersteld van depressie of een depressie hadden bij start van het onderzoek (n = 104). De resultaten toonden aan dat over het algemeen zelfcompassie toenam, terwijl positief affect stabiel bleef en negatief affect gedurende MBCL afnam. Bovendien werden er geen week-tot-week effecten gevonden tussen zelfcompassie en daaropvolgend positief affect, noch omgekeerd. Hoewel er tevens geen effecten bleken van negatief affect op zelfcompassie, werd er wel bewijs gevonden voor het omgekeerde: een hogere mate van zelfcompassie tijdens iedere sessie voorspelde minder negatief affect bij de daaropvolgende sessie.
3. Discussie

3.1. “Hoe werkt MBCT bij depressie”

3.1.1. Affect

Theorie suggereert dat mindfulness toeneemt tijdens MBCT (Segal et al., 2012), wat werd bevestigd door de resultaten uit Hoofdstuk 2 van dit proefschrift. Deze bevinding is ook consistent met de huidige literatuur (van der Velden et al., 2015). Naast de toename van mindfulness, werd in het huidige proefschrift ook een toename gevonden in de mate van ervaren positief affect gedurende de MBCT. Bovendien werd gevonden dat sterkere toenames in mindfulness samenhangen met sterkere toenames in positief affect. Dit komt overeen met de mindfulness-to-meaning theorie (MMT; Garland et al., 2015) die stelt dat mindfulness een positieve wederkerige relatie heeft met positief affect (meer mindfulness leidt tot meer ervaren positief affect, wat weer leidt tot meer mindfulness, etc.) en een negatieve wederkerige relatie met negatief affect (meer mindfulness leidt tot minder ervaren negatief affect, wat weer leidt tot meer mindfulness, etc.). Dit kan een goed uitgangspunt zijn voor mensen om zich vervolgens bloot te stellen aan moeilijkere emoties tijdens MBCL voor depressie, gezien Segal e.a. (2012) eerder hebben gesuggereerd dat het beoefenen van (zelf) compassie zonder een basis in mindfulness, mogelijk kan leiden tot een verhoogde kwetsbaarheid bij mensen met depressie.

Onverwacht nam negatief affect niet af gedurende MBCT (Hoofdstuk 2). Dit is in strijd met bevindingen uit eerdere onderzoeken, bijvoorbeeld Batink et al. (2013), die vonden dat negatief affect de werkzaamheid van MBCT voor depressie medieerde. Een verklaring voor huidig resultaat zou kunnen zijn dat er ook geen duidelijk effect van MBCT op de ernst van depressieve klachten is gevonden in de klinische onderzoeken waaruit de huidige gegevens zijn afgeleid (Huijbers et al., 2015, 2016). Wellicht had dit te maken met het feit dat uitsluitend mensen aan het onderzoek meededen die hersteld waren van de depressie bij aanvang, waardoor er minder ruimte voor verbetering overblijft. Een andere reden zou kunnen zijn dat de mindfulness trainers gemiddeld genomen minder hoge competentie scores hadden in deze studies vergeleken met eerdere studies die zijn verricht (Kuyken et al., 2008, 2015; Segal et al., 2010). Een andere verklaring zou kunnen zijn dat deelnemers leerden om negatief affect te observeren zonder dit direct te willen veranderen of over te blijven piekeren. Volgens de MMT (Garland et al., 2015) helpt mindfulness om het aandachtsveld te verbreden: waarbij eerst de focus lag op alleen het negatieve, komt er ook ruimte voor het positieve waardoor er een meer evenwichtige kijk ontstaat op wat er gebeurt. Dit raakt aan een paradox van mindfulness onderzoek. Er wordt vaak gebruik gemaakt van negatieve uitkomstmaten, zoals vermindering van depressieve symptomen, hoewel dit misschien niet de meest geschikte uitkomstmaat is voor mindfulness onderzoek. Bij het ontwikkelen van
Mindfulness leert men ervaringen op een niet-oordelende, vriendelijke en accepterende manier te benaderen in plaats van ernaar te streven de ervaringen zelf te veranderen. Daarom zijn uitkomstmaten die attitude, veerkracht en welzijn of tevredenheid met het leven omvatten, wellicht geschikter.

Uit het huidige proefschrift bleek dat negatief affect een barrière zou kunnen vormen voor het ontwikkelen van mindfulness tijdens MBCT voor depressie (Hoofdstuk 2). Alhoewel eerdere studies de samenhang tussen mindfulness en daaropvolgend negatief affect hebben onderzocht, zijn omgekeerde relaties van negatief affect op mindfulness minder bestudeerd en laten deze gemengde resultaten zien (o.a. Gotink et al., 2016; Snippe et al., 2015). Een voordeel van de analyses die in dit proefschrift werden geëxporteerd, is dat de relaties tussen mindfulness en positief/negatief affect in beide richtingen gelijktijdig werden gemodelleerd binnen één model, terwijl werd gecontroleerd voor het algemene verloop van de variabelen over de gehele interventie. Indien het algemene verloop van de variabelen over tijd niet wordt meegenomen in de analyse kan dit leiden tot het vinden van week-tot-week effecten die er in werkelijkheid niet zijn (Voelkle, 2008). De mogelijke belemmerende rol van de mate van negatief affect op het ontwikkelen van mindfulness vraagt om verder (replicatie) onderzoek voordat klinische implicaties hieruit kunnen worden afgeleid. Bij voorkeur met het gebruik van meerdere metingen van beide variabelen in de tijd en het liefst ook na de interventieperiode, waarbij gebruik gemaakt dient te worden van geavanceerde statistische technieken (o.a. de ALT analyse methode). Kortom, positief affect speelt een prominente rol in MBCT voor depressie, waarbij negatief affect een barrière kan vormen om mindfulness te ontwikkelen. De resultaten zijn echter voorlopig en moeten eerst worden gerepliceerd voordat aanbevelingen voor de klinische praktijk kunnen worden gedaan.

3.1.2. Mindfulness beoefening
Tegen de verwachting in werd in het huidige proefschrift het veronderstelde effect van de frequentie van de formele mindfulness beoefening op depressieve klachten niet teruggevonden (Hoofdstuk 3). Dit is in tegenstelling tot een systematische review en meta-analyse door Parsons et al. (2017), die een kleine maar significante relatie vonden tussen de mate van formele mindfulness beoefening en verbeteringen na MBCT en MBSR bij een breed scala aan klinische en niet-klinische populaties. Bij verdere inspectie van de afzonderlijke studies die in de meta-analyse waren opgenomen en de relatie tussen formele mindfulness beoefening en zowel korte- als langetermijnresultaten van MBCT bij depressie onderzochten, lieten de meeste studies positieve effecten zien (Crane et al., 2014; Hawley et al., 2014; van Aalderen et al., 2012; Geschwind et al., 2012). Er waren echter ook studies die deze relatie niet terugvonden (Bondolfi et al., 2010; Shallcross et al., 2015).
Een verklaring voor de verschillen in de gevonden resultaten zou de mate van beoefening kunnen zijn, alsmede de sterke afname in beoefening in de loop van de tijd. Het minder oefenen na een interventie blijft een veelvoorkomend probleem in de klinische praktijk (Bondolfi et al., 2010; Gaynor et al., 2006). Segal et al. (2019), suggereren dat een blijvend effect van MBCT op de lange termijn langdurige beoefening behoeft, ook na de interventie. We kunnen echter de mogelijke generalisatie van adaptieve coping vaardigheden over tijd hierbij niet uitsluiten. Het kan zijn dat individuen in de loop van de tijd de neiging hebben om minder formele maar juist meer informele mindfulness oefeningen te doen (o.a. Bondolfi et al., 2010). Daarnaast zou de verklaring van een omgekeerde U-curve in de effectiviteit van mindfulness beoefening een overkoepelend verklarend raamwerk kunnen bieden voor de gevonden mix van positieve en nul bevindingen in mindfulness onderzoek (Britton, 2019). Er is bijvoorbeeld gesuggereerd dat MBCT minder effectief is voor mensen met zeer weinig of juist zeer veel depressieve klachten (Kuyken et al., 2016; van Dam et al., 2018). Het is aan te bevelen om in toekomstig onderzoek de effecten van therapietrouw prospectief en gerandomiseerd gecontroleerd te onderzoeken in plaats van via secundaire analyses (Dimidjian & Segal, 2015). Zo zou de effectiviteit tussen groepen die verschillende hoeveelheden mindfulness beoefening bevatten (waaronder helemaal geen beoefening) met elkaar kunnen worden vergeleken. Soortgelijk onderzoek in cognitieve gedragstherapie (CGT; Beck et al., 1979), toonde aan dat het verrichten van huiswerk resulteerde in betere behandelings-effecten ten opzichte van diegenen die dat niet deden (Kazantzis et al., 2010). Bovendien kan naast de kwantiteit van beoefening ook de kwaliteit van beoefening invloed hebben op uitkomsten (Kazantzis et al., 2016). Zoals eerder besproken, omvat mindfulness niet alleen zelfregulatie van aandacht voor de huidige ervaring (‘wat’), maar omvat het ook een open, nieuwsgierige, accepterende en niet-oordelende houding (‘hoe’) ten opzichte van iemands ervaring (Baer et al., 2019). Recent onderzoek gericht op de kwaliteit van beoefening laat een aanvullend effect zien van de kwaliteit bovenop kwantiteit van beoefening op mindfulness (Hassed et al., 2020) en uitkomstmaten (Del Re et al., 2013; Goldberg et al., 2014, 2020). Daarom wordt aanbevolen om zowel de frequentie en hoeveelheid tijd besteed aan oefenen (de kwantiteit) als de houding waarmee men oefent (de kwaliteit) mee te nemen in toekomstig onderzoek naar de impact van mindfulness beoefening.

Het huidige proefschrift vond geen effecten van formele mindfulness oefeningen op de mate van depressieve symptomen, maar omgekeerde effecten werden wel gevonden: meer depressieve symptomen op ieder meetmoment (0, 3, 6, 9, 12 en 15 maanden) leek samen te hangen met het minder frequent uitvoeren van formele mindfulness beoefening tijdens de daaropvolgende perioden van drie maanden bij personen met recidiverende depressie na MBCT (Hoofdstuk 3). Dit is een opmerkelijke bevinding, aangezien eerder gevonden
negatieve relaties tussen mindfulness beoefening en uitkomsten werden geïn-
terpreteerd als dat meer mindfulness beoefening zou leiden tot een verbetering van resultaten, ondanks dat er bij de meeste onderzoeken alleen voor en na de interventie metingen waren verricht (Parsons et al., 2017). Tot op heden is een omgekeerd effect niet eerder onderzocht in MBCT voor depressie, wat zou kunnen leiden tot nieuwe inzichten in de relatie tussen formele mindfulness beoefening en depressieve klachten bij MBCT voor mensen met recidiverende depressie. De huidige bevinding dat depressieve klachten mogelijk het beoefenen van mindfulness belemmeren, komt overeen met de eerdere bevinding uit Hoofdstuk 2 dat negatief affect een barrière zou kunnen vormen om mindfulness te ontwikkelen tijdens MBCT voor depressie. Daarnaast lijkt het ook in lijn met de bevindingen van Banerjee et al. (2018) die vonden dat een hogere mate van rumineren en piekeren samenhangt met een verminderde aanwezigheid bij de groepssessies en het minder uitvoeren van mindfulness oefeningen, wat vervolgens het verder ontwikkelen van mindfulness zou kunnen belemmeren. Kwalitatief onderzoek naar belemmerende en ondersteunende factoren die een rol spelen bij mindfulness beoefening, zou meer inzicht kunnen geven in de onderliggende processen. Tot op heden hebben kwalitatieve studies gerapporteerd dat een gebrek aan ondersteuning uit de groep, fysiek ongemak, uitgeput of gedesoriënteerde voelen, zelftwijfel en langer durende oefeningen belemmerend kunnen werken in het uitvoeren van mindfulness oefeningen. Als ondersteunende factoren kwamen naar voren: voorkennis over mindfulness, positieve overtuigingen, motivatie, ervaren positieve gevolgen (o.a. bevordering in welzijn, verandering in zelfcompassie en een toegenomen gevoel van keuzevrijheid voor gedachten) en mogelijkheden om beoefening op lange termijn te faciliteren zoals het bijwonen van opfrissessies en retraites na de training (Banerjee et al., 2017; Dobkin et al., 2012; Langdon et al., 2011; Lomas et al., 2015). Uit een kwalitatieve studie over mindfulness-beoefening na MBCT door Langdon et al. (2011), bleek dat men eerst cognities en gevoelens die konden werken als obstakels voor beoefening diende te omzeilen om daadwerkelijk te starten met oefenen en het ‘gewoon te doen’. Dit sluit aan bij het welbekende advies over beoefenen “You don’t have to like it, you just have to do it” (Kabat-Zinn, 1990).

Concluderend lijkt de wisselwerking tussen mindfulness beoefening en uitkomsten misschien niet zo eenvoudig als eerder werd verondersteld. Dit onderstrept het belang van replicatiestudies en het publiceren van negatieve studieresultaten. Daarnaast wijzen de huidige studieresultaten erop dat depressieve klachten mogelijk een belemmerende factor kunnen zijn voor mindfulness beoefening, wat overeen lijkt te komen met de mogelijk belemmerende rol van negatief affect in het verder ontwikkelen van mindfulness bij MBCT voor depressie.
3.2. “Voor wie werkt MBCT bij depressie?”
Tijdens MBCT leert men cognitieve processen die mogelijk kunnen leiden tot depressie (o.a. rumineren) te herkennen en van een afstand te aanschouwen, waarna deze gemakkelijker kunnen worden losgelaten. Het huidige proefschrift laat zien dat MBCT + gebruikelijke zorg mogelijk gunstiger is dan gebruikelijke zorg alleen voor personen bij wie de eerste depressie op jongere leeftijd aanving en er sprake is van een sterkere mate van rumineren en daarnaast voor diegenen met een lagere kwaliteit van leven (Hoofdstuk 4). Dit is in lijn met het onderliggende theoretische model, ook wel de ‘differentiële activeringshypothese’ genoemd (Teasdale, 1988). Dit model gaat ervan uit dat de kwetsbaarheid voor depressie toeneemt met elke depressieve periode, omdat eerdere patronen van negatief denken iedere keer gemakkelijker toegankelijk worden zodra je je neerslachtig voelt. Bovendien komen de huidige bevindingen overeen met eerdere onderzoeken die suggereren dat de effecten van MBCT voor depressie kunnen worden gemodereerd door kwetsbaarheidsfactoren zoals personen met drie of meer eerdere depressieve perioden, eerste depressie op jongere leeftijd (Ma & Teasdale, 2004; Teasdale et al., 2000), vroeg opgelopen psychotrauma (Kuyken et al., 2015; Williams et al., 2014) en meer schommelingen in depressieve klachten (Segal et al., 2010). Hoewel het huidige onderzoek personen onderzocht met een breed scala aan depressieve klachten bij aanvang, moet worden opgemerkt dat mensen met zeer ernstig depressieve klachten (≥37 punten op de HRSD-17; Hamilton, 1960) niet waren geïncludeerd. Voor deze specifieke groep mensen kan dan ook geen uitspraken worden gedaan over de vraag of MBCT bij depressie van toegevoegde waarde kan zijn of dat het mogelijk geen of een negatief effect zou kunnen hebben.

Tegen de verwachting in vond het huidige proefschrift geen aanwijzingen voor een hogere mate van effectiviteit van MBCT bij mensen met meer depressieve klachten (Hoofdstuk 4). Dit lijkt in tegenspraak te zijn tot de individuele patiënt-data (IPD) meta-analyse van Kuyken et al. (2016), die dit wel onderschreef met betrekking tot het risico op terugval. Het lijkt ook in tegenspraak te zijn met de tegenovergestelde bevindingen van het huidige proefschrift dat depressieve klachten mogelijk het beoefenen van mindfulness belemmeren (Hoofdstuk 3) en dat negatief affect een belemmerende factor zou kunnen zijn om mindfulness te ontwikkelen bij personen met recidiverende depressie (Hoofdstuk 2). Echter, de IPD-meta-analyse was beperkt tot personen met recidiverende depressie die (gedeeltelijk) waren hersteld van hun depressie, waardoor het bereik van depressieve klachten in de onderzochte populatie bij aanvang werd beperkt en mogelijk overeen zou kunnen komen met de opwaartse helling van de omgekeerde U-curve (Britton, 2019; ter Avest et al., 2019). Bovendien kunnen de verschillende statistische benaderingen de verschillen in gevonden resultaten verklaren. De meeste onderzoeken naar mogelijke moderaatoren van het effect van de interventie veronderstelden lineaire relaties
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en tweeweg interactie-effecten (o.a. Kuyken et al., 2016), waarbij geen onderscheid kon worden gemaakt tussen kwantitatieve en kwalitatieve behandeling-subgroep interacties. In het huidige proefschrift werd gebruik gemaakt van de QUINT methode, die zich richt op het identificeren van kwalitatieve behandeling-subgroep interacties, die niet-lineaire relaties mogelijk maakt en rekening houdt met mogelijke effecten van hogere-orde interacties. Andere gevonden moderatorvariabelen (rumineren, leeftijd van de eerste depressie en kwaliteit van leven) bleken een sterkere invloed op de uitkomst van de interventie te hebben dan depressieve klachten bij aanvang, die niet als duidelijke moderator naar voren leek te komen.

Concluderend bleek uit het huidige proefschrift de sterkste evidentie voor de kwetsbaarheidsfactoren leeftijd van aanvang van depressie en mate van rumineren als moderatoren van het effect van MBCT voor depressie, waarbij personen die op jongere leeftijd een eerste depressie doormaken en een sterke mate van rumineren vertoonden meer kans hadden om baat te hebben bij MBCT ter aanvulling op gebruikelijke zorg.

3.3. “Hoe werkt MBCL bij depressie?”

Volgens de theorie zou zelfcompassie toenemen tijdens MBCL (van den Brink & Koster, 2015; Segal et al., 2012). Dit werd inderdaad bevestigd in een eerdere studie naar MBCL bij personen met recidiverende depressie (Schuling, Huijbers, van Ravesteijn, Donders, et al., 2020) en bleek ook uit secundaire analyses van die studie die week-tot-week verbeteringen in zelfcompassie aantonen, zoals gerapporteerd in dit proefschrift (Hoofdstuk 5). Deze bevindingen zijn ook consistent met overig onderzoek dat tot op heden is verricht (Ferrari et al., 2019). Zoals verwacht nam negatief affect af tijdens MBCL voor depressie en dit werd voorafgegaan door een toename in zelfcompassie (Hoofdstuk 5). Dit is in lijn met eerdere (experimentele) onderzoeken (o.a. Diedrich et al., 2014). In MBCT ontwikkelt men een niet-oordelende houding ten opzichte van zichzelf en anderen en wordt men zich meer bewust van zowel positieve als negatieve emoties, gedachten en lichamelijke gewaarwordingen en de bijbehorende automatische reacties. Volgens een recent kwalitatief onderzoek naar de meerwaarde van MBCL bij mensen met recidiverende depressie (Schuling, Huijbers, van Ravesteijn, Kuyken, & Speckens, 2020) gaven deelnemers echter aan dat ze tijdens MBCL een meer ‘neutrale’ observerende houding ten opzichte van moeilijke emoties, gedachten en lichamelijke gewaarwordingen aannamen. Gezien in MBCT de actieve uitnodiging ontbrak om ongemak te benaderen, was het mogelijk om sterk gewortelde vermijdingspatronen te blijven inzetten. Het kan zijn dat personen met recidiverende depressie meer expliciete instructies en oefeningen nodig hebben om een compassievolle houding te ontwikkelen ten opzichte van zichzelf en anderen, vooral tijdens negatieve ervaringen, aangezien er vaak sprake is van zelfkritiek en gevoelens van schaamte, schuld en minder-
waardigheid (Gilbert et al., 2008, 2012; Gilbert & Procter, 2006). MBCL richt zich expliciet op het ontwikkelen van (zelf)compassie doordat men zich opzettelijk blootstelt aan onaangename gevoelens, gedachten en lichamelijke gewaarwordingen, waarbij men nieuwe manieren leert om met het ongemak te zijn: door te verzachten en te kalmeren, op een niet-oordeelende en vriendelijke manier (van den Brink & Koster, 2015).

Er lijken duidelijke verschillen te zijn gevonden tussen MBCT en MBCL in de trajecten van positief en negatief affect (Hoofdstuk 2 en 5), wat suggereert dat er mogelijk verschillende affectieve processen ten grondslag liggen aan MBCT en MBCL voor depressie. Het kan zijn dat positief affect een meer prominente rol speelt bij MBCT voor depressie, wat een mooie aanvulling zou kunnen zijn bij bestaande therapieën voor depressie, zoals antidepressiva en cognitieve therapie, aangezien wordt gesuggereerd dat deze therapieën negatief affect effectievere herstellen dan positief affect (Dunn et al., 2020). Gezien eerdere studies aantonen dat herstel van positief affect minstens zo belangrijk is als het verminderen van negatief affect bij personen die herstellen van een depressie (Demyttenaere et al., 2015; Zimmerman et al., 2006) en bestaande reguliere behandelingen niet leiden tot een normalisering van de mate van positief affect (Dunn et al., 2020), is er nog ruimte voor verdere verbetering. Naast MBCT zijn er verschillende medicijnen (o.a. Jamerson et al., 2003; Lally et al., 2015; Tomarken et al. 2004) en aangepaste psychotherapieën die gericht zijn op positief affect en welzijn in opkomst (o.a. Geschwind et al., 2019, Craske et al., 2019; Ruini & Fava, 2012; Dunn et al., 2019; Chaves et al., 2017). Het kan zijn dat het verder normaliseren van de mate van ervaren positief affect leidt tot een meer gelijkmoedige gemoedstoestand en daarmee verbetering van kwaliteit van leven.

Terwijl positief affect een meer prominente rol speelt bij MBCT, lijkt het cultiveren van (zelf)compassie tijdens MBCL meer expliciet gericht op negatief affect. Dit zijn echter voorlopige resultaten welke eerst dienen te worden gereduceerd voordat aanbevelingen voor de klinische praktijk kunnen worden gedaan. Bovendien, gezien MBCL niet direct werd vergeleken met een andere actieve controleconditie als vervolg op MBCT, geeft dit weinig informatie over de specificiteit van MBCL. Ten slotte was de onderzoekspopulatie, waarbij MBCL volgde op eerder ontvangen MBCT, pragmatisch van aard. Zo werd deelname aan MBCL aangeboden aan alle voormalige MBCT deelnemers die voldeden aan de in- en exclusiecriteria. Daardoor is er weinig bekend over de kenmerken van degenen die zich aanmeldden versus degenen die dat niet deden, wat ervoor zorgt dat een mogelijke selectiebias niet kan worden uitgesloten (zelfselectie van deelnemers voor wie MBCT mogelijk minder effectief was).
3.4. Sterke punten, beperkingen en aanbevelingen

3.4.1. Statistiek
Een sterk punt van het huidige proefschrift is het gebruik van geavanceerde statistische methoden. Door gebruik te maken van herhaalde metingen en de ALT analyse techniek, kon een duidelijk onderscheid worden gemaakt tussen het algemene verloop van iedere variabele en de wederkerige effecten tussen variabelen van week tot week. Dit maakte het mogelijk om processen tussen mindfulness/zelfcompassie en positief/negatief affect in de loop van de training gedetailleerder te bestuderen in vergelijking met eerdere pre-post studies, waardoor de kans wordt vergroot om een mogelijk oorzakelijk verband hieruit af te leiden (Voelkle, 2008).

Naast de ALT analyse methode werd de QUINT methode toegepast. Het proefschrift vond aanwijzingen dat MBCT ter aanvulling op gebruikelijke zorg gunstiger is dan gebruikelijke zorg alleen voor diegenen die op jongere leeftijd een eerste depressie doormaken en meer rumineren, en voor hen met een lagere kwaliteit van leven. Voordat definitieve toewijzingscriteria kunnen worden geformuleerd en geïmplementeerd in de klinische praktijk, dienen de huidige bevindingen te worden gerepliceerd en bij voorkeur ook langetermijnresultaten te worden meegenomen in toekomstig onderzoek. Momenteel breidt het gebied van gepersonaliseerde psychologische interventies zich snel uit en nieuwe benaderingen, zoals network estimation techniques (Boschloo et al., 2019), machine learning (Lutz et al., 2019), en het gebruik van grote hoeveelheden aan data uit de dagelijkse praktijk (Kessler et al., 2019) zijn veelbelovende ontwikkelingen, die een verschuiving veroorzaken van een generaliserende naar een meer individuele benadering (Hofmann & Hayes, 2019). Hoewel nieuwe statistische benaderingen kunnen bijdragen aan de kennis voor wie bestaande therapieën het meest effectief zouden kunnen zijn, kunnen ze mogelijk ook leiden tot meer kennis over mogelijke onderliggende werkingsmechanismen. Dit kan vervolgens wellicht weer leiden tot het combineren van effectieve elementen uit verschillende interventies om zo effectiever op het onderliggende proces in te grijpen (Hofmann & Hayes, 2019; Rosen en Davison, 2003).

3.4.2. Design en populatie
De bevindingen in dit proefschrift brengen het onderzoeksveld verder door gebruik te maken van prospectieve studie designs met herhaalde metingen op zowel de korte als lange termijn. Bovendien waren de meeste onderzoeken gebaseerd multicenter RCT's en die waren ingebed in de algemene klinische praktijk waar weinig exclusiecriteria op van toepassing waren. Deze real-life setting vergroot de generaliseerbaarheid van de huidige bevindingen naar mensen met (recidiverende) depressie in zowel de tweede- als de derdelijnszorg. Er waren ook enkele beperkingen.
Ten eerste zijn er geen procesgegevens van een (actieve) controle groep verzameld. Hierdoor kan niet worden vastgesteld of de relaties die in de huidige onderzoeken werden gevonden specifiek zijn voor MBCT en MBCL. Toekomstig onderzoek dient procesgegevens te verzamelen van zowel een interventie als een (bij voorkeur actieve) controle groep om de specificiteit van verandering te bepalen. Daarnaast wordt het aangemoedigd om gebruik te maken van experience sampling methoden (ESM; Larson & Csikszentmihalyi, 1983). Hierbij wordt frequent gemeten over een kleinere tijdsspanne, om zo nog nauwkeuriger veranderingsprocessen tijdens MBCT en MBCL in kaart te brengen. Bovendien zou het waardevol zijn om uitkomstmaten (o.a. depressieve symptomen, kwaliteit van leven) ook in het model op te nemen om met meer zekerheid uitspraken te kunnen doen over de rol van mindfulness, zelfcompassie en affect als mogelijke werkingsmechanismen in MBCT en MBCL (Kazdin, 2007).

Ten tweede onderzocht het huidige proefschrift alleen de invloed van mindfulness beoefening in termen van kwantiteit en ontbraken er gegevens over de kwaliteit van beoefening. Om meer duidelijkheid te krijgen over de relatie tussen mindfulness beoefening en uitkomsten, is het aan te bevelen om in toekomstig onderzoek kwaliteit van mindfulness beoefening routinematig te beoordelen als aanvulling op de kwantiteit. Idealiter zou toekomstig onderzoek de kwaliteit van mindfulness beoefening op consistente wijze operationaliseren en meten, zodat de vergelijking van studieresultaten wordt bevorderd. De kwaliteit van beoefening kan bijvoorbeeld worden beoordeeld met de 7-item Practice Quality-Mindfulness (PQM; Del Re et al., 2013) of met de single-item PQM (Goldberg et al., 2020) om de belasting van deelnemers te verminderen wat mogelijk kan leiden tot minder ontbrekende data of het afhaken van deelnemers. Meer recent is de Mindfulness Adherence Questionnaire (MAQ; Hassed et al., 2020) ontwikkeld, die naast formele en informele mindfulness beoefening ook een duidelijk onderscheid maakt tussen de kwaliteit en kwantiteit van beoefening.

Ten derde dient onderzoek naar de werkingsmechanismen van MBCT en MBCL bij mensen met een huidige en chronisch therapiresistente depressie verder te worden onderzocht. In het huidige proefschrift werd MBCL aangeboden als vervolg op MBCT. Alhoewel eerder onderzoek gesuggereerde dat personen met relatief ernstige depressieve symptomen vooral baat kunnen hebben bij een sequentiële (op elkaar volgende) benadering (Cuijpers et al., 2020), is toekomstig onderzoek nodig om dit met betrekking tot MBCT en MBCL bij depressie te bevestigen. Dit kan bijvoorbeeld worden gedaan door de effectiviteit en het werkingsmechanisme van MBCT en MBCL bij depressie direct met elkaar te vergelijken. Om verder onderscheid te maken of de volgorde van interventies ertoe doet, zouden beide interventies in een cross-over studie kunnen worden aangeboden. Alhoewel Segal et al. (2012) suggereerden dat het beoefenen van zelfcompassie zonder eerst een basis te hebben ontwikkeld in mindfulness
kwetsbaarheid kan veroorzaken bij mensen met een (terugkerende) depressie, zou het aanbieden van MBCL in een eerder stadium of als een op zichzelf staande behandeling het behandeltraject aanzienlijk kunnen verkorten voor personen met een hoge mate van zelfkritiek en/of de neiging om te vermijden (Schuling, Huijbers, van Ravesteijn, Donders, et al., 2020). Bovendien zou dit kunnen leiden tot een verdere verlaging van de zorgkosten, gezien Schuling, Huijbers, van Ravesteijn, Donders, et al. (2020) ontdekten dat MBCL deelnemers minder gebruik maakten van de gezondheidszorg dan degenen in de controle groep, behalve als het gaat om bezoeken aan de huisarts.

3.4.3. Meetinstrumenten
Dit proefschrift is gebaseerd op data die verkregen is door middel van zelfrapportage vragenlijsten wat mogelijk kan hebben geleid tot recallbias (specifieke dingen wel/niet herinneren) en response bias (sociaal wenselijk antwoorden). Hoewel er redelijk wat evidentie is gevonden dat vragenlijsten veranderingen in mindfulness tijdens MBI’s kunnen oppikken (Goldberg et al., 2018), is het tot op heden moeilijk gebleken om consensus te bereiken over de precieze definitie van mindfulness (Baer et al., 2019) en wordt de validiteit van mindfulness vragenlijsten nog steeds betwist (Bergomi et al., 2013; Grossman & van Dam, 2011; van Dam et al., 2018). Sommige onderzoekers suggereren bijvoorbeeld dat de betekenis van vragen in zelfrapportage vragenlijsten voor mindfulness anders zullen worden geïnterpreteerd naarmate iemand meer ervaring heeft met mindfulness (Grossman & van Dam, 2011; van Dam et al., 2009). Daarnaast staat de Self-Compassion Scale (SCS) ter discussie. Zo zijn er onderzoekers die beweren dat het negatieve domein van de SCS, die de subschalen zelfoordeel, isolatie en overidentificatie bevat, de totale score voor zelfcompassie ‘besmet’, aangezien dit negatieve domein matig tot sterk correleert met psychopathologische constructen zoals negatief affect, depressieve klachten en rumineren (o.a. López et al., 2015; Muris et al., 2018). Andere onderzoekers ondersteunen echter het idee dat zowel de negatieve als de positieve subschalen de relatieve balans vertegenwoordigen van medelevende en niet-medelevende reacties op lijden en dat beiden een belangrijke bijdrage leveren aan het algemene concept van zelfcompassie (o.a. Krieger et al., 2016; Neff, 2016). Voor toekomstig onderzoek wordt aanbevolen om gelijktijdig zowel zelfrapportage vragenlijsten als meer objectieve data te verzamelen zoals gedragsmaten (Hadash & Bernstein, 2019) en fysieke, biologische en neurowetenschappelijke gegevens (van Dam et al., 2018) om de validiteit verder te onderzoeken. Ten slotte lijkt het, met betrekking tot het meten van affect, belangrijk om ook meer subtiele emoties op te nemen in toekomstig onderzoek (o.a. kalm, ontpidden), aangezien wordt aangenomen dat met name deze emoties toenemen tijdens meditatie (Jones et al., 2018).
Gezien MBI's geworteld zijn in de boeddhistische psychologie, kan het tevens interessant zijn om verder voort te bouwen op deze oude wijsheid. Moderne interventies kunnen bijvoorbeeld gebaat zijn bij het integreren van oefeningen die, naast compassie en vriendelijkheid, explicieter vreugde en gelijkmoedigheid cultiveren, wat mogelijk van toegevoegde waarde kan zijn voor mensen met recidiverende depressie. Bovendien zou het, in de context van het bestuderen van therapietrouw, interessant kunnen zijn om de vijf hindernissen in overweging te nemen die terug te vinden zijn in de boeddhistische leer. Dit zijn vijf mentale factoren die vooruitgang in meditatiebeoefening belemmeren: zintuiglijk verlangen, afkeer, rusteloosheid en zorgen, vermoeidheid of gebrek aan energie en twijfel of gebrek aan vertrouwen. Deze factoren zouden in toekomst onderzoek meegenomen kunnen worden om beter begrip te krijgen waarom wel of juist niet mindfulness oefeningen worden uitgevoerd. Het kan bijvoorbeeld zijn dat de neiging om naar plezierige ervaringen te zoeken, het lastiger kan maken om te oefenen indien er moeilijke of ongemakkelijke gevoelens of sensaties aanwezig zijn.

3.5. Klinische implicaties
Er zijn verschillende klinische implicaties die kunnen worden afgeleid uit het huidige proefschrift. Ten eerste bleek positief affect een duidelijke rol te spelen bij MBCT voor depressie, wat suggereert dat een verdere verfijning van MBCT voor depressie mogelijk zou kunnen zijn door meer nadruk te leggen op oefeningen die positief affect cultiveren, of zelfs het programma aan te passen door de sectie over prettige ervaringen verder uit te breiden, bijvoorbeeld door oefeningen vanuit de positieve psychologie toe te voegen. Ten tweede benadrukken de huidige bevindingen dat depressieve klachten mogelijk belemmerend kunnen werken bij het uitvoeren van mindfulness oefeningen en het ontwikkelen van mindfulness. Het kan van toegevoegde waarde zijn om deze problematiek in een vroeg stadium in de klinische praktijk te bespreken en regelmatig hierop terug te komen zodat de begeleiding hierop eventueel kan worden aangepast. Misschien kan een intensievere monitoring van nut zijn voor degenen met meer depressieve klachten (bijvoorbeeld met behulp van apps). Ten derde, alhoewel replicatie gerechtvaardigd is, zouden personen met een hoge mate van rumineren en een jonge leeftijd ten tijde van de eerste depressie vooral baat kunnen hebben bij MBCT als toevoeging op gebruikelijke zorg (bijvoorbeeld antidepressiva). Tot slot lijkt het erop dat MBCL zich met name richt op negatief affect via een (verdere) toename van zelfcompassie. Gezien resterende depressieve klachten, zoals bijvoorbeeld negatief affect, een belangrijke voorspeller zijn van een terugval van depressie, ondersteunt deze bevinding de potentiële klinische relevantie van MBCL en de mogelijke invloed ervan op terugvalpercentages. Toekomstig onderzoek zal moeten uitwijzen wie er in het bijzonder baat zouden kunnen hebben bij MBCL, en of MBCL bij voorkeur wordt
aangeboden als een aanvullende behandeling na MBCT voor depressie (of vice versa), of dat MBCL kan worden aangeboden als een op zichzelf staande interventie. Bovendien zou het interessant zijn om te onderzoeken of het explicieter integreren van zelfcompassie in MBCT de effectiviteit ervan kan verbeteren.

3.6. Conclusie
Dit proefschrift omvat verschillende studies naar de dynamische wisselwerking tussen mindfulness en affect bij MBCT en tussen zelfcompassie en affect bij MBCL voor depressie, het effect van formele mindfulness oefeningen bij MBCT voor depressie en het differentiële interventie effect van MBCT bij mensen met depressie. Voorlopig bewijs suggereert dat positief affect bij MBCT en negatief affect bij MBCL een prominentere rol lijkt te spelen. Bovendien is het effect van formele mindfulness oefeningen misschien niet zo eenduidig als verwacht, waarbij mogelijk omgekeerde effecten ook een rol kunnen spelen. Ten slotte kan MBCT naast gebruikelijke zorg gunstiger zijn voor diegenen die meer rumineren en op jongere leeftijd hun eerste depressieve periode doormaken. Deze bevindingen kunnen leiden tot een verdere verfijning van MBCT voor depressie en het gerichter aanbieden van MBCT bij deze populatie.
Referenties


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Aanwezigheid tijdens de PhD, die was soms hard nodig 😊. Kyle, I am sure you did not expect to end up in this dissertation. Although, our paths led us to other parts of the world, every now and then you crossed my mind and helped me with translating parts of papers and the website of the practice. Thank you for your endless support.

I am realizing that this acknowledgement is already way too long, so I would therefore like to briefly thank the rest of the (chosen) family (though no less heartfelt or valuable): Romane, Simone, André, Cathy, Esra, Natalie, Jessica (who?!), Saira, Ramón, Marjolein, Devan, Femmie, Coen, Marije, Mark, Daan, Rodrigo, Edo, Paula, Tijs, Petra, Hennie, Roos, Suze, Beer, Marcel, Rachela, Jeff, Nikki, Joanna, Carin, Joke, Charl, Dirk-Jan, Mechteld, Anita, Hermieke en Els (wanneer gaan we weer eens piano spelen?). In case I forgot to mention you; will you visit me soon? It probably has been far too long since we have seen each other!

Dan de familie. Om mij aan mijn woord te houden en deze dankbetuiging niet al te lang meer te laten worden, richt ik mij op het gezin. Om te beginnen Rosa; bij ons in de familie beter bekend als ‘aanloop zus’. Wat hebben we een mooi parallel proces gelopen tijdens de afronding van onze proefschriften en wat waren de kleine pauze-loopjes waardevol tijdens de lockdown! Ik ben erg blij met onze lange vriendschap (volgens mij zijn we onderhand ook de 25 jaar vergeten te vieren... oh ooh... time flies, maar gelukkig hebben we fun 😊). Ik heb bewondering voor jouw keuzes gedreven door passie en flow, waarbij jij je niet laat weerhouden door angst. Je inspireert en doet, terwijl je blijft voelen. Ik voel me geprezen met zo’n mooie lieve vriendin als jij.

Dan Tessa, ook wel ‘kleine grote zus’ genoemd. Wat was het heerlijk om samen te wonen en af en toe mee te kunnen eten als ik weer van hot naar her aan het rennen was gedurende het begin van de PhD. Ook kleine grote zusjes worden volwassen. Aan de ene kant moeilijk en pijnlijk, want daar hoort ook loslaten bij, maar aan de andere kant ook oh zo wonderbaarlijk mooi. Op momenten dat ik je weer zie, wordt ik vaak geraakt door de krachtige en gepassioneerde vrouw die voor me staat en hoe je nu weer in een andere vorm contact maakt. Dank je wel voor jouw heerlijke humor, nuchterheid, inspiratie, liefde en support.

Natuurlijk ook Milou en Chantal, ook wel ‘zussen’ genoemd. Lieve Chan en Mi, het was altijd weer gezellig als ik jullie tegenkwam bij Dorien en Tim: heerlijk gek doen, lekker lachen en spelletjes spelen. Ik heb bewondering voor jullie veerkracht en doorzettingsvermogen. De laatste jaren zijn jullie steeds meer op jullie zelf gegaan en zien we elkaar geleidelijk aan wat minder, maar weet: uit het oog is zeker niet uit het hart.

En natuurlijk lieve Dorien en Tim, wat hebben jullie een grote rol gespeeld en dan met name gedurende het afgelopen jaar. De deur staat bij jullie altijd
open om binnen te lopen en (soms ietwat langer dan gepland) te blijven plakken. Wat is het fijn om me zo af en toe terug te kunnen trekken uit de stad en in contact met jullie en de natuur te komen. Het is van onschatbare waarde om zo'n veilige haven te hebben. Dank jullie wel voor jullie onvoorwaardelijke liefde.

Shlomi, although we have been apart for a long time since corona struck the earth, you have supported me through and through. I love your humor, your ability to put things into perspective, your fearlessness when talking the truth, and your alignment with your soul. Thank you for being you.

Marleen J. ter Avest was born in Amsterdam, the Netherlands, on the 21st of July in 1989. She finished secondary education at Damstede College in 2007 and started her studies in Medicine at the Free University (VU) Amsterdam. During the medical internships she realized that she was less driven by ‘making people better but more by ‘helping people dealing better with whatever they are facing in life’. She firmly decided to switch to Psychology, and this is where it all began. Practicing mindfulness helped her to make this decision consciously by getting more in touch with her feelings and desires, and by becoming less affected by other people’s opinions. Back then, she was not yet aware to what extent mindfulness was going to affect her life.

In 2017 she graduated cum laude from Clinical Psychology, and directly afterwards she started her PhD on the working mechanisms of mindfulness-based cognitive therapy and mindfulness-based compassionate living for depression combined with the 1.5 years postgraduate mindfulness teacher training program at the Center for Mindfulness, department of Psychiatry, Radboud University Medical Center.

While finishing up her PhD in 2020, Marleen joined the Association of Mindfulness-Based Trainers of the Netherlands as a member of the scientific committee, she attended the mindfulness-based compassionate living teacher training program, and started her own practice Note to Mind. Lastly, to foster the resilience of people who work in health care, she volunteered at the Radboudumc Center for Mindfulness and Compassionate Care & Mindful Medicine by giving online mindfulness and compassion meditations to healthcare professionals.

Marleen will continue combining practice with research. Besides providing mindfulness and compassion courses at her own practice, she started as a post-doctoral researcher in the spring of 2021 studying the working mechanisms of mindfulness in children with ADHD and their parents at the Radboud University Medical Center, Donders Institute for Brain, Cognition and Behavior, department of Cognitive Neuroscience. In the future, Marleen aspires to keep combining practice with research, ideally with an increasing focus on compassion.
List of publications


Not included in this thesis


## PhD portfolio

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<thead>
<tr>
<th>Activities</th>
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<tr>
<td>Research meetings Radboudumc Center for Mindfulness: attendee, presenter and coordinator</td>
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<tr>
<td>Grand Rounds Radboudumc Psychiatry: attendee and presenter</td>
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<td>Stress meetings Radboudumc Stress-related disorders: attendee and presenter</td>
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<td>Donders Discussions 2019 and 2020: attendee</td>
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<td>Lectures on psychometrics, working mechanisms and neuroscience postgraduate mindfulness teacher training Radboudumc Center for Mindfulness: lecturer</td>
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<td>Cognitive Therapy and Research: reviewer</td>
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<td>Mindfulness-Based Compassionate Living: attendee</td>
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<td>Congress Society of Psychotherapy Research Amsterdam (June 28-30, 2018): attendee and presenter</td>
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Data management statement

This thesis is based on the results of previous human randomized-controlled trials (RCTs), which were conducted in accordance with the principles of the Declaration of Helsinki. All RCTs were approved by the Medical Ethics Committee of Arnhem-Nijmegen for all participating sites and/or the Medical Ethical Committee of local hospitals in Nijmegen, the Netherlands (2008/242; 2005/284; 2012/339; 2013/220).

Data and meta-data of each successive study from this thesis is stored at a separate subfolder of the folder ‘H:\Research\Co-MinD study’, which is securely stored on the H-server of the Radboud University Medical Center, department of Psychiatry. This folder and subfolders can only be accessed by authorized personnel, as to be determined by the management of the department of Psychiatry.

The original data of all RCTs will be saved for 15 years after termination of each successive RCT. Using these patient data in future research is only possible after a renewed permission by the patient as recorded in the informed consent. The datasets analyzed during this thesis are available from the corresponding author on reasonable request.
Donders Graduate School for Cognitive Neuroscience

For a successful research Institute, it is vital to train the next generation of young scientists. To achieve this goal, the Donders Institute for Brain, Cognition and Behavior established the Donders Graduate School for Cognitive Neuroscience (DGCN), which was officially recognized as a national graduate school in 2009. The Graduate School covers training at both Master’s and PhD level and provides an excellent educational context fully aligned with the research program of the Donders Institute.

The school successfully attracts highly talented national and international students in biology, physics, psycholinguistics, psychology, behavioral science, medicine and related disciplines. Selective admission and assessment centers guarantee the enrolment of the best and most motivated students.

The DGCN tracks the career of PhD graduates carefully. More than 50% of PhD alumni show a continuation in academia with postdoc positions at top institutes worldwide, e.g. Stanford University, University of Oxford, University of Cambridge, UCL London, MPI Leipzig, Hanyang University in South Korea, NTNU Norway, University of Illinois, North Western University, Northeastern University in Boston, ETH Zürich, University of Vienna. Positions outside academia spread among the following sectors: specialists in a medical environment, mainly in genetics, geriatrics, psychiatry and neurology. Specialists in a psychological environment, e.g. as specialist in neuropsychology, psychological diagnostics or therapy. Positions in higher education as coordinators or lecturers. A smaller percentage enters business as research consultants, analysts or head of research and development. Fewer graduates stay in a research environment as lab coordinators, technical support or policy advisors. Upcoming possibilities are positions in the IT-sector and management position in pharmaceutical industry. In general, the PhDs graduates almost invariably continue with high-quality positions that play an important role in our knowledge economy.

For more information on the DGCN as well as past and upcoming defenses, please visit: https://www.ru.nl/donders/graduate-school/phd/.
Wat het is

Het is onzin
zegt het verstand

Het is wat het is
zegt de liefde

Het is ongeluk
zegt de berekening
Het is alleen maar verdriet
zegt de angst
Het is uitzichtloos
zegt het inzicht

Het is wat het is
zegt de liefde

Het is belachelijk
zegt de trots
Het is lichtzinnigheïd
zegt de voorzichtigheid
Het is onmogelijk
zegt de ervaring

Het is wat het is
zegt de liefde

Erich Fried - 1983
Vertaling: Remco Campert