Mechanisms of action in mindfulness-based cognitive therapy (MBCT) and mindfulness-based stress reduction (MBSR) in people with physical and/or psychological conditions: A systematic review

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Abstract

Background: Recently, there has been an increased interest in studying the effects of mindfulness-based interventions for people with psychological and physical problems. However, the mechanisms of action in these interventions that lead to beneficial physical and psychological outcomes have yet to be clearly identified. **Purpose:** The aim of this paper is to review, systematically, the evidence to date on the mechanisms of action in mindfulness interventions in populations with physical and/or psychological conditions. **Method:** Searches of seven databases (PsycINFO, Medline (Ovid), Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, AMED, clinicaltrials.gov) were undertaken in June 2014 and July 2015. We evaluated to what extent the studies we identified met the criteria suggested by Kazdin for establishing mechanisms of action within a psychological treatment (2007, 2009). **Results:** We identified four trials examining mechanisms of mindfulness interventions in those with comorbid psychological and physical health problems and 14 in those with psychological conditions. These studies examined a diverse range of potential mindfulness mechanisms, including mindfulness and rumination. Of these candidate mechanisms, the most consistent finding was that greater self-reported change in mindfulness mediated superior clinical outcomes. However, very few studies fully met the Kazdin criteria for examining treatment mechanisms. **Conclusion:** There was evidence that global changes in mindfulness are linked to better outcomes. This evidence pertained more to interventions targeting psychological rather than physical health problems. While there is promising evidence that MBCT/MBSR intervention effects are mediated by hypothesised mechanisms, there is a lack of methodological rigour in the field of testing mechanisms of action for both MBCT and MBSR, which precludes definitive conclusions.

Keywords: MBCT, MBSR, mechanisms, physical conditions, psychological conditions, systematic review

Introduction

Long-term physical and mental health problems affect a significant proportion of the population, place an enormous burden on health care systems, are a very significant cost to society and cause immeasurable suffering. It is estimated that 46% of people in the UK with mental health problems also suffer from long-term physical conditions, such as heart conditions, stroke, diabetes and cancer (Naylor et al., 2012). This comorbidity is responsible for poor medical outcomes (Katon, 2011; Kisely, Smith, Lawrence, & Maaten, 2005; Wright et al., 2008), significant decrements in quality of life (Fortin et al., 2006; Moussavi et al., 2007; Sareen. et al., 2006) and increased costs of health care (Naylor et al., 2012). Therefore, there is a need to develop integrated treatments that can effectively treat people with comorbid mental and physical health presentations. It is increasingly argued that there could be some overlap in the biological, behavioural and psychosocial mechanisms linked to these physical and psychological conditions (Carlson, 2012; DE Hert et al., 2011; Dickens, 2015; Miller, Chen, & Cole, 2009). Consequently, researchers are increasingly trying to develop integrated mind-body theoretical models that can potentially capture the shared mechanisms and support the development of effective treatments for physical conditions that have mental health co-morbidity.

Mindfulness-based interventions were developed for people with chronic physical problems, who were managing pain, low mood and health-related anxiety. Mindfulness is most typically defined as "paying attention in a particular way: on purpose, in the present moment, and non-judgementally" (Kabat-Zinn, 1994, p.4). An operational definition of mindfulness would include at least three components: attentional control, the intention of attentional control (e.g., to decenter from negative thinking) and attitudes that are being trained (e.g. approach orientation and non-judgment). Mindfulness-Based Stress Reduction (MBSR) has been used since 1979 as a training vehicle for the relief of pain and distress in

people with chronic health problems (Kabat-Zinn, 1990, 2013). Mindfulness-Based Cognitive Therapy (MBCT) (Segal, Williams, & Teasdale, 2013, 2002) integrates MBSR with cognitive science and Cognitive Behavioural Therapy. It was initially developed as a relapse prevention treatment in those with a high risk of depression recurring, but has since been adapted to a range of different populations and contexts. Both MBSR and MBCT incorporate a range of formal mindfulness practices as a key method for training attentional control as well as the non-judgemental attitudinal dimensions of mindfulness (Crane et al., 2017) MBSR has been found to have positive effects on pain, anxiety and stress in people with chronic disorders, such as fibromyalgia, coronary artery disease, pack pain and arthritis (Grossman, Niemann, Schmidt, & Walach, 2004; Rosenzweig et al., 2010). Preliminary evidence suggests that MBCT can decrease depression, anxiety and fatigue in some physical conditions, such as coronary heart disease (O'Doherty et al., 2015), diabetes (Van Son, Nyklíček, Pop, & Pouwer, 2011; van Son et al., 2014) and cancer (Van Der Lee & Garssen, 2012). Moreover, recent systematic reviews have indicated that MBSR and MBCT have small to medium effect sizes on psychological and physical symptoms across a range of chronic somatic conditions including cancer, cardiovascular disorders and arthritis (Abbott et al., 2014; Bohlmeijer, Prenger, Taal, & Cuijpers, 2010; Hofmann, Sawyer, Witt, & Oh, 2010).

In addition to research evaluating clinical efficacy, there is also a need to understand the mechanisms of action of these mindfulness interventions (Craig et al., 2008; Moore, Audrey, Barker, & Bond, 2014). A greater understanding of the mechanisms through which interventions bring about change will enable these interventions to be refined, which will potentially increase their potency and provide "larger effect sizes at lower cost or risk" (Kraemer, Wilson, Fairburn, & Agras, 2002, p. 878). Moreover, it will shed light on the theories that explain how these conditions arise.

A mechanism is defined as "the process that is responsible for change", while a mediator is "an intervening variable that may account statistically for the relationship between independent variable and dependent variable" (Kazdin, 2007, p.3). Kazdin (2007, 2009) proposes essential criteria for identifying mechanisms or mediators of action in psychotherapy. To begin with, there needs to be a clear association between change in the proposed mechanism/mediator and the proposed outcome (strong correlation criterion). In addition, the outcomes and mediating variables need to be measured at multiple time points, thus making it possible to establish that change in the mediator precedes change in the outcome (temporal precedence criterion). Manipulation designs (where a specific mechanism is increased or decreased), active and/or dismantling designs (where intervention elements targeting a specific mechanism are left out) need to be utilised to determine the specificity of effects (specificity criterion). Further, a dose-response relationship needs to be observed, such that the more a mechanism is targeted, the greater the degree of change in the outcome observed (gradient criterion). The findings should be replicable; ideally by an independent research group (consistency criterion). Kraemer suggests that randomised controlled trials (RCTs) are needed to test the mechanisms or mediators routinely and that experimental studies need to take into account their results in their designs (Kraemer et al., 2002).

There is as yet no consensually agreed unifying theoretical framework of how MBCT/MBSR effect change, but rather a breadth of theoretical models. A recent editorial suggested that there is some consensus that MBCT/MBSR helps people "learn that habitual reactive patterns stem from unhelpful habits of the mind; that fear, denial and discrepancy-based thinking create and exacerbate distress; and that skilful ways of relating to experience can be developed through awareness, wise discernment and practice which offer the potential for (moments of) freedom from reactivity" (Crane et al., 2017).

Several early studies have started to explore the mechanisms in MBCT/MBSR (Batink, Peeters, Geschwind, van Os, & Wichers, 2013; Geschwind, Peeters, Drukker, van Os, & Wichers, 2011; Nyklícek & Kuijpers, 2008;Vøllestad et al., 2011). To date most mechanisms studies have either not explicitly drawn on a particular theoretical model, or have drawn on different models and selected out particular mechanisms and defined these with varying degrees of precision. Moreover, they have failed to employ robust designs to assess the proposed mechanisms (Gu, Strauss, Bond, & Cavanagh, 2015; van der Velden et al., 2015).

It is as yet unclear whether mechanisms of action in MBCT/MBSR are shared across physical and psychological health conditions or are specific to particular physical or psychological health conditions. Some researchers think that there are potential common or universal mechanisms of action in MBCT/MBSR regardless of whether the specific disorder is physical (Carlson, 2012) or psychological (Teasdale, Segal, & Williams, 2003). A narrative review (Carlson, 2012) of mindfulness interventions in physical conditions has indicated that mechanisms such as mindful attention, acceptance and exposure are important in understanding how MBCT/MBSR are effective for different physical conditions. Other researchers suggest that some mechanisms of action are disorder-specific. For example, Loucks and his colleagues in their recent review (Loucks et al., 2015) put forward some mechanisms that might explain how mindfulness works with cardiovascular disorders (CVD), including attentional control of some of the risk factors of CVD and self-awareness of cardiac experiences that are potentially modifiable. The delineation of universal and specific vulnerabilities that may also be mechanisms of change leads to the generation of key hypotheses that can inform both primary research and interpretation of secondary research (Teasdale et al., 2003). In terms of vulnerability, unhelpful repetitive thinking hijacking attention could be universal (Watkins, 2008), while in people with a history of depression

cognitive reactivity, characterised by negative self-referential thoughts, might be a specific vulnerability (Segal et al., 2013). In terms of the hypothesised mechanisms, learning to stabilise attention (a universal mechanism), which refers to our capacity to cultivate and stabilise or focus attention in the body (Williams & Kabat-Zinn, 2013),could be a pre-requisite to first recognising cognitive reactivity (a specific mechanism in this population) and then decentering from negative thinking (an emotion regulation strategy). Cognitive reactivity is defined as 'the degree to which a mild dysphoric state reactivates negative thinking patterns" (Raes, Dewulf, Van Heeringen, & Williams, 2009, p.623)

Recently, Van der Velden et al. (2015) conducted a systematic review of the mechanisms of MBCT in RCTs looking at how MBCT produced its effects on both relapse prevention and acute depression in people with major depressive disorders (MDD). The results showed good evidence supporting the mediating role for mindfulness, rumination, worry, compassion, meta-awareness with preliminary evidence for attention, memory specificity, self-discrepancy, emotional reactivity as well as positive and negative affect. This review only considered MDD not physical conditions and primarily focused on depression outcomes. Although, the review mentioned some of Kazdin criteria, it did not systematically evaluate each study against these. Another recent systematic review and meta-analysis, conducted by Gu et al. (2015), tested the mechanisms of both MBSR/MBCT on mental health and wellbeing outcomes, including for those with primary physical health problems (e.g. cancer). In this review, RCTs or quasi-experimental design studies were included and they found strong evidence for cognitive and emotional reactivity, moderate evidence for mindfulness, rumination, and worry as potential mechanisms of change, and preliminary but insufficient evidence for self-compassion and psychological flexibility. This review involved using a well-established method of mediation analysis and had a quantitative assessment of change in the outcome and mediators. However, the review had some

limitations, such as not considering the methodological quality, not commenting on Kazdin's criteria in detail and considering only mechanisms with a strong theoretical rationale, thus excluding some potential more exploratory variables. In addition, even though the review targeted a broad range of populations, including people with cancer, it did not focus on whether the same mechanisms play a role in depression versus depression in the context of long term conditions.

There is therefore a need for a further systematic review of mechanisms of action in mindfulness interventions that deals with these shortcomings. In this review, we further explore the evidence, to date, on mechanisms of action in MBCT/MBSR interventions for populations with physical and/or psychological conditions. We included studies that focused on populations with physical and/or psychological conditions to assess whether the evidence for mechanisms accounting for psychological symptom improvement has been found both in those with psychological and physical health presentations. We looked at whether the same mechanisms have been identified across different populations (primarily depression or primarily physical health), which would suggest they may be universal. Also, we aimed to assess methodological adequacy of these studies according to the Kazdin criteria for examining mechanisms of change in treatments. We approached the mechanisms of action in an exploratory (rather than theory driven) way, that is, simply identifying and reporting the mechanisms/mediators that were reported in the identified studies. Moreover, we considered the recommendations mentioned in Gu and her colleagues review in terms of publication bias and variation in the nature of the outcome variable (acute versus relapse prevention; physical or psychological). The aim of this work is to usefully frame future primary research.

Method

Inclusion and exclusion criteria

The systematic review was conducted following the general principles published by the NHS Centre for Reviews and Dissemination (CRD, 2009) and reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher, Liberati, Tetzlaff, & Altman, 2009). It included published randomised controlled trials (RCTs), and controlled trials (CTs) that aimed to examine potential mechanisms or mediators of change in MBCT/MBSR in adults diagnosed with physical and/or psychological conditions. Studies using shortened forms of either MBCT or MBSR were excluded. No language or date restrictions were applied for this review. Details of the inclusion and exclusion criteria are presented in Table 1.

Identification of studies

Search strategy. The first electronic search of seven databases (PsycINFO, Medline (Ovid), Cochrane Central Register of Controlled Trials, EMBASE, CINAHL, AMED, clinicaltrials.gov) was undertaken in June 2014 and we conducted an update search in July 2015. The search strategy varied across the databases, but the same keywords applied throughout. An example of the search strategy is presented in Appendix A.

Study selection. After removing duplicates, the titles and abstracts were screened independently by MA and TK, with the aim of identifying potentially relevant studies. During this phase, inclusion and exclusion criteria were applied and disagreement was resolved through discussion with a third reviewer, RA. Subsequently, full texts of the promising studies were obtained and their reference lists were examined. In the second phase of screening, the full texts were assessed further for eligibility by MA and checked by RA.

Data extraction. We collected the characteristics of studies using the PICOS (**P**opulation, **I**ntervention, **C**omparator, **O**utcomes and **S**tudy design) framework. The

population features included age, gender, sample size and whether it was a psychological or physical condition. Intervention covered whether the intervention used was MBCT or MBSR and if had been administered as its developers had intended or had been adapted. Comparator features consisted of the number of study arms and type of control group (waitlist, other active intervention or treatment as usual). The outcomes pertained to the main findings in terms of physical and/or psychological aspects, whilst the study design included whether it was a randomised controlled trial (RCT) or a controlled trial (CT). We additionally extracted all information that would enable us to evaluate how well the Kazdin criteria (2007, 2009) were met. Data extraction was conducted by MA and checked by RA.

Data synthesis. The aims of this review were not to examine the effectiveness or efficacy of interventions, but rather, to describe and evaluate potential mechanisms or mediators. We anticipated identifying studies that used a range of different interventions, with possible different mechanisms or mediators of action in different populations. We anticipated that pooling the data would distract from the main aims of the review, would be difficult to interpret, and would not add value. Therefore, where sufficient data was available we decided to classify data by population type and then evaluate the status of the evidence for each hypothesized mechanism/mediator within each population type.

Risk of bias in RCTs

The methodological quality of each included study was assessed using the Cochrane 'risk of bias' tool (Higgins et al., 2011). Each study was evaluated based on certain parameters, such as random sequence generation, allocation concealment, blinding and selective reports. The risk of bias in the RCTs' evaluation was conducted by MA and checked by RA.

Conceptual framework for abstracting and interpreting studies

We developed a framework derived from the recommendations put forward by Kazdin (2007, 2009), which both informed the data extraction and the interpretation of the findings. This framework included the following questions:

1. Did the study use a theory or treatment rationale to articulate the mechanism through which the intervention is hypothesised to work? This includes:

   - Were hypotheses about the mechanism of change articulated?

   - Were the hypothesised processes of change articulated, defined and operationalised?

2. Did the study use process measures that assess the constructs, if necessary, from a variety of perspectives? A variety of perspectives means here the study's use of a variety of assessment methods in addition to self-report measures, which could include experimental or neuroscience measures".

3. Did the study design ensure the hypotheses could be addressed? This includes:

   - Making explicit that changes in processes are specifically targeted by the treatment;

   - That changes occur during treatment;

   - That these changes precede change in the outcome;

   - Using different time-points assessments.

4. Did the study use appropriate statistical analysis?

Results

Studies flow

The electronic searches of seven databases retrieved 3,290 titles and abstracts. After adjusting for duplicates and reviewing the titles and abstracts, 3,234 studies were removed. In the first phase of the screening for eligibility, 56 abstracts and titles were screened against the inclusion and exclusion criteria, resulting in 15 studies being excluded for the following reasons: five were not MBCT or MBSR, two focused on healthy populations, two were short MBSR (six weeks), four did not examine mechanisms or mediators and two were not randomised controlled trials or controlled trials. In the second phase, 35 of the 41 full texts were obtained while six were conference abstracts rather than published papers and the necessary information was not available. The 35 full texts were screened further against the inclusion and exclusion criteria. In this phase, 17 studies were excluded for the following reasons: four for not being MBCT or MBSR, four focused on healthy populations, four used short MBSR (four-six weeks), three were not randomised controlled trials or controlled trials, one did not examine mechanisms or mediators and one tested moderators of MBCT. Finally, four studies with physical conditions populations and 14 studies with psychological conditions populations met the inclusion criteria of this review (see Figure 1).

Studies focused on populations with physical conditions

   Characteristics of the studies.

Table 2 summarises the characteristics of the included studies that focused on people with physical conditions and co-existing psychological problems. Four studies met the review criteria: three focused on people with cancer (Bränström, Kvillemo, Brandberg, & Moskowitz, 2010; Labelle, Campbell, & Carlson, 2010; Labelle, Campbell, Faris, & Carlson, 2015) and one (O'Doherty et al., 2015) targeted people with coronary heart disease (CHD). One study (Bränström et al., 2010) employed an RCT design and three used a CT design

(Labelle et al., 2010, 2015; O'Doherty et al., 2015). All the studies compared MBSR/MBCT to waitlist control. The sample sizes ranged from 71 to 211 with a total of 71 randomised and 405 non-randomised. Two studies included only females (n=148) (Bränström et al., 2010; Labelle et al., 2010).

Two out of the four included studies examined more than one mediator, which were mindfulness skills (n=4), rumination (n=2) and cancer-related worry (n=1). All the studies used self-report questionnaires to assess the proposed mediators. Three (Bränström et al., 2010; Labelle et al., 2010, 2015) made some adaptations to the MBSR original manual so as to make it appropriate for people with cancer, but with the same length of course, whilst the only study that used MBCT followed the programme as outlined by Segal et al. (2002, 2013).

Mechanisms/mediators in studies with physical conditions populations.

Mindfulness, rumination and worry. Mindfulness, as a potential mediator, was tested in the all of these studies and rumination was assessed in two. Of the four studies looking at mindfulness as the mediator, two (Bränström et al., 2010; O'Doherty et al., 2015) showed it mediated the effects of MBCT/MBSR on perceived stress, posttraumatic avoidance, positive state of mind, current depression, anxiety, psychosocial adjustment to illness, mood and health-related quality of life. In these studies, mindfulness was assessed by different measures that have different conceptual backgrounds. For example, the Kentucky inventory of mindfulness (KIMS) (Baer, 2004) and five-facet mindfulness questionnaire (FFMQ) (Baer et al., 2008) were developed based on the assumption that mindfulness is a multifaceted construct, including facets such as observing, describing, acting with awareness, non-judgment and non-reactivity. While the mindful attention awareness scale (MAAS) was developed with a single-factor structure (receptive attention to and awareness of present events and experience) (Brown & Ryan, 2003). The other two studies (Labelle et al., 2010, 2015) found no mediation effect of mindfulness on depression, experiential avoidance and

stress symptoms. Both studies (Labelle et al., 2010, 2015) that assessed rumination as a mediator found it to be a significant mediator of MBSR for depression, experiential avoidance and stress symptoms (Labelle et al., 2010, 2015).

Bränström and his colleagues (2010), in their RCT with two time-points (pre-post), tested whether mindfulness skills would mediate the effects of adapted-MBSR in females with cancer (n=71). The results indicated that the positive effects of the MBSR intervention on stress, posttraumatic avoidance and positive states of mind were mediated by significant increases in mindfulness skills. A study by O'Doherty et al. (2015) used a controlled trial with three time-points (pre-post- follow up) to evaluate the effectiveness of MBCT on people with coronary heart disease (CHD) and current depression and tested whether mindfulness would lead to changes in outcomes. The results revealed that the MBCT group when compared to the waiting list group showed improvements for current depression, anxiety, psychological adjustments to illness, quality of life and mindfulness, with these improvements being correlated significantly with the increases in mindfulness.

Labelle et al. (2010) in a controlled study of 77 females with cancer using two time-points, found that mindfulness did not mediate the significant effect of adapted-MBSR on depressive symptoms, while rumination did. Consistent with this result, a recent controlled study (Labelle et al., 2015) with three time-points (pre, mid, and post intervention), showed that early decreases in rumination and cancer-related worry mediated the effects of adapted-MBSR on the outcomes, while mindfulness skills did not.

Studies focused on populations with psychological conditions

Characteristics of studies.

 Table 3 shows the characteristics of the included studies that focused on people with psychological conditions (depression and anxiety). 14 published trials met the review criteria, three of which used the same dataset (Batink, Peeters, Geschwind, van Os, & Wichers, 2013;

van Aalderen et al., 2012; van den Hurk et al., 2012). All the studies employed an RCT design. The sample sizes ranged from 29 to 219 with a total of 1,122 randomised males and females. Four studies compared MBCT to treatment as usual (TAU), four compared MBCT (n=3) or MBSR (n=1) to waitlist, three studies compared MBSR to active groups (aerobic exercise, stress management), one compared MBCT plus discontinuation of antidepressant medication to maintenance antidepressant medication (mADM), one study used the depression relapse active monitor (DRAM) as a control group and one had three arms: MBCT, mADM and a placebo. Among the depression studies, the majority focused on recurrent MDD, whereas one (van Aalderen et al., 2012) targeted recurrent and current depression. The studies used different criteria to establish MDD, such as the Structured Clinical Interview for DSM-IV (SCID) and the Hamilton Rating Scale for Depression (HRSD). All studies followed the MBCT/MBSR programmes, as outlined by Segal et al. (2002, 2013) and Kabat-Zinn (1990, 2013).

The majority of the studies (n=11) examined two or more mediators. Those examined included mindfulness skills (n= 8), rumination (n=5), positive affect (n=2), worry (n=2), cognitive function and reactivity (n=2), emotional reactivity (n=1), attentional processes (n=1), self-compassion (n=1), decentering (n=2), self-referential brain network (n=1), brain activation and connectivity (n=1). With regard to measuring the mediators, the majority of the studies (n=10) relied on self-report. Emotional and cognitive tasks in addition to self-report measures were used to assess attentional processes as well as emotional and cognitive reactivity (n=3), whilst two studies used fMRI.

Mechanisms/mediators in studies with psychological conditions populations.

Anxiety disorders.

Mindfulness and decentering. Two studies examined mindfulness as the mechanism of change for MBSR in people with anxiety disorders. Vøllestad, Sivertsen, and Nielsen

(2011) looked at mindfulness as a mediator of the relationship between MBSR and improvements in anxiety, worry and depression in a randomised controlled trial for people with anxiety disorders. The results indicated that during MBSR significant increases in mindfulness skills mediated the relationship between MBSR and anxiety and worry, but not depression when compared to waitlist control. Another randomised study (Hoge et al., 2015) that compared adapted-MBSR to stress management education (SME) in people with generalised anxiety disorders (GAD), found that a significant increase in decentering was a mediator for MBSR in relation to anxiety, while significant increases in mindfulness skills mediated the effects of MBSR on worry when compared to a stress management group. In this study, decentering is defined as "a metacognitive capacity of individuals to observe items that arise in the mind (e.g., thoughts, feelings, memories, etc.) as mere psychological events" (Hoge et al., 2015, p.229).

Brain network and connectivity. Goldin, Ziv, Jazaieri, & Gross (2012) tested the correlation between self-referential brain networks and improvements in social anxiety symptoms in people undertaking MBSR compared with a group undertaking aerobic exercise (AE). The fMRI and self-referential encoding task results showed that significant changes in self-views as well as dorsomedial pre- frontal cortex (DMPFC) activity during negative self-view were correlated with significant reductions in social anxiety in the MBSR group. Hölzel et al. (2013) found that people undergoing MBSR, when compared to a stress management group, showed changes in ventrolateral prefrontal regions (VLPFC) activation and amygdala–prefrontal connectivity and these were associated with improvements in generalised anxiety disorder.

Depression.

Mindfulness. Six RCTs indicated that MBCT led to a significant decrease in residual depressive symptoms (Batink et al., 2013; Bieling et al., 2012; Kuyken et al., 2010; Shahar, Britton, Sbarra, Figueredo, & Bootzin, 2010; van Aalderen et al., 2012) and relapse (Kearns et al., 2015; Kuyken et al., 2010). These effects were found to be mediated by significant increases in overall mindfulness (Kearns et al., 2015, Kuyken et al., 2010; Shahar et al., 2010), acceptance without judgment (Batink et al., 2013; van Aalderen et al., 2012) and curiosity (Bieling et al., 2012).

Rumination. Rumination refers to "a mode of responding to distress that involves repetitively and passively focusing on symptoms of distress and on the possible causes and consequences of these symptoms"(Nolen-Hoeksema, 1991,p1).Two MBCT studies indicated that significant reductions in depression were mediated by rumination (van Aalderen et al., 2012) and brooding as a component of rumination (Shahar et al., 2010), while the outcomes of other studies have determined that the effects of MBCT were not mediated by rumination as a total score (Batink et al., 2013; Bieling et al., 2012; Kearns et al., 2015) or reflective pondering, as a component of rumination (Shahar et al., 2010).

Worry, affect and self-compassion. Worry refers to "a chain of thoughts and images that are affectively negative and relatively uncontrollable" (Borkovec, Robinson, Pruzinsky, & DePree, 1983. p10).Two MBCT studies using the same dataset (Batink et al., 2013; van Aalderen et al., 2012) tested worry as a proposed mediator of change by using self-report measures and found that it mediated the effects of MBCT on depressive symptoms. Regarding affect, two studies assessed whether increased positive affect acted as a mediator of the effect of MBCT on depression, using experience sample methods (ESM). The first (Geschwind, Peeters, Drukker, van Os, & Wichers, 2011), showed that increased positive affect (PA), activity pleasantness, and reward experience (SE) were associated with decreases in depression. The second (Batink et al., 2013), found that an increase in positive affect and a decrease in negative affect were mediated MBCT effects on depression. In another study, learning self-compassion was found to have a mediating role in the relationship between MBCT participation and depression over a 15 months follow up period (Kuyken et al., 2010). "Self-compassion is being touched by and open to one's own suffering, not avoiding or disconnecting from it, generating the desire to alleviate one's suffering and to heal oneself with kindness" (Neff, 2003, p.87).

Cognitive and emotional reactivity. Kuyken et al. (2010) found that high levels of cognitive reactivity predicted a poorer outcome in terms of depressive symptoms and relapse rate in the m-ADM group, but for the MBCT group this link between reactivity and outcome was weakened. With regards to emotional reactivity which is defined as 'progressively prolonged or intensified negative affect in response to stress'" (Britton et al., 2012, p. 366), Britton, Shahar, Szepsenwol, & Jacobs (2012) conducted a laboratory study to test emotional reactivity to a social stress task in people with recurrent depression. The results indicated that improvements in emotional reactivity were mediated the relationship between MBCT and depression.

Cognitive function and attentional processing. Jermann et al. (2013) examined five cognitive functions (autobiographical memory, shifting abilities, dysfunctional attitude, mindful attention and rumination), using a combination of cognitive tasks and self-report measures. They found that the participants in the MBCT group showed a significant decrease in dysfunctional attitudes at 9 months follow up. Van den Hurk and his colleagues (2012) tested different components of attentional processing (alerting, orienting and executive attention) by using an attentional network test. The results indicated that MBCT led to reductions in depression and rumination and increases in mindfulness skills when compared to TAU, but no significant differences in components of attention between MBCT and TAU were found. In terms of testing the mediating role of attentional processing, the results suggested that attentional processing did not mediate the relationship between MBCT and depression when compared to the TAU group.

Risk of bias in the RCTs

Risk of bias assessments are shown in Tables 4 and 5. Regarding the studies with physical conditions populations, the majority had shortcomings regarding sequence generation, allocation concealment and power calculation. However, most did adequately describe eligibility criteria and data collection tools valid. For the studies regarding psychological conditions, the majority adequately described sequence generation, allocation concealment and selective reporting. These studies also effectively reported eligibility criteria, power calculations, compliance with intervention and data collection tools valid.

Evaluating the ability of the studies to assess mechanisms or mediators

Each study was also evaluated based on our previously mentioned framework (see Tables 6 and 7). In this section, we present, first, whether each included study was able to meet the eight criteria of this review framework and then, we report how well all of them met the four questions that represent the eight criteria. With regards to the studies pertaining to

physical conditions, that by Bränström et al. (2010), which targeted females with cancer, met five of the eight criteria of this review, but it did not reflect different perspectives in terms of assessing mediators of MBSR. In addition, two time-point assessments were used, which meant that they were not able to prove that the change in their proposed mediator (mindfulness skills) preceded the observed changes in the study outcomes. The study by Labelle et al. (2010) that also studied females with cancer met five criteria, but could not meet 3, 6 or 7 . The authors relied on self-report measures to assess their mediators (mindfulness and rumination) and used two time points, which meant that temporal precedence could not be established and therefore, true mediation could not be tested. Labelle and her colleagues in their recent study (2015) with people with cancer met seven criteria however, they used only self-report measures to assess rumination, mindfulness skills and worry as proposed mediators of the effects of MBSR. The study by O'Doherty et al. (2015) that focused on people with coronary heart disease met six criteria, but did not satisfy 3 and 8. The correlation analysis that was used in this study was not able to test the full mediation of effects of MBCT on depression.

Regarding the studies focussed on psychological conditions, the studies that targeted people with anxiety disorders (Goldin et al., 2012; Hoge et al., 2015; Hölzel et al., 2013; Vøllestad et al., 2011) met between five and six of the eight criteria. These studies used two assessments, hence being unable to show the temporal precedence between mediators and outcomes. In terms of studies that targeted people with depression using MBCT, Kuyken et al., (2010) met all the eight criteria of this review framework, whilst others (Bieling et al., 2012; Kearns et al., 2015) met seven and could not meet criterion 3. The studies by Batink et al. (2013), Shahar et al. (2010), van Aalderen et al. (2012) van den Hurk et al. (2012) met five criteria and had limitations in term of relying on self-repost measures, using just two time points and not showing the temporal precedence. The studies by Geschwind et al. (2011) and

Jermann et al. (2013) met only four of the eight criteria, not being able to satisfy criteria 3,6,7, 8 having shortcomings in terms of not using enough time point assessments, not showing the temporal precedence and not using the appropriate statistical analyses.

Did the study use a theory?

The mechanisms need to be identified based on a theory or treatment rationale for articulating the mechanisms through which the treatment is hypothesised to work (Kazdin, 2007). While all studies reported using some theory, very few articulated a coherent account of universal and/or specific vulnerabilities driving the problems or explained exactly how MBCT/MBSR would target these mechanisms. We found that the studies with participants with physical conditions, especially those focusing on cancer populations, represented good attempts to develop models that linked mindfulness and emotions regulation as mediators for MBSR effects on cancer. There is a need for further studies that consider clearly articulated mechanisms, such as those proposed in reviews conducted by Carlson et al. (2012) and Loucks et al. (2015). With regards to studies focussed primarily on psychological condition, the majority with depression populations used a well-designed theoretical model of MBCT intervention for recurrent depression. However, many looked at a single mediator and did not consider the issue of universal versus specific vulnerabilities or the inter-play between different mechanisms.

Did the study use process measures that assess the constructs, if necessary, from a variety of perspectives?

The use of measures that can take into account different viewpoints, such as experimental and neuropsychological measures, is another important matter that needs to be considered (Kazdin, 2007). All the included studies used some form of measures to assess the mediators; however, there was wide variability in the types used. We found that the studies of physical conditions (n=4) relied completely on self-report measures to assess mediators, such

as mindfulness, rumination and cancer-related worry. In the studies of psychological conditions, whilst the majority (n=10) used self-report measures, we did find some examples of more objective measures, such as fMRI and laboratory tests, to assess self-referential brain network, brain connectivity as well as emotional and cognitive reactivity.

Did the study design ensure the hypotheses can be addressed?

It is worth noting that the best design is one that can assess changes over different time points within an RCT design (Kazdin, 2007). Even though the majority of the studies (n=15) were RCTs, which is considered as the gold standard for testing efficacy and effectiveness, the number of time assessments included in these was not optimal to for testing mechanisms or mediators. Only two of the five studies focusing on populations with physical conditions (Labelle et al., 2015; O'Doherty et al., 2015) and three of the depression and anxiety studies (Bieling et al., 2012; Kearns et al., 2015; Kuyken et al., 2010) used three or more time points. The majority of the studies looked at changes from Time 1 to Time 2 in both constructs, meaning temporal precedence (change from Time 1 to Time 2 in the mediator predicts change between Time 2 and Time 3 in the outcome) could not be established (and reverse causality remained a possibility). However, all the studies in this review failed to assess the changes over several time points.

Did the study use appropriate statistical analyses?

Some statistical criteria have been suggested that can help in testing mediation effects (Kazdin, 2007, 2009; Kraemer et al., 2002). For example, establishing significant relationships between the intervention, the proposed mediator and the outcome, as well as between the proposed mediators and the outcomes. Another important criterion is establishing the precedence between the changes in mediators and changes in outcomes. In this review, we found that whilst the majority of studies used some form of mediation analyses, the rest employed analyses that could not test mediation. Moreover, it was not

possible to conduct a full test for mediation due to insufficient time points in the majority of the studies.

Discussion

In this review, we first aimed to review the potential mechanisms of change in MBCT and MBSR for people with physical and/or psychological conditions. A second aim was to see whether there are universal mechanisms of mindfulness interventions that apply across populations/conditions as well as specific mechanisms that pertain to a particular population/condition. The evidence from the included studies was evaluated based on Kazdin's framework (Kazdin, 2007, 2009). The results of the review are consistent with the two recent reviews (Gu et al., 2015; van der Velden et al., 2015). While there is promising evidence that MBCT/MBSR treatment effects are mediated by hypothesised mechanisms, such as mindfulness and rumination, there is a lack of methodological rigour in the field of testing mechanisms and mediators of action in both MBCT and MBSR that precludes definitive conclusions.

Moreover, the lack of a consensually agreed theoretical framework of what universal and specific mechanisms drive change in MBCT/MBSR means that we do not, as yet, have the basis for articulating what degree of change, in which mechanisms (e.g., orienting attention, executive control, compassion), through which components of MBCT/MBSR (e.g. particular formal mindfulness practices) drive change, with which populations (e.g., adults with recurrent depression, health related anxiety), for which aims (e.g., reduce depressive relapse). Our findings provide insights that can inform future experimental and mechanisms studies embedded in trials to better articulate these elements.

Moreover, our review highlights that less attention has been given to studying the mechanisms of change through MBCT/MBSR in populations with physical conditions when compared to populations with psychological ones. Moreover, the few studies examining

physical health conditions focused primarily on psychological symptoms outcomes such as stress, anxiety and depressive symptoms and neglected physical health outcomes.

In two out of the four studies, mindfulness and rumination seem to mediate the effects of MBCT/MBSR on perceived stress, posttraumatic avoidance, depression, positive state of mind and psychosocial adjustment to illness for people with physical conditions (heart conditions and cancer). However, only one out of the four physical studies focused on mediating factors that were specifically related to the populations, namely cancer-related worry in a cancer population (Labelle et al., 2015). Examining mechanisms that are specific to a population or intervention is essential to test whether universal and specific vulnerabilities/mechanisms are being targeted.

In the studies of psychological conditions, we found that depression has received much attention with regards to mechanisms of action in MBCT, while anxiety has received most attention in relation to MBSR. The majority of the included studies considered mindfulness as a universal mediator. In most, mindfulness shows potential as a mediator of change in MBCT/MBSR for people with depression, anxiety and stress. In addition to mindfulness, rumination, worry and self-compassion have been investigated for mediation effects. Other proposed mediators, such as attention and emotional reactivity, were assessed to a lesser degree. To assess attention and reactivity well requires experimental paradigms that the majority of the studies to date have not included. Moreover, studies sometimes used different measures of the same outcome; for example, in depression relapse some prevention studies used depressive relapse/recurrence whilst others used residual depressive symptoms as a proxy. It is possible that different mechanisms could be at play for each of these.

There was evidence that global changes in mindfulness were linked to better outcomes. This evidence pertained more to interventions targeting psychological rather than physical health problems.

Some variables hold up strongly as a candidate universal mechanism or mediator of change in MBCT/MBSR across psychological and physical populations (e.g. enhancing mindfulness) whilst others seem promising as specific to particular populations (e.g. decentring from negative thinking with depression). Moreover, there may be universal mechanisms that have specific manifestations in a given population (e.g., repetitive thinking as a universal mechanism; in recurrent depression, the focus is on the causes, meanings and consequences of depression whereas in cardiovascular disorders it may be on the causes, meaning, consequences around physical health). These hypotheses need to be tested in future work.

Most studies relied on self-report measures and very few were adequately powered to examine mediation. Triangulation of measures and sufficient power will enable more exploratory examination of as yet "unknown" mechanisms. For example, the two studies that examined neuroscience mechanisms suggested particular brain networks as candidate mechanisms. These studies suggest that there could be a range of possibilities regarding how MBCT/MBSR interventions produce their effects and future work might usefully triangulate across neuroscience, experimental and self-report measures.

An important feature we highlighted in our review was the constituent studies' design with regard to the timeline of changes. In this regard, it was found that majority of studies did not establish a timeline that would provide a full test of mediation. This means that the findings of such studies regarding the role of a specific mediator are just preliminary and future research needs to ensure temporal sequencing of assessments that enables change in mechanisms to be assessed separately and temporally before change in outcomes. Many of the included studies were conducted with the primary aim of assessing the effectiveness of MBCT/MBSR interventions, with identifying mechanisms being a secondary goal. Furthermore, some studies that tested mediators in detail were post hoc analyses using

datasets obtained from effectiveness studies. As discussed above, it is essential to design mechanisms studies that choose time points and time scales so as to uncover the temporal relationships between mediators and outcomes over short and long-term trajectories of change.

In the majority of the studies, both MBCT and MBSR demonstrated significant reductions in the proposed mediators and targeted outcomes compared to the different control groups (active, waitlist) as well as for different populations (physical and psychological). This suggests that there are associations between the intervention, the mediator and the outcome. However, a significant relationship between the mediator and the outcome was not supported in some of the studies. This inconsistency we argue provides fertile ground for hypothesis generation that can be tested in improved study designs. Recently, there has been a growing interest in causal mediation analysis that includes methods for dealing with multiple mediators (Tingley, Yamamoto, Hirose, Keele, & Imai, 2014). Such methods should be considered in future studies aimed at testing multiple mediators. Moreover, there has been growing interest in developing models that can test what works for whom.

Strengths and limitations

This review was aimed at understanding mechanisms of change in MBCT and MBSR when used for people with physical and/or psychological conditions. This work has the potential to shed light on the theory underpinning the conditions that MBCT/MBSR seek to address as well as enhancing outcomes by enabling these interventions to be better targeted at both universal and specific vulnerabilities. For this review, we assessed the quality of the appropriate studies based on Kazdin's (2007, 2009) recommended framework for enhancing methodological quality in this area.

There are several limitations of this review. First, we reviewed only randomised and non-randomised controlled studies. Other types of studies, such as observational and case

studies, might produce more detailed data concerning the mechanisms of how and the reasons why MBCT/MBSR interventions can lead to change. A second limitation is that the main targeted population in this review comprised adults with diagnosed physical and/or psychological conditions. Focusing on other types of population, such as healthy people or children, might highlight different mechanisms underlying mindfulness interventions at different stages of the lifespan and with different profiles of universal and specific vulnerability. Thirdly, only published studies were included in this review and so there might be some publication bias in the findings. Fourth, this review did not consider the fidelity of the MBCT and MBSR, nor how they were implemented by participants. We hypothesize that this would significantly influence the mechanisms and mediators being examined and is essential for future work to incorporate.

Recommendations

This review suggests that the field of testing mechanisms of mindfulness interventions might benefit from delineating universal and specific vulnerabilities in populations with physical and/or psychological conditions, so that we can better understand what any mindfulness-based intervention can change and what a mindfulness-based intervention adapted for particular populations specifically change. The emerging theoretical framework for MBCT/MBSR draws on aspects of cognitive science (e.g., attention and executive control and decentering) and trans-diagnostic work (e.g. repetitive thought and experiential avoidance. This emerging model is being clarified and developed as empirical understanding is built. Future mechanisms studies should clearly articulate which aspect of this framework and which specific mechanisms they are investigating. The second point is that following the criteria suggested by Kazdin (2007, 2009) could assist researchers when conducting future studies aimed at identifying mechanisms of change in interventions. More recent developments in conceptual thinking and methodology can further enhance this field. Future

research in this area might benefit from this focus on universal and specific mechanisms and triangulating experimental, neuroscience and self-report measures to test potential biological, psychological and social processes that might lead to a better understanding of how MBCT/MBSR interventions work in populations with physical and/or psychological conditions. Finally, researchers need to build in sufficient time points in their study designs so as to be able to determine the shape and temporal sequencing of change.

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Table 1

Inclusion/exclusion criteria of the review

	Inclusion criteria	Exclusion criteria
Types of trials	Randomised controlled trial and controlled trial aimed at examining mechanisms or mediators of change	Case-control trials, cohort trials, cross-sectional trials, case reports, series and qualitative trials
Types of publication	Published trials reported in any language	Non-published trials and dissertations
Types of participants	Adults, 18 years and older, diagnosed with a physical health condition and/or, diagnosed with any psychological problem	Children and healthy people
Types of interventions	Studies of MBCT as specified by Segal et al., (2002, 2013) and MBSR as outlined by John Kabat-Zinn (1990)	Other mindfulness interventions and short duration MBCT or MBSR
Types of outcomes	Any	
Types of comparators	Any comparator. This might include inactive control such as treatment as usual (TAU) and waiting list or active group, such as antidepressants or other psychological interventions	

Studies identified through electronic searches (Total 3290)

Duplications and non-relevant studies (N=3234)

Titles and abstracts screened against inclusion/ exclusion criteria (N=56)

Studies excluded (N= 15):

- Not MBSR/MBCT (N=5)
- Mechanism/ mediator not studied (N=4)
- Healthy populations (N=2)
- Not RCT or CT (N=2)
- Not full length interventions (N=2)

Full texts for screening (N=41)

Studies excluded (N=23)

- Full papers unavailable (6)
- Not MBSR/MBCT (N=4)
- Mechanism/mediator not studied (N=2)
- Healthy populations (N=4)
- Not RCT or CT (N=3)
- Not full-length interventions (N=4).

18 studies included:

- Physical conditions studies (N= 4)
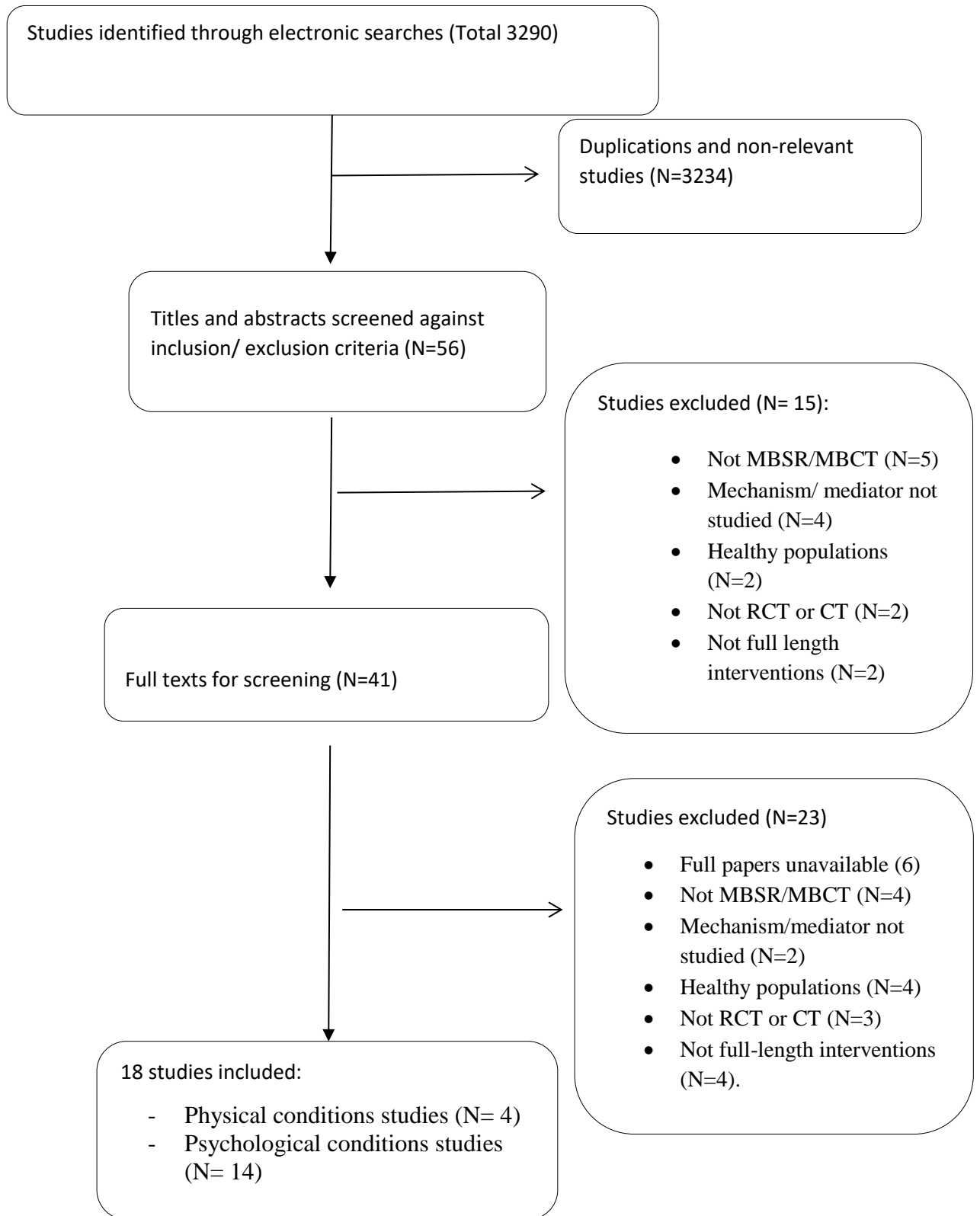- Psychological conditions studies (N= 14)

Figure 1. Flow of studies identification and eligibility determination

Table 2

Characteristics of studies with physical conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Bränström et al., 2010 Sweden	N = 71 Male (n=1) and female (n=70) (Mean age 52 yrs.)	MBSR 8 weeks	Cancer	RCT	Adapted MBSR versus waitlist control	Two time-points (pre and post treatment)	• Mindfulness (Five-Facet Mindfulness Questionnaire/ FFMQ)	Baron & Kenny method	Psychological outcomes. -Primary (perceived stress) -Secondary (depressive symptoms, anxiety, posttraumatic avoidance symptoms and positive states)	• MBSR led to significant improvements in perceived stress, posttraumatic avoidance symptoms, positive states of mind and mindfulness compared to the control group.	• MBSR effects on perceived stress, posttraumatic avoidance symptoms and positive states of mind were mediated by increases in mindfulness skills.
Labelle et al., 2010 Canada	N = 77 Female (Mean age 53 yrs.)	MBSR 8 weeks	Cancer	CT	Adapted MBSR versus waitlist control	Two time-points (pre and post treatment)	• Mindfulness (Mindful Attention Awareness Scale (MAAS) • Rumination (Rumination-Reflection Questionnaire -Rumination Subscale/RRQ)	- Change scores - Baron & Kenny method - Nonparametric Bootstrapping (Preacher & Hayes method)	Psychological outcomes. -Primary (depressive symptoms)	•People in MBSR showed significant decreases in depressive symptoms and rumination and increases in mindfulness compared to the control group.	• MBSR effect on depression was mediated by a decrease in rumination • Significant changes in mindfulness did not show a mediating role.

Table 2 cont.

Characteristics of studies with physical conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Labelle et al., 2015 Canada	N = 211 Male and female (Mean age 53 yrs.)	MBSR 8 weeks	cancer	CT	Adapted MBSR versus waitlist control	Three time-points (pre, mid and post treatment)	• Mindfulness (Mindful Attention Awareness Scale (MAAS) and Five-Facet Mindfulness Questionnaire (FFMQ) • Rumination (Rumination-Reflection Questionnaire -Rumination Subscale/RRQ). • Worry (Penn State Worry Questionnaire/ PSWQ).	Two-level hierarchical linear model (HLM)	Psychological outcomes. -Primary (stress symptoms and mood disturbance) -Secondary (mindfulness, rumination, worry and experiential avoidance)	•MBSR group showed a significant decrease in stress, mood disturbance, rumination, worry, experiential avoidance and increases in mindfulness skills.	• Decreases in rumination and worry (cancer-related worry) mediated the effects of MBSR on outcomes. • Changes in total of mindfulness measure did not mediate the effects of MBSR on outcomes. .
O'Doherty et al. 2015 Ireland	N = 117 Male and female (Mean age 59 yrs.)	MBCT 8 weeks	Coronary heart disease (CHD) and current MDE	CT	MBCT versus waitlist control	Three time-points (pre, post and 6-month follow up)	• Mindfulness (Mindful Attention Awareness Scale/MAAS)	Correlation analysis	Psychological outcomes. -Primary (current MDD in people with CHD) -Secondary (psychological adjustment and quality of life)	•MBCT group demonstrated significant improvements in depression, anxiety, psychological adjustment, mood, quality of life and mindfulness.	• The study found that significant associations between improvements in (depression, anxiety, psychological adjustment, quality of life and mood) and changes in mindfulness.

Table 3

Characteristics of studies with psychological conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Batink et al. 2013 Netherlands	N = 130 Male and female (Mean age 44 yrs.)	MBCT 8 weeks	Current residual depressive symptoms after at least one episode of MDD	RCT	MBCT + TAU versus TAU alone	Two time-points (pre and post treatment)	• Mindfulness skills (Kentucky Inventory of Mindfulness/KIMS) •Worry (Penn State Worry Questionnaire/PSWQ) • Rumination (Rumination on Sadness Scale/RSS) •Positive affect (PA) and negative affect (NA) (experience sampling method-ESM)	- Sobel-Goodman mediation analysis. - Multiple regression analysis	Psychological outcomes. -Primary (residual depressive symptoms)	•MBCT group had significant decreases in depressive symptoms, worry and rumination and an increase in mindfulness skills.	• Effects of MBCT on depressive symptoms were mediated by - An increase in a mindfulness skill (accept without judgment). - A decrease in worry. - An increase in positive affect. - A decrease in negative affect. • Rumination did not mediate a decrease in depressive symptoms.
Bieling et al. 2012 Canada	N = 84 Male and female (Mean age 44 yrs.)	MBCT 8 weeks	Recurrent depression with current residual depressive symptoms	RCT	MBCT versus maintenance antidepressants (mADM) versus placebo	Three time-points (pre, post and 6-month follow up)	• Decentering (Toronto Mindfulness Scale) • Curiosity (Toronto Mindfulness Scale) •Wider Experiences (Experiences Questionnaire •Rumination (Experiences Questionnaire)	Multiple regression	Psychological outcomes. -Primary (relapse rate and residual depressive symptoms)	• No differences between MBCT and mADM groups in terms of depression outcomes.	•MBCT group showed increases in wider experiences and curiosity and these increases predicated depression at follow up. •Decentering and rumination did not have a mediating role.

Table 3 cont.

Characteristics of studies with psychological conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Britton et al., 2012 USA	N = 52 Male and female (Mean age 48 yrs.)	MBCT 8 weeks	Recurrent depression with residual depressive symptoms	RCT	MBCT versus waitlist control	Two time-points (pre and post treatment)	•Emotional reactivity to social stress (laboratory-based stress induction + STAI-YI)	Preacher and Hayes approach	Psychological outcomes. -Primary (residual depressive symptoms).	•MBCT led to significant decreases in depression and emotional reactivity.	• Significant decreases in emotional reactivity mediated the effects of MBCT on depression.
Geschwind et al. 2011 Netherlands	N = 130 Male and female (Mean age 44 yrs.)	MBCT 8 weeks	Current residual depressive symptoms after at least one episode of MDD	RCT	MBCT versus waitlist control	Two time-points (pre and post treatment).	• Activity pleasantness (Experience Sampling Method-ESM) • Positive affect (ESM) • Pleasant activity (ESM) • Reward experience.	Correlation analysis	Psychological outcomes. -Primary (residual depressive symptoms).	•MBCT group showed significant improvements in depressive symptoms, affect, activity pleasantness and reward, worry and rumination.	• Significant decreases in depression were associated with increases in: - Positive affect. - Activity pleasantness. - Reward experience.

Table 3 cont.

Characteristics of studies with psychological conditions populations

Author, year and country	Population	Inter- vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Goldin et al. 2012 USA	*N* = 56 Male and female (Mean age 32 yrs.)	MBSR 8 weeks	Social Anxiety Disorder	RCT	MBSR versus Active control (Aerobic exercise/ AE)	Two time-points (pre and post treatment)	• Self-referential brain network (Self-Referential Encoding Task) + fMRI	Multiple regression	Psychological outcomes. -Primary (social anxiety symptoms)	•MBSR group showed an increase in positive self-views and decrease in negative self-views when compared to a AE group.	• Significant changes in self-views as well as dorsomedial pre- frontal cortex (DMPFC) activity during negative self-view were correlated with significant reductions in social anxiety in the MBSR group
Hoge et al. 2015 USA	*N* = 38 Male and female (Mean age 38 yrs.)	MBSR 8 weeks	Generalised Anxiety Disorder	RCT	Adapted - MBSR versus active control (stress management education/ SME)	Two time-points (pre and post treatment)	• Mindfulness (Five-Facet Mindfulness Questionnaire/F FMQ) • Decentering (Experience Questionnaire /EQ)	Multiple mediation model and Preacher and Hayes approach	Psychological outcomes. -Primary (anxiety symptoms)	•MBSR group had a significant decrease in generalised anxiety.	• Effect of MBSR on anxiety was mediated by an increase in decentering . • Effect of MBSR on worry was mediated by increases in mindfulness (awareness and non-reactivity).
Holzel et al. 2013 USA	N = 29 Male and female (Mean age 36 yrs.)	MBSR 8 weeks	Generalised Anxiety Disorder	RCT	MBSR versus active control (stress management education: SME)	Two time-points (pre and post treatment)	• Brain activation and connectivity (fMRI)	Multiple regression	Psychological outcomes. -Primary (generalised anxiety symptoms)	• People in MBSR showed changes in ventrolateral prefrontal regions (VLPFC) activation and amygdala–prefrontal connectivity.	• The changes in ventrolateral prefrontal regions (VLPFC) activation and amygdala–prefrontal connectivity were associated with improvements in generalised anxiety disorder.

Table 3 cont.

Characteristics of studies with psychological conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Jermann et al. 2012 Switzerland	N = 60 Male and female (Mean age 45 yrs.)	MBCT 8 weeks	Recurrent depression 3 groups (remitted people had an MBCT course). Depressed group and non-depressed group.	RCT	MBCT versus TAU	Three time-points (pre, post and 9 month follow up) for only MBCT group. One assessment for depressed and non-depressed groups.	• Cognitive functioning: - Autobiographical memory (Autobiographical Memory Test/AMT) - Shifting abilities (PM task) - Dysfunctional attitude (Dysfunctional Attitude Scale/DAS) - Mindfulness Attention (Mindfulness Attention Awareness Scale/MAAS)	Correlation analysis	Psychological outcomes. Cognitive functioning.	•MBCT group showed significant decrease in depressive symptoms, and dysfunctional attitude.	MBCT group showed a significant decrease in dysfunctional attitudes at 9 months follow up.
Kearns et al. 2015 Australia	N = 203 Male and female (Mean age 48 yrs.)	MBCT 8 weeks	Recurrent depression	RCT	MBCT versus depression relapse active monitoring (DRAM).	Three time-points (pre, post and 2 years follow-up)	•Rumination (Rumination Response Style Questionnaire/PRS). •Mindfulness (Five-Facet Mindfulness Questionnaire/FFMQ).	-Baron & Kenny method -Non-parametric Boot-strapping Preacher & Hayes	Psychological outcomes. -Primary (relapse rate)	•MBCT group showed significant reductions in relapse rate.	• MBCT effects on depressive relapse were mediated by significant increases in mindfulness. • Rumination did not mediate the relationship between MBCT and depression outcomes.

Table 3 cont.

Characteristics of studies with psychological conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Kuyken et al., 2010 UK	*N* = 123 Male and female (Mean age 49 yrs.)	MBCT 8 weeks	Recurrent depression with residual depressive symptoms	RCT	MBCT+ discontinuation of antidepressants (ADM) versus maintenance antidepressants (mADM)	Three time-points (pre, post and 15 month follow up)	•Mindfulness skill (Kentucky Inventory of Mindfulness/KIMS) •Self-compassion (self-Compassion Scale/SCS) •Cognitive reactivity (laboratory task + Dysfunctional Attitude Scale/DAS).	Mediation and moderation analytic framework (Kraemer method)	Psychological outcomes. -Primary (relapse rate and residual depressive symptoms).	• The effects of MBCT were similar to mADM in terms of relapse and residual depressive symptoms.	•MBCT's effects were mediated by significant increases in: -Mindfulness -Self-compassion. •High reactivity predicted a worse outcome for mADM group, but this relationship did not show up in MBCT group.
Shahar et al., 2010 USA	*N* = 52 Male and female (Mean age 47 yrs.)	MBCT 8 weeks	Recurrent depression with residual depressive symptoms	RCT	MBCT versus waitlist control	Two time-points (pre and post treatment)	• Brooding (Rumination Response Scale/RSQ) • Reflective pondering (Rumination Response Scale/RSQ) • Mindfulness (The Mindful Attention Awareness Scale/MAAS)	Preacher and Hayes approach	Psychological outcomes. -Primary (residual depressive symptoms).	• People in MBCT group reported significant decreases in depression compared to waitlist group.	•The relationship between MBCT and depression was mediated by -increases in mindfulness. -decreases in brooding. •Reflective pondering did not play a role in the mediation.

Table 3 cont.

Characteristics of studies with psychological conditions populations

Author, year and country	Population	Inter-vention	Disorders	Study design	Comparator	Time-point assessments	Mediators studied (Assessment tool)	Statistical analysis used	Outcomes targeted	Outcome of Intervention	Findings in relation to 'mechanism of intervention'
Van Aalderen et al. 2012 Netherlands	N = 219 Male and female (Mean age 48 yrs.)	MBCT 8 weeks	Current or recurrent depression	RCT	MBCT + TAU versus TAU alone	Two time-points (pre and post treatment).	•Rumination (Rumination on Sadness Scale/RSS) •Worry (Penn State Worry Questionnaire/PSWQ) •Mindfulness skills (Kentucky Inventory of Mindfulness/KIMS).	Preacher and Hayes approach	Psychological outcomes. -Primary (residual depressive symptoms or current depressive symptoms).	•MBCT group showed significant decreases in depressive symptoms, worry and rumination and an increase in mindfulness skill.	•The relationship between MBCT and depression was mediated by -A decrease in rumination; -A decrease in worry; - An increase in a mindfulness skill (accept without judgment).
Van den Hurk et al. 2012 Netherlands	N=71 Male and female (Mean age 49 yrs.)	MBCT 8 weeks	Recurrent depression	RCT	MBCT + TAU versus TAU alone	Two time-points (pre and post treatment)	•Attentional processing (Attentional Network Test).	Correlation analysis	Psychological outcomes. -Primary (residual depressive symptoms or current depressive symptoms).	•MBCT led to reductions in depressive symptoms and rumination and increases in mindfulness when compared to TAU. • No significant differences between MBCT and TAU in components of attention	•Attentional processing did not mediate the relationship between MBCT and depression.
Vøllestad et al. 2011 Norway	N=76 Males and female (Mean age 43 yrs.)	MBSR 8 weeks	Anxiety disorders	RCT	MBSR versus waitlist control	Two time-points (pre and post treatment	•Mindfulness (Five-Facet Mindfulness Questionnaire/FFMQ)	-Baron & Kenny method -Non-parametric Boot-strapping (Preacher & Hayes)	Psychological outcomes. -Primary (acute anxiety symptoms). -Secondary (worry and trait anxiety).	•MBSR group showed significant decreases in anxiety, depression and worry and an increase mindfulness.	•Effects of MBSR on acute anxiety, worry and trait anxiety, but not depression were mediated by increases in mindfulness.

Table 4

Risk bias in studies with physical conditions

Study	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Eligibility criteria specified	Power calculation	Compliance with interventions	Data collection tools valid	All participants accounted for
Bränström et al. 2010	Low	Unclear	High	High	Low	Low	Yes	Yes	Unclear	Yes	Yes
Labelle et al. 2010	High	High	High	High	Low	Low	Yes	Unclear	Yes	Yes	Yes
Labelle et al. 2015	High	High	High	High	Low	Low	Yes	Unclear	Unclear	Yes	Yes
O'Doherty et al. 2015	High	High	High	High	Low	Low	Yes	Yes	Yes	Yes	Yes

Table 5

Risk bias in studies with psychological conditions

Study	Random sequence generation	Allocation concealment	Blinding of participants	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Eligibility criteria specified	Power calculation	Compliance with interventions	Data collection tools valid	All participants accounted for
Batink et al. 2013	Low	Low	High	Unclear	Low	Low	Yes	Yes	Yes	Yes	Yes
Bieling et al. 2012	Low	Low	High	Low	Low	Low	Yes	Unclear	Yes	Yes	Yes
Britton et al. 2012	Low	Low	High	High	Low	Low	Yes	Yes	Yes	Yes	Yes
Geschwind et al. 2011	Low	Low	High	Low	Low	Low	Yes	Yes	Yes	Yes	Yes
Goldin et al. 2012	Low	Unclear	High	High	Low	Low	Yes	Yes	Unclear	Yes	Yes
Hoge et al. 2015	Low	Low	High	Low	Low	Low	Yes	Unclear	Yes	Yes	Yes
Hölzel et al. 2013	Unclear	Unclear	High	Low	Low	Low	Yes	Unclear	Yes	Yes	Yes
Jermann et al. 2013	Low	Low	High	Low	Low	Low	Yes	Yes	Yes	Yes	Yes
Kearns et al. 2015	Low	Low	High	Low	Low	Low	Yes	Yes	Yes	Yes	Yes
Kuyken et al. 2010	Low	Low	High	Low	Low	Low	Yes	Yes	Yes	Yes	Yes
Shahar et al. 2010	Low	Low	High	High	Low	Low	Yes	Yes	Unclear	Yes	Yes
Van Aalderen et al. 2012	Low	Low	High	Unclear	Low	Low	Yes	Yes	Yes	Yes	Yes
Van den Hurk et al. 2012	Low	Low	High	Unclear	Low	Low	Yes	Yes	Yes	Yes	Yes
Vøllestad et al. 2011	Unclear	Unclear	High	High	Low	Low	Yes	Unclear	Yes	Yes	Yes

Table 6

Evaluation of studies with physical conditions populations based on the review framework

Study name	1. Did the study use a theory?	2. Did the study use measures to assess the mediators?	3. Did the study use measures that can reflect different perspectives?	4. Did changes in processes are specifically targeted by MBCT/MBSR?	5. Did changes in potential mediators occur during the MBCT/MBSR?	6. Did changes in mediators precede changes in outcomes?	7.Did the study use enough time-point assessments?	8. Did the study use an appropriate statistical analysis?	Total of scores
Bränström et al. 2010	1	1	0	1	1	0	0	1	5
Labelle et al. 2010	1	1	0	1	1	0	0	1	5
Labelle et al. 2015	1	1	0	1	1	1	1	1	7
O'Doherty et al. 2015	1	1	0	1	1	1	1	0	6

Note: 1= Yes, 0=No

Table 7

Evaluation of studies with psychological conditions populations based on the review framework

Study name	1. Did the study use a theory?	2. Did the study use measures to assess the mediators?	3. Did the study use measures that can reflect different perspectives?	4. Did changes in processes are specifically targeted by MBCT/MBSR?	5. Did changes in potential mediators occur during the MBCT/MBSR?	6. Did changes in mediators precede changes in outcomes?	7. Did the study use enough time-point assessments?	8. Did the study use an appropriate statistical analysis?	Total of scores
Batink et al 2013	1	1	0	1	1	0	0	1	5
Bieling et al. 2012	1	1	0	1	1	1	1	1	7
Britton et al. 2012	1	1	1	1	1	0	0	1	6
Geschwind et al. 2011	1	1	0	1	1	0	0	0	4
Goldin et al. 2012	1	1	1	1	1	0	0	1	6
Hoge et al. 2015	1	1	1	1	1	0	0	1	6
Hölzel et al. 2013	1	1	0	1	1	0	0	1	5
Jermann et al. 2013	1	1	0	1	1	0	0	0	4
Kearns et al. 2015	1	1	0	1	1	1	1	1	7
Kuyken et al. 2010	1	1	1	1	1	1	1	1	8
Shahar et al. 2010	1	1	0	1	1	0	0	1	5
Van Aalderen et al. 2012	1	1	0	1	1	0	0	1	5
Van den Hurk et al. 2012	1	1	1	1	1	0	0	0	5
Vøllestad et al. 2011	1	1	0	1	1	0	0	1	5

Note: 1= Yes, 0=No

Appendix A

Keywords and example of Search strategy

Database Name:

Reviewer: ……………………………

Date	Search term	Initial results	Cleaned results	Articles read	Potential related article	EndNote Exported
	mindfulness.					
	mbsr.					
	mbct.					
	(mindfulness and randomi*ed controlled trial*).ti,ab.					
	(mbsr and randomi*ed controlled trial*).ti,ab.					
	(mbct and randomi*ed controlled trial*).ti,ab.					
	(mindfulness and controlled trial*).ti,ab.					
	(mbsr and controlled trial*).ti,ab.					
	(mbct and controlled trial*).ti,ab.					
	(mindfulness and clinical trial*).ti,ab.					
	(mbsr and clinical trial*).ti,ab.					
	(mbct and clinical trial*).ti,ab.					
	(mindfulness and randomi*ed).ti,ab.					
	(mbsr and randomi*ed).ti,ab.					
	(mbct and randomi*ed).ti,ab.					
	(mindfulness and randomly).ti,ab.					

Database: Name:

Reviewer: …………………………

Date	Search term	Initial results	Cleaned results	Articles read	Potential related article	EndNote Exported
	(mbsr and randomly).ti,ab					
	(mbct and randomly).ti,ab					
	(mindfulness and randomi*ed efficacy trial*).ti,ab.					
	(mbsr and randomi*ed efficacy trial*).ti,ab.					
	(mbct and randomi*ed efficacy trial*).ti,ab.					
	(mbsr and randomi*ed controlled trial* and mechanism*).ti,ab.					
	(mbsr and randomi*ed controlled trial* and mediator*).ti,ab.					
	mbct and randomi*ed controlled trial* and mechanism*).ti,ab.					
	(mbct and randomi*ed controlled trial* and mediator*).ti,ab.					
	(mbsr and controlled trial* and mechanism*).ti,ab.					
	(mbsr and controlled trial* and mediator*).ti,ab.					
	(mbct and controlled trial* and mechanism*).ti,ab.					
	(mbct and controlled trial* and mediator*).ti,ab.					
	(mbsr and clinical trial* and mechanism*).ti,ab.					
	(mbsr and clinical trial* and mediator*).ti,ab.					

Database Name:

Reviewer: ……………………………

Date	Search term	Initial results	Cleaned results	Articles read	Potential related article	EndNote Exported
	(mbct and clinical trial* and mechanism*).ti,ab.					
	(mbct and clinical trial* and mediator*).ti,ab.					
	(mbsr and randomi*ed and mechanism*).ti,ab.					
	(mbsr and randomi*ed and mediator).ti,ab.					
	(mbct and randomi*ed and mechanism*).ti,ab.					
	(mbct and randomi*ed and mediator).ti,ab.					
	(mbsr and randomly and mechanism*).ti,ab					
	(mbsr and randomly and mediator*).ti,ab					
	(mbct and randomly and mechanism*).ti,ab					
	(mbct and randomly and mediator*).ti,ab					
	(mbsr and randomi*ed efficacy trial* and mechanism*).ti,ab.					
	(mbsr and randomi*ed efficacy trial* and mediator).ti,ab.					
	(mbct and randomi*ed efficacy trial* and mechanism*).ti,ab.					
	(mbct and randomi*ed efficacy trial* and mediator*).ti,ab.					