How do mindfulness-based programmes improve anxiety, depression and psychological distress? A systematic review

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Abstract



This study aimed to systematically review studies which conducted a controlled mediation analysis in order to examine the potential mechanisms which underlie mindfulness-based programme's (MBPs) effects on anxiety, depression and psychological distress in any health or mental health population. Searches of six databases (Medline (Ovid), PsycINFO, Cochrane Central Register of Controlled Trials, EMBASE, Cinahal Plus and Cochrane Reviews) were undertaken in September 2020. After removing duplicates, 2052 records were screened, of these 1822 were excluded based on the abstract and 230 were further assessed for eligibility against the full study inclusion criteria. Full texts were acquired for the 11 studies which met the inclusion criteria. The quality of the methodologies of each of these 11 studies were assessed using the Cochrane risk of bias tool (Higgins et al., 2011). The quality of the findings from each study relating to the hypothesised mechanisms of action of the MBP reviewed were evaluated using Alsubaie et al. (2017)'s framework for abstracting and interpreting mechanistic study quality, derived from recommendations made by Kazdin (2007, 2009). We found preliminary evidence that MBCT/ MBSR treatment effects on anxiety and depression may be mediated by hypothesised mechanisms, such as mindfulness, rumination, worry, self-compassion, cognitive reactivity, aversion, attention regulation skills and positive affect. An overall lack of methodological rigour does preclude us from making any definitive conclusions on causality. The results from this study do however provide some insights into what the potential causal pathways connecting MBPs with improved anxiety and depression might be.

Keywords Mindfulness · Anxiety · Depression · Psychological distress · Mechanisms

Depression and anxiety are both common mental health disorders (The World Health Organisation (WHO), 2017). Depression is a state of low mood and aversion to activity that can affect a person's thoughts, behaviour, feelings and sense of wellbeing (American Psychiatric Association (APA), 2013). The latest Diagnostic and Statistical Manual of Mental Disorders (DSM-5) outlines the criterion needed for a person to be diagnosed with a Major Depression Episode (MDE) (APA, 2013). The DSM-5 requires that a person should be experiencing five or more depressive symptoms within a two week period (APA, 2013). One of these symptoms should be either (1)

depressed mood or (2) loss of interest or pleasure (APA, 2013). The secondary symptoms of MDE are significant weight loss or gain, slowing down of thought and physical movement, fatigue or loss of energy, feelings of worthlessness or excessive guilt, diminished concentration levels and suicidality (APA, 2013). Anxiety is an emotion characterised by feelings of tension, worried thoughts and physical changes like palpitations (APA, 2013). There are a number of distinct anxiety disorders which are grouped together in the DSM-5 as they share the same fear, worried and anxiety-related behaviours e.g. Generalised Anxiety Disorder and Social Anxiety Disorder (APA, 2013). The WHO (2017) estimates that 4.4% of the worldwide population have a depressive disorder and 3.6% have an anxiety disorder, which equates to a worldwide prevalence of approximately 322 and 254 million people respectively. Psychological distress is a nonspecific negative emotion that includes a combination of both anxious and depressive feelings (Bjerkeset et al., 2020; Kessler et al., 2003). These common mental health

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disorders can have a significant negative impact on all aspects of a person's life, including physical, psychological, social, sexual and occupational elements (Kimball et al., 2005; National Collaborating Centre for Mental Health, 2011). The psychological impact of some acute and chronic health conditions, have been identified as being just as debilitating as the physical symptoms, significantly affecting mental and emotional functioning (Hayes & Koo, 2010; Kurd et al., 2010; Greenberg, 2007). This can lead to a significant proportion of patients with acute and chronic health conditions also suffering from depression, anxiety and psychological distress (Kurd et al., 2010; Greenberg, 2007; Schmitt & Ford, 2007). Common mental health conditions such as depression and anxiety, particularly when coupled with a comorbid physical health condition, can place a chronic burden on health care systems and society as a whole, e.g. through lower work productivity and a more significant number of missed workdays (Ayala et al., 2014).

Mindfulness-based programmes (MBP), particularly since the start of this century, have experienced a marked increase in popular interest and an exponential research growth trajectory in health and mental health disciplines such as psychology, psychiatry and medicine (Goldberg et al., 2018; Grossman et al., 2004). This increased interest appears to be due to their capacity to support the biopsychosocial adjustment of health and mental health of patients through a relatively brief costeffective programme (Goldberg et al., 2018; Grossman et al., 2004). This has led to three MBPs being developed to target depression, anxiety or psychological distress in specific populations, or have been subsequently adopted to support these conditions in health and mental health populations. Mindfulness-based stress reduction (MBSR) is an eight-week programme which provides intensive training in mindfulness meditation (Kabat-Zinn, 1990, 2013). MBSR was developed in 1979 to support the alleviation of stress, distress (including feelings of anxiety and depression) and the pain which can accompany chronic health conditions (Kabat-Zinn, 1990, 2013). Mindfulness-Based Cognitive Therapy (MBCT) derived from MBSR is an eight-week evidencebased systematic programme which integrates aspects of CBT for depression with training in mindfulness meditation (Segal et al., 2002). MBCT was specifically developed as a programme to prevent recurrent depression (Segal et al., 2002) but has subsequently been adapted to a range of health and mental health populations (Alsubaie et al., 2017). Mindfulness-Based Relapse Prevention (MBRP) whose programme components are derived from MBCT, combines mindfulness meditation training with cognitive behavioural relapse prevention to target negative mood, craving and substance use relapse (Bowen et al., 2010).

Reviews have found that MBSR has positive effects on the anxiety, depression and psychological distress levels of a range of patients with health conditions, including cancer patients and survivors (Xunlin et al., 2020) and fibromyalgia (Kozasa et al., 2012). Preliminary evidence suggests that MBCT can decrease depression and anxiety and psychological distress in a number of physical conditions, such as coronary heart disease (O'Doherty et al., 2015), diabetes (van Son et al., 2014), cancer (Van Aalderen et al., 2012) and psoriasis (Maddock et al., 2019a). Meta-analyses have found that MBSR and MBCT have a moderate to large effects on anxiety (Goldberg et al., 2018; Khoury et al., 2013) and depressive disorders (Goldberg et al., 2018; Khoury et al., 2013; Kuyken et al., 2016). The evidence for the effectiveness of MBRP on mental health outcomes is more limited and contains mixed results. In a feasibility pilot study, Zgierska et al. (2008) found that MBRP reduced the anxiety and depression symptoms of people with alcohol dependence issues. Witkiewitz and Bowen (2010) however, found no significant changes in depression in individuals with a substance use disorder as a result of completing an MBRP programme from pre to post-programme versus TAU. Zemestani and Ottaviani (2016) found that MBRP was effective in reducing rates of depression and anxiety in patients with co-morbid depression and substance use disorders (Zemestani & Ottaviani, 2016). The differences in these studies may be explained by the severity of depression at baseline in both studies. In Witkiewitz and Bowen (2010) study participants were experiencing mild depressive symptoms, with participants in Zemestani and Ottaviani (2016) experiencing severe depressive symptoms at baseline (both studies used the BDI-II), perhaps leading to a floor effect in Witkiewitz and Bowen (2010).

It remains unclear which mechanisms of MBPs are responsible for changes in anxiety, depression and psychological distress, though the evidence base is growing (Montgomery et al., 2016). A mechanism is 'the process that is responsible for change' (Kazdin, 2007: 3). A mediation effect occurs when a third variable explains the relationship between an independent and a dependent variable (Hayes, 2018a, 2018b). Kazdin (2007, 2009) identified the key criteria needed in order to identify the mediators/mechanisms of therapeutic programmes. Research examining what the potential mediators/mechanisms of MBCT/MBSR/MBRP's effects on depression, anxiety and psychological distress are, is likely to lead to: (1) a better understanding of possible causal relationships and the processes that predict and mediate the relationships between mindfulness variables, depression, anxiety and psychological distress (Kazdin, 2007; Svendsen et al., 2017; Van der Velden et al., 2015); (2) a greater identification of potential treatment moderators - improving the accuracy of matching of therapies to patients that will benefit from the treatment (Hayes-Skelton & Wadsworth, 2015; Shapiro & Jazaieri, 2015); and 3) support the optimisation of MBPs' therapeutic effects, or the development of new and more efficient MBPs, in which the mindfulness variables that were found to be most active could be intensified and refined, and the inactive or redundant MBP programme components could be discarded (Baer et al., 2006; Brown, 2015; Kuyken et al., 2010).

There have been three systematic reviews, which have explored what the mechanisms of MBPs are on changes in anxiety, depression and psychological distress. Van der Velden et al. (2015) conducted a systematic review exploring MBCT's mechanisms of change in the treatment of major recurrent depressive disorder. Van der Velden et al. (2015) found that changes in worry, rumination, mindfulness, compassion or meta-awareness due to MBCT participation were either associated with, predicted or had a mediated effect on depression. A number of other variables were also highlighted as having a potential role to play in how MBCT participation may improve depression, these were: emotional reactivity, attention, momentary positive and negative affect, memory specificity and self-discrepancy (Van der Velden et al., 2015). This review contained both RCT and quasi-experimental studies, which did not contain a control group in their subsequent mediation analyses, and also did not systematically evaluate each study against Kazdin (2007, 2009)'s criteria for mediation analysis. Gu et al. (2015) conducted a systematic review, which examined how MBCT and MBSR might improve mental health (including stress, mood states, anxiety and depression as outcomes) and wellbeing. Gu et al. (2015) found evidence for the roles of rumination, worry, mindfulness, psychological flexibility and self-compassion as being potential mediators of change in mental health and wellbeing through participation in these MBPs. This review also contained both RCT and quasi-experimental studies, which did not contain a control group in their subsequent mediation analyses, and also did not systematically evaluate each study against Kazdin (2007, 2009)'s criteria for mediation analysis. Alsubaie et al. (2017) carried out a systematic review which explored the change mechanisms in MBCT and MBSR in people with physical and/or psychological conditions. Alsubaie et al. (2017) found promising preliminary evidence that mindfulness mediated MBSR and MBCT's effects on depression, anxiety and stress. Decentering was also deemed to be a potential mediator of change in MBCT/MBSR in people in anxiety. Alsubaie et al. (2017) also found evidence that mindfulness, worry, self-compassion, positive effect, cognitive and emotional reactivity may mediate the effects of MBCT/MBSR on depressive disorders, with more mixed evidence for rumination. This review also contained both RCT and quasi-experimental studies, which did not contain a control group in their subsequent mediation analyses. Alsubaie et al. (2017) developed a conceptual framework based on the recommendations put forward by Kazdin (2007, 2009) and evaluated each study against it. This framework did have limitations, in that it did not include all of criteria required by Kazdin (2007, 2009) to help demonstrate mediation e.g. showing a gradient in which greater activation of a proposed mediator is associated with increases or decreases in the outcome, helping to make the case for the proposed mediator. Using this conceptual framework, Alsubaie et al. (2017) noted that the limited rigour contained in the methodologies of the reviewed studies restricted the extent to which conclusions could be drawn on what the mechanisms/mediators of MBPs treatment effects in people with physical and/or psychological conditions were.

This systematic review will build on the work of Van der Velden et al. (2015), Gu et al. (2015) and Alsubaie et al. (2017). Anticipating, as Gu et al. (2015) did, that as time goes by, that the number and quality of MBP mediation studies would increase, this systematic review will aim to explore the current best quality evidence available on which mechanisms of MBPs change any form of anxiety, depression and psychological distress. As this review will focus on any form of anxiety, depression or psychological distress, across a range of health and mental health populations, the authors expect to examine evidence for potential disorder specific (Loucks et al., 2015), and universal mediating variables (Teasdale et al., 2003). This review will build on the work of Van der Velden et al. (2015), Gu et al. (2015) and Alsubaie et al. (2017) by only including studies which used more robust tests of mediation in their research design. We included RCT studies, as these are the gold-standard method to produce reliable results with minimum bias (Van Breukelen, 2006). Nonrandomised controlled trials can detect associations between an intervention and an outcome; however, they cannot rule out that an association is caused by a third factor linked to both the outcome and the intervention (Sibbald & Roland, 1998). The statistical mediation analyses of nonrandomised data provide less convincing evidence of the potential role of mediators as causal processes (MacKinnon, 2008). More definite conclusions about mediation can be attained from randomised designs which compare the intervention to the control group, as a stronger case for the specificity of effects on the mediating variables and outcomes to the treatment can be made (Kazdin, 2007). We aimed to identify potentially significant causal pathways between MBPs mediators and anxiety, depression and psychological distress, which were as far as possible, not caused by systematic differences between the intervention or control group or other potential confounding factors, e.g. the passage of time (Sibbald & Roland, 1998). This would allow our findings to be based on more rigorously designed studies and decreased heterogeneity in methods and quality across studies (Gu et al., 2015). Studies which used RCT designs were thus included if their subsequent mechanistic analyses was one which was recommended within the literature on mediation analysis and included a control condition as a form of moderating variable (Hayes, 2018a, 2018b). This method of analysis would allow us to disentangle more clearly the nature of the relationships between the potential mediators and the examined outcomes (Hayes, 2018a, 2018b). This meant that previously common statistical methods of mediation such as Baron and Kenny's (1986) causal-steps approach, which are now actively discouraged in mediation analysis literature (Memon et al., 2018) due to this approach not testing the significance of a specific indirect effect and not quantifying the magnitude of the mediation effect, nor accommodating models with inconsistent mediation (Hayes, 2009; Rungtusanatham et al., 2014), if used as the sole mediation method, would not be included. With this mind, we identified any appropriate statistical mediation analysis, as one that could assess the indirect effects of the proposed mediating variable on the examined outcome, within an RCT design, where the control group could operate as a moderating variable e.g. Preacher and Hayes' bias-corrected nonparametric bootstrapping techniques (Hayes, 2018a), or the mediation and moderation statistical analytic framework recommended by Kraemer et al. (2002) for RCTs. As MBRP was initially designed to improve

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mood and its role in the relapse process with people with substance use issues, we included this in our review. This MBP was not included in the reviews conducted by Van der Velden et al. (2015), Gu et al. (2015) or Alsubaie et al. (2017). In line with the work of Alsubaie et al. (2017), we also aimed to assess the methodological rigour and the adequacy of the studies reviewed to examine mechanisms of change in MBPs in anxiety, depression and psychological distress. Even though their framework does have limitations, in order to aid comparability, we used the same comprehensive conceptual framework developed by Alsubaie et al. (2017), based on the recommendations put forward by Kazdin (2007, 2009), to inform data extraction and to assess methodological rigour.

Methods

Inclusion and Exclusion Criteria

This systematic review was conducted following the general principles published by the NHS Centre for Reviews and Dissemination (2001), and reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher et al., 2009). The inclusion and exclusion criteria are outline in Table 1 below.

 Table 1
 Inclusion/exclusion criteria for the review

	Inclusion Criteria	Exclusion Criteria
Types of trials	change in anxiety, depression or psychological distress, using a well-established method of mediation analysis, which included both an analysis of an MBP and a control group.	Non-randomised trials, uncontrolled trials, case-control trials, cohort trials, cross-sectional trials, longitudinal studies, case reports, series and qualitative trials. Any randomised controlled trial, which conducted a mediation analysis but did not include an analysis of both
	These studies were required to engage in an assessment, at a minimum, of pre–post-change in any hypothesised mechanisms and any form of anxiety, depression or psychological distress.	an MBP and control group.
Types of publications	Published trials reported in English.	Non-published trials and dissertations
Types of participants	Adults, 18 years and older, with any form of anxiety, depression or psychological distress and/or diagnosed with a related health co-morbidity and the RCT is examining levels of anxiety, depression and psychological distress.	Children and adults who do not have any form of anxiety, depression or psychological distress and/or diagnosed with a related health co-morbidity and the RCT is not examining levels of anxiety or depression or psychological distress.
Types of interventions	MBSR, MBCT or MBRP.	Other mindfulness programme or MBSR, MBCT or MBRP programmes which were of a shorter duration.
Types of outcomes	Anxiety, depression or psychological distress.	
Types of comparators	Any comparator. This might include inactive control groups such as treatment as usual (TAU) and waiting list or active control groups, such as anti-depressants or other psycho- logical interventions.	

Search Strategy

The electronic search of six databases (Medline (Ovid), PsycINFO, Cochrane Central Register of Controlled Trials, EMBASE, Cinahal Plus and Cochrane Reviews) was undertaken in September 2020. The search strategy varied across the databases, but the same keywords applied throughout. The number of publications, which emerged from each database, is outlined in Table 2 below. Two reviewers (AM and CB) independently assessed all potentially relevant articles for inclusion.

Study Selection and Data Extraction

The results of all search strategies for the interventions component of the review were imported to the screening tool, Rayyan (Ouzzani et al., 2016). After removing duplicates, the titles and abstracts were screened independently by AM and CB, to identify potentially relevant studies. During this phase, inclusion and exclusion criteria (see Table 1) were applied, and disagreement was resolved through discussion. Subsequently, full texts of the promising studies were obtained, and AM and CB examined their reference lists. A PRISMA diagram, which outlines the study selection process, is presented in Fig. 1 below.

To be included in this review, MBPs had to: 1) have mindfulness meditation, e.g. body scan, as a core practice component; and 2) have been developed to target mood, depression, anxiety or psychological distress; or 3) have an evidence base on its impact on these outcomes. By consequence, three MBPs, Mindfulness-based Stress Reduction (MBSR; Kabat-Zinn, 1982), Mindfulness-Based Cognitive Therapy (MBCT; Segal et al., 2002); and Mindfulness-Based Relapse Prevention (MBRP; Bowen et al., 2010) were included. Other potentially relevant interventions such as dialectical behavioural therapy (DBT; Linehan, 1993), and compassion-focussed therapy (CFT; Gilbert, 2010) which focus on developing a mindful attitude (Alsubaie et al., 2017) rather than the formal practice of mindfulness meditation were not included in this review.

A data extraction tool which examined the characteristics of each study based on the PICOS (Population, Intervention,

Table 2 Database searches	Database	Publications
	Medline	747
	PsycINFO	468
	CINAHAL PLUS	316
	Embase	1218
	Cochrane Reviews	181
	Cochrane Trials	1099
	Other (hand searching)	0
	Total:	4026

Comparator, Outcomes and Study) design framework was developed) (Higgins & Green, 2011). Data extraction was conducted by CB and checked by AM.

Quality Appraisal

The quality of the methodologies undertaken in each RCT study, which accompanied the mechanistic analysis, was assessed using the Cochrane risk of bias tool (Higgins et al., 2011). This quality assessment tool contains seven domains, which assess the risk of biased findings due to sequence generation, allocation concealment, blinding of participants and personnel, outcome assessment, incomplete outcome data, selective reporting and other biases. AM and CB conducted the risk of bias and quality appraisals. The quality of the findings from each of the included studies were reviewed using Alsubaie et al. (2017)'s framework for abstracting and interpreting MBP mechanistic study quality. These criteria included the following questions: 1) Did the study use a theory to articulate the mechanism through which the intervention is hypothesised to work?; 2) Did the study use measures to assess the mechanisms?; 3) Did the study use measures that can reflect different perspectives?; 4) Did changes in processes that are specifically targeted by the MBP occur?; 5) Did changes in potential mechanisms occur during the MBP?; 6) Did changes in mechanisms precede changes in outcomes?; 7) Did the study use enough time-point assessments?, and 8) Did the study use an appropriate statistical analysis? Each yes answer received a score of 1, reflecting that it had met the criteria.

Data Analysis and Synthesis

We anticipated that when all the included RCTs and mechanistic analyses had been reviewed, that there would be too much heterogeneity in MBPs, populations examined, mediators and outcomes measured for a robust meta-analysis to be conducted. Therefore, a modified narrative synthesis was conducted (Popay et al., 2006), which focused on the MBP, it's outcome focus and evaluated the status of the evidence for each hypothesised mediator or mechanism on each outcome. This involved: (1) developing a preliminary synthesis, i.e. through organising the included studies in terms of programme type, outcome focus and direction of their effects; (2) exploring relationships in the data, i.e. considering factors that may explain any similarities or differences in the nature of the effects in the included studies; and (3) assessing the robustness of the synthesis, i.e. through assessing the strength of the evidence for the effects of each MBP on each outcome, and on the effects of the MBPs on the mechanistic relationships between the hypothesised predictor, mediating variables and the outcomes (Popay et al., 2006). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009) were also utilised.

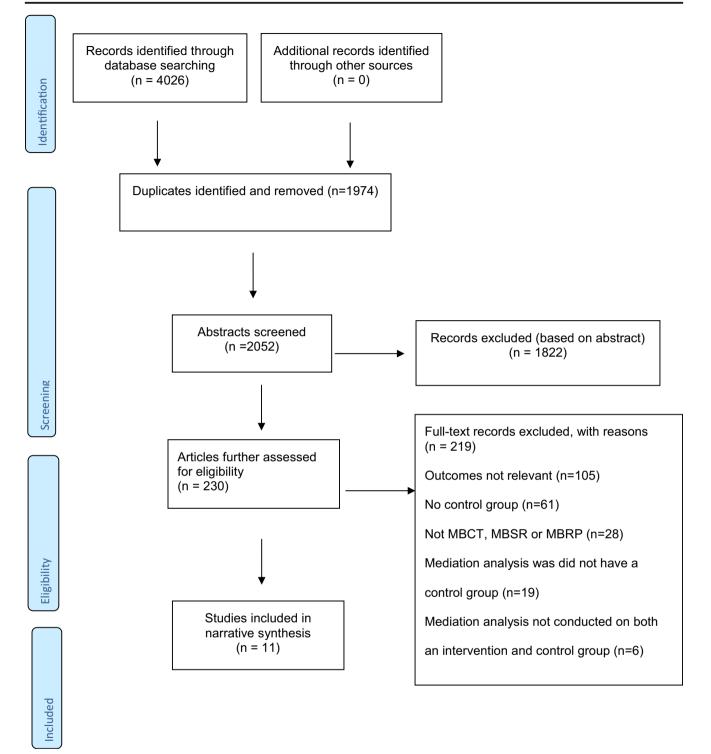


Fig. 1 PRISMA Flow Diagram (Moher et al., 2009)

Results

The database searches led to be 4026 study titles and abstracts being retrieved. After reviewing the abstracts and screening for duplicates, 1974 studies were discarded. The initial phase of screening of the remaining studies against the inclusion and exclusion criteria led to another 1822 studies being removed. In the second phase, the remaining 230 studies were further assessed for eligibility against the inclusion and exclusion criteria. Of these, 219 studies were excluded for the following reasons: outcomes not relevant (n = 105), no control group (n = 61), the programme was not MBCT, MBSR or MBRP (n = 28), mediation analysis was not from an RCT (n = 19), mediation analysis not conducted on both an intervention and control group (n = 6). Finally, 11 studies met the inclusion criteria of this review (see Fig. 1).

Study Characteristics

The characteristics of the included studies are outlined in the data extraction table below. Eight studies contained a controlled mediation analysis of MBCT (Kuyken et al., 2010; Shahar et al., 2010; Van Aalderen et al., 2012; McManus et al., 2012; Batink et al., 2013; Haenen et al., 2016; Cladder-Micus et al., 2018; Maddock et al., 2019b), three a controlled mediation analysis of MBSR (Vøllestad et al., 2011; Goldin et al., 2016; Morrison et al., 2019) and we found no studies which contained a controlled mediation analysis of MBRP. The sample sizes ranged from 45 to 205, with a total of 1197 randomised participants. The majority of studies (n = 9) examined two or more mediators. Among the 5 studies (Batink et al., 2013; Cladder-Micus et al., 2018; Kuyken et al., 2010; Shahar et al., 2010; van Aalderen et al., 2012) which examined the effectiveness of MBCT on recurrent depression outcomes, three studies (Batink et al., 2013; Cladder-Micus et al., 2018; van Aalderen et al., 2012) compared MBCT with treatment as usual (TAU), one used a waitlist control group (Shahar et al., 2010) with only one study (Kuyken et al., 2010) using an active control group. These studies examined a number of potential mechanisms of action: Mindfulness skills (n = 5), rumination or facets of rumination (n = 3) e.g. brooding, worry (n = 2), cognitive reactivity (n = 2), self-compassion (n = 1), positive affect (n = 1) and negative affect (n = 1). Among the studies which examined the effectiveness of MBCT on depression and anxiety, one (Haenen et al., 2016) used a waitlist, and another (Maddock et al., 2019b) used a TAU control condition. The study (McManus et al., 2012) which focussed on health anxiety as an outcome used a TAU control condition. These studies examined a number of potential mechanisms of action: Mindfulness or facets of mindfulness (n = 3), self-compassion (n = 1), acceptance (n = 1), aversion (n = 1), attention regulation (n = 1), non-attachment (n = 1), rumination (n = 1) and worry (n = 1). The two studies (Goldin et al., 2016; Morrison et al., 2019) which examined the effectiveness of MBSR on social anxiety used an active control condition (Group Cognitive Behavioural Therapy - GCBT) with the study examining the effectiveness of MBSR on different forms of anxiety (Vollestad et al., 2011) using a waitlist control condition. These studies examined a number of potential mechanisms of action: mindfulness skills (n = 2), affective empathy (n = 1), cognitive empathy (n = 1), cognitive reappraisal frequency and selfefficacy (n = 1), cognitive distortions (n = 1), subtle avoidance (n = 1)= 1), attention focusing (n = 1) and brooding (n = 1).

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Findings in relation to 'mechanism of intervention'	•Enhancement of mindfulness and self-compassion from pre to post MBCT programme had mediated effect on depressive symptoms but not relapse rate at 15 month follow up. •Improved cognitive reactivity had mediated effect on depressive symptoms and relapse rate at not of provided and mediated effect on depressive symptoms and relapse rate at not follow up. 15 month follow up.	×
Outcome of the intervention	The effects of MBCT were similar to m-ADM in terms of relapse and residual depressive symptoms.	
Statistical Analysis used	Mediation and moderation analytic framework (Kraemer method)	
Time-point assessments	Three time-points (Pre, post and 15 month follow up)	
Mediators studied (and Time-point assessment tool) assessme	Mindfulness skills Kentucky Inventory of Mindfulness (KIMS) Self-compassion Self-compassion Scale (SCS) Cognitive reactivity Laboratory task	Brooding
Outcomes of interest targeted	Relapse rate and depressive symptoms Hamilton Rating Scale for Depression (HRSD) Structured for DeSM-IV Depressive thinking style Dysfintetional Attitude Scale (DAS)	
Intervention Comparator	MBCT + discontinuation of anticepressants (ADM) versus maintenance ADM	
Intervention	MBCT	MBCT
Participants Population no./- clinical popula- tion (number, gender, mean age)	Recurrent depression with residual depressive symptoms	
Participants no./- clinical popula- tion (number, gender, mean	N = 123 Male and female (Mean age 49 yrs.)	N = 45
Title of review, authors, country	How does mindfulness-based cognitive therapy work? (Kuyken et al., 2010)	

Mechanisms of change in mindfulness-based cognitive therapy for depression: Preliminary evidence from a randomized controlled trial. (Shahar et al., 2010)	Males and Females (Mean age 47 yrs)	Recurrent depression with residual depressive symptoms	MBCT versus waitlist control	Depressive symptoms Beck Depression Inventory (BDI)	Rumination Response Scale (RRS) Reflective pondering Scale (RRS) Scale (RRS) Mindfulness skills The Mindfulness skills The Mindfulness scale (MAAS)	Two time-points (Pre 1 and post-treatment)	Bootstrapping: Preacher and Hayes	MBCT group reported significant decreases in depression compared to waitlist group.	 MBCTs effects were mediated by: Reductions in brooding (an aspect of rumination). Increases in midfulness. Reeflective pondering did not play a mediating role.
The efficacy of mindfulness-based cognitive therapy in recurrent depressed patients with and without a current depressive episode: a randomized controlled trial. (van Aalderen et al., 2012)	N = 205 Male and Female (Mean age 48 yrs.)	Depression - 3 MBCT or more depressive episodes	MBCT versus TAU	Depressive symptoms Hamilton Rating Scale for Depression (HAMD) Beck Depression Inventory (BDI)	Rumination Rumination on Sadness Scale (RSS) Worry Penn State Worry Questionnaire (PSWQ) Mindfulness skills Kentucky Inventory of Mindfulness (KLMS)	Six time points Preament, and post treatment, 3, 6, 9 and 12 months follow up.	Bootstrapping: Preacher and Hayes	Post Treatment: Patients in the MBCT+TAU group reported decreased depressive symptoms, worry, runniation and increased mindfulness skills (observation, acting with awareness, and acceptance without judgement) compared with patients receiving TAU alone.	•MBCTs effects from pre to post programme were mediated by increased acceptance without judgement and decreased levels of rumination and worry.
How does MBCT for depression work? (Batink et al., 2013)	 N = 130 Male and female partici- partici- quarts 44 yrs.) 	Current residual MBCT depressive symptoms asymptoms ome episode of Major Depressive Disorder	MBCT + TAU versus TAU alone	Residual depressive symptoms Hamilon Depression Rating Scale (HDRS). Inventory of Depressive Symptoms (Self-Rating: IDSSR 30) IDSSR 30)	Mindfulness skills Kentucky Inventory of Mindfulness (KJMS) Worry Penn State Worry Questionnaire (PSWQ) Positive affect (PA) and negative affect (PA) and negative affect (Two time points (Pre- and post- treatment)	Sobel-Goodman mediation anahysis. Multiple regression anahysis	ad ecreases vorry skills. skills.	•MBCT effects were mediated by: An increase in mindfulness skills. The effect of the increase of mindfulness skills mindfulness skills mindfulness skills mindfulness skills mindfulness skills in worry and positive affect but not mediated by changes in worry scores on depressive symptoms was mediated by changes in worry scores on depressive symptoms was mediated by changes in positive and negative effect. •Rumination did not play a mediating role.
Cognitive reactivity as outcome and working mechanism of mindfulness-based cognitive therapy for recurrently depressed patients	N = 115 Males and Females (Mean age 48 yrs)	Depression - MBCT remitted patients or currently depressed with 3 or more	MBCT versus TAU	Depressive Symptoms The Hamilton Rating Scale for Depression (HAMD) Beck Depression Inventory (BDI)	Cognitive Reactivity The Leiden Index of Depression Sensitivity Revised (LEIDS-R) Mindfulness skills The Kentucky Inventory of	Two time-points (Pre 1 and post-treatment)	Bootstrapping: Preacher and Hayes	MBCT group reported significant decreases in cognitive reactivity and depressive symptoms versus TAU.	 MBCTs effects were mediated by reductions in cognitive reactivity, which decreased depressive symptoms.

(continued)

	 Mediation analysis showed that pre to post MBCT programme: changes in total mindfulness facets of observing and non-reactivity to inner experience mediated changes in depressed mood. Changes in total mindfulness and the observing facet of mindfulness and the observing facet of mindfulness mediated changes in anxiety scores. MBCT to follow up (six months hence) that changes in total mindfulness along with mindfulness facets of non-judging of inner experience and acting with avareness scores mediated changes in arxious and depressed mood scores. 	•MBCTs effects on anxiety were meditated by: -Increases in self-compassion. -Increased mindfulness and reduced aversion were found to be significantly associated with reduced anxiety when mediated by reduced worry.
	MBCT group reported significant increases in mindfulness facets and decreases in and depressed and anxious mood versus a waitlist control.	MBCT group reported significant increases in mindfulness, attention regulation, self-compassion, acceptance, non-attachment and decreases in attachment, worry, rumination, anxiety and depression versus TAU.
	Bootstrapping: Preacher and Hayes	Bootstrapping: Preacher and Hayes
	Four time points (pre, mid, post treatment, 6 months follow-up)	Two time- points (pre- and post- treatment)
Mindfulness (KJMS)	Mindfulness skills The Five Facet Mindfulness Questionnaire (FFMQ)	Mindfulness The Southampton Mindfulness Questionnaire (SMQ) Attention regulation The Experiences Questionnaire (EQ) Self-Compassion Self-Compa
	Anxious and Depressed Mood Profile of Mood States (POMS-SF)	Depression and Anxiety Hospital Anxiely and Depression Scale (HADS)
	MBCT versus waitlist control	MBCT + TAU versus TAU alone
	MBCT	MBCT
depressive episodes	Anxiety and depression (Mood)	Anxiety and depression
	N = 139 Males and Females (Mean age 57 yrs.)	N = 101 Males and Females (Mean age 44 yrs.)
in remission. (Cladder-Micus et	Mindfuness facets as differential mediators of short and long-term effects of Mindfulness-Based Cognitive Therapy in diabetes outpatients: Findings from the DiaMind randomized trial. (Haenen et al., 2016)	Testing a moderated mediation model of MBCT's effects for psoriasis patients. (Maddock et al., 2019a,b)

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	•Mediation analysis showed that pre to post MBCT change in mindfuhress mediated the decreases in symptoms of health anxiety.	 Mediation analyses pre to post programme indicated that: Mindfulness fully mediated changes in acute anxiety symptoms, and partially mediated changes in worry and trait anxiety. Mindfulness did not mediate changes in mediate changes in 	•Mediation analyses revealed that: -Post MBSR and CBGT changes in
	MBCT group reported significant increases in mindfulness post programme but not after a 1 year follow up period. MBCT group reported significantly lower health anxiety versus the US control group period. MBCT did inprove general anxiety or depression versus the US control versus the US control versus	group. The MBSR group showed significantly positive changes in depression severity, acute anxiety acute anxiety symptoms and trait arxiety along with mindfulness and worry post programme. Treatment gains were maintained 6 months post MBCT programme.	CBGT and MBSR both resulted in similar significant improvements in
	Bootstrapping: Preacher and Hayes	Bootstrapping: Preacher and Hayes	Bootstrapping: Preacher and Hayes
	Three time points (pre, post treatment, 1 year follow up)	Self-report measures for both groups were collected at baseline, at the start of treatment, midway through treatment. A follow-up assessment using the same measures was conducted 6 months after treatment.	Baseline, during treatment, at post-treatment completion and
	Acceptance subscale (PHLMS) Non-attachment The Non-Attachment Scale (NAS) Rumination The 12-item rumination subscale from the Rumination Reflection Questionnaire (RRQ) Worry Penn State Worry Questionnaire (RRQ) Worry Penn State Worry Questionnaire (RRQ) Worry Penn State Worry Questionnaire (FFMQ)	Mindfulness skills Five-Factor Mindfulness Questionnaire (FFMQ)	Mindfulness skills using the Five Facet Mindfulness
	Anxiety (Health anxiety) and Depression The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-1) The Short Health Anxiety Inventory (SHAI) The Whiteley Index (WI) The Beck Anxiety and Depression Inventories (BAI)	Anxiety Beck Anxiety Inventory (BAI); The Spielberger State Trait Anxiety Inventory (ATAI); Depression Inventory (BDI-II) Symptom Checklist 90eRevised Edition (SCL-90-R)	Social anxiety Liebowitz Social Anxiety
	MBCT + usual services (unrestricted services) versus unrestricted services (US) alone.	MBSR versus waitlist control	Cognitive-Behavioural Group Therapy (CBGT) versus
	MBCT	MBSR	MBSR
	Health Anxiety	Anxiety - patients with panic disorder with or without agoraphobia (PD/AG), social anxiety disorder (SAD), and generalized anxiety disorder (GAD) and	Depression Social Anxiety
	N = 74 Males and Females (Mean age 43 yrs)	N = 76 Males and females (Mean age 43 yrs)	<i>N</i> = 108 Males and Females
(continued)	A randomized clinical trial of mindfulness-based cognitive therapy versus unrestricted services for health anxiety (hypochondriasis) (McManus et al., 2012)	Mindfulness-based stress reduction for patients with anxiety disorders: evaluation in a randomized controlled trial (Vøllestad et al., 2011)	Group CBT versus MBSR for social anxiety disorder: A randomized

(Goldin et al., 2016)	(Mean age 34 yrs)		MBSR versus waitlist control	Scale-Self-Report (LSAS-SR)	Questionnaire (FFMQ) Attention	every 3 months during 1-year follow-up		social anxiety post MBSR programme and 1 year post	mindfulness skills, attention focussing and shifting,
					Attentional Control Scale (ATTC) Brooding The Brooding subscale	-		MBSR programme versus the waitlist control. CBGT and MBSR also	cognitive reappraisal frequency, subtle avoidance behaviours and
					of the Ruminative Responses Scale (RRS)			significantly improved mindfulness skills.	cognitive distortions versus the waitlist control group
					Cognitive reappraisal frequency and			attention focussing and shifting,	predicted changes in social anxiety
					cognitive reappraisal self-efficacy			eappraisal and sy, subtle	symptoms. -Post programme CBGT (but not
					Emotion Regulation Questionnaire (FRO)			avoidance behaviours, cognitive distortions	MBSR) changes in brooding (a maladantive form of
					Cognitive Distortions Cognitive Distortions			and brooding (a maladaptive form of	rumination) and reappraisal
					Questionnaire (CD-OI IEST)			rumination) comnared to the	self-efficacy medicted changes in
					Subtle Avoidance			waitlist control.	social anxiety
					Subue Avoidance Frequency				symptotic versus waitlist control.
					Examination (SAFE)				-Increases in reappraisal self-efficacy and
									decreases in avoidance
									behaviours mediated the impact of CBGT
									social anxiety symptoms.
Changes in Empathy N = Mediate the Effects Ma of Cognitive-Behavio- unal Group Therapy but Not Mindfulness-Based Stress Reduction for Social Anxiety Disorder (Morrison et al., 2019)	<i>N</i> = 81 Social Anxiety Males and Females (Mean age 33 yrs)	MBSR	CBGT versus MBSR versus wait-list control	Social anxiety The Liebowitz Social Anxiety Scale – Short-form (LSAS-SR) Anxiety Disorders Interview Schedule for DSM-IV – Lifetime version (ADIS-IV-L)	Affective Empathy; Cognitive Empathy Modified version of the empathic accuracy (EA) task	Baseline, post treatment/wait-list (N = 81), and 1-year follow-up (N = 37).	Bootstrapping: Preacher and Hayes	Relative to both MBSR and wait-list, CBGT resulted in significant improvements in positive affective empathy both post programme and after a 1 year follow up period. There were no significant different differences between the three groups in cognitive empathy or negative	•The improvement in Provement in pathy in CBGT versus MBSR post programme mediated lower social anxiety post programme and at 12-month follow-up.

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	McManus et al. (2012)	Low	Low	High	High	Low	Low	Yes	Yes	Yes	Yes	Yes
	Batink et al. (2013)	Low	Low	High	High	Low	Low	Yes	Yes	Yes	Yes	Yes
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People with Remitted Depression with at Least 3 Prior Episodes of Depression – MBCT

Kuyken et al. (2010) in a mediation and moderation analysis of MBCT (with discontinuation of anti-depressant medication) versus maintenance anti-depressant medication in patients with recurrent depression found that MBCT improved mindfulness, self-compassion and cognitive reactivity versus the control group from baseline to post programme. Kuyken et al. (2010) found that MBCT weakened the link between cognitive reactivity (changes from pre to post MBCT programme) and depressive symptoms and relapse rate at 15 month follow up. Kuyken et al. (2010) also found that increased mindfulness and self-compassion (pre to post MBCT programme changes) had a mediating role in the relationship between MBCT participation and depression symptoms at 15 month follow up but not with relapse rate. Kuyken et al. (2010) was the only study which focussed on depression as an outcome and used measures which reflected different perspectives and performed mediation analysis in an appropriate temporal sequence i.e. that the MBP changed the mediator prior to a test being conducted on associated changes in the outcome at a subsequent time-point. This makes this study the highest quality available and thus more value should be ascribed to their findings relative to the others that focussed on depression as an outcome. Cladder-Micus et al. (2018) supported Kuyken et al. (2010) by finding that MBCT significantly decreased cognitive reactivity and depressive symptoms versus a TAU control group post programme in recurrently depressed patients in remission. Cladder-Micus et al. (2018) found that changes in cognitive reactivity mediated the relationship between MBCT participation and depressive symptoms from pre to post programme. Cladder-Micus et al. (2018) also reported that MBCT significantly changed mindfulness scores; however, they did not report a mediation analysis of mindfulness on depression even though it would likely have been a candidate potential mechanism. Shahar et al. (2010) found that MBCT versus waitlist control significantly increased mindfulness and decreased brooding (a facet of rumination) and depressive symptoms in patients with major depressive disorder and remitted patients from pre to post programme. Shahar et al. (2010) also found that reflective pondering (another facet of rumination) did not change significantly versus the waitlist control group. Shahar et al. (2010) found that reductions in brooding and increases in mindfulness mediated the effects of MBCT on depressive symptoms from pre to post programme. Van Aalderen et al. (2012) found that MBCT versus TAU significantly improved depressive symptoms, rumination, worry and improved three of the four mindfulness skills (observation, acting with awareness, acceptance without judgement but not describing) in recurrently depressed patients with and without a current depressive episode. Van Aalderen et al. (2012) found that pre to post programme changes in rumination, worry and the mindfulness skill 'accept without judgement' scores mediated the relationship with post MBCT programme depression levels versus the TAU control condition. Batink et al. (2013) in a group of adults with current residual depressive symptoms after at least one episode of major depressive disorder found that depressive symptoms were mediated by mindfulness - measured with KIMS - specifically the acceptance without judgement subscale of this measure, following an MBCT programme. They also found that the effect of mindfulness on depressive symptoms was mediated by changes in worry, measured by the PSWO, and positive affect but not negative effect. The effect of the PSWQ score on depressive symptoms was mediated by changes in positive and negative effect. Rumination was not found to be a significant mediator of MBCT on depressive symptoms in this study. Batink et al. (2013) also conducted a mediation analysis on two subgroups, one which had experienced two or less major depressive episodes and the other which had experienced three or major depressive episodes. In the subgroup with two or fewer episodes, Batink et al. (2013) found that the effect of MBCT on depressive symptoms was mediated by total KIMS scores, specifically the acceptance and awareness subscales. The effect of KIMS on depressive symptoms was mediated by changes in PSWQ scores. The effect of PSWQ on depressive symptoms was mediated by changes in positive effect. The effect of MBCT on depressive symptoms in the subgroup with three or more episodes of major depression was only mediated by positive affect. The fact that the proposed mediators and outcomes were measured simultaneously in Cladder-Micus et al. (2018), Shahar et al. (2010), Van Aalderen et al. (2012) and Batink et al. (2013) using only two time points (pre and post MBCT) means that these studies cannot establish and assert claims of causality between their hypothesised mediators of change and depressive symptoms of people with remitted depression (Hayes, 2018a, 2018b). These studies do however help to narrow down what the potential mediators of MBCT's effects are on the depressive symptoms of people with remitted depression generally, and for subgroups of people with 3 or more previous episodes of major depressive disorder (Kazdin, 2007).

Health Populations - Depression and Anxiety Symptoms - MBCT

Maddock et al. (2019b) in a group of psoriasis patients tested but did not find any significant direct effects of post MBCT programme changes scores in acceptance, aversion, self-compassion, attention regulation, non-attachment or mindfulness all of which changed significantly versus a TAU control group (Maddock et al., 2019a) - on depression. Maddock et al. (2019b) also tested if changes in each of these domains of mindfulness had a mediated effect on changes in depression through changes in worry and rumination post programme, but did not find any significant mediated relationships. Maddock et al. (2019b) did find that increased self-compassion scores as a result of participation in an MBCT programme directly predicted changes in anxiety scores post programme. Maddock et al. (2019b) also found that changes in aversion and mindfulness scores, independently, significantly predicted changes in anxiety scores post programme through mediated changes in worry scores.

Haenen et al. (2016) examined the effects of MBCT on various facets of mindfulness and on the mood of patients with type 1 and type 2 diabetes. Haenen et al. (2016) conducted assessments of each at pre-programme (T1), mid-programme (4 weeks: T2), post-programme (8 weeks: T3) and follow-up (6 months post-intervention: T4). Haenen et al. (2016) found that from pre to post MBCT programme that changes in total mindfulness and the mindfulness facets of observing and non-reactivity to inner experience mediated changes in depressed mood. Haenen et al. (2016) also found that pre to post MBCT programme changes in total mindfulness and the observing facet of mindfulness also mediated changes in anxiety scores. Haenen et al. (2016) found that from post MBCT to follow up that changes in total mindfulness along with mindfulness facets of non-judging of inner experience and acting with awareness scores mediated changes in anxious and depressed mood scores.

Health Anxiety - MBCT

McManus et al. (2012) found that MBCT versus TAU significantly increased mindfulness (measured by the FFMQ) from pre to post-programme. McManus et al. (2012) conducted a pre to post programme mediation analysis and found that this change in mindfulness mediated the relationship between MBCT and health anxiety in those who were diagnosed with hypochondriasis using the DSM-IV-TR (American Psychiatric Association, 2000).

Anxiety Disorders - MBSR

Vøllestad et al. (2011) found that MBSR versus waitlist control significantly improved anxiety symptoms, worry, depressive symptoms and mindfulness from pre to post-programme in people with anxiety disorders. Vøllestad et al. (2011) assessed mindfulness, which was their mediator of interest at pre, mid and post MBSR programme. Vøllestad et al. (2011) found that mindfulness did not change significantly from pre to mid programme. This lack of a significant finding meant that they could not test for true mediation using the midpoint data. Vøllestad et al. (2011) conducted a pre to post programme mediation analysis and found that mindfulness mediated acute anxiety symptoms, trait anxiety and worry but not depression severity.

Social Anxiety Disorder (SAD) - MBSR

In a three-armed RCT with people with social anxiety disorder, Goldin et al. (2016) found that MBSR and CGBT significantly improved SAD post treatment and 1 year post treatment versus a waitlist control group. Goldin et al. (2016) conducted a mediation analysis on pre and post treatment changes and found that post MBSR and CBGT changes in mindfulness skills, attention focussing and shifting, cognitive reappraisal frequency, subtle safety behaviours and cognitive distortions versus the waitlist control group predicted changes in social anxiety symptoms. Goldin et al. (2016) also found that post programme CBGT changes in brooding and reappraisal self-efficacy predicted changes in social anxiety symptoms versus the waitlist control. They did not find a similar significant relationship in changes in these variables due to MBSR programme participation and changes in social anxiety symptoms versus the waitlist control group. Goldin et al. (2016) then compared CBGT and MBSR and found evidence that reappraisal self-efficacy and decreases in safety behaviours mediated the effect of CBGT (vs. MBSR) on social anxiety. These results indicate that though decreases in subtle safety behaviours was a significant mediator of both MBSR and CBGT's effects on social anxiety, the decreases in subtle safety behaviours experienced by the CBGT participants had a stronger mediated effect on social anxiety than the decreases experienced by the MBSR programme participants. Morrison et al. (2019) in a 3-armed RCT examined if empathy was a mediator of MBSR or CBGT effects on SAD post treatment and during a 12 month follow up period. Morrison et al. (2019) found that CBGT significantly improved positive affective empathy versus MBSR and a waitlist control post-intervention. This improvement was maintained in CBGT after 12 month follow up period versus MBSR. Positive effective empathy after MBSR was not found to be significantly different from the waitlist control post-intervention. Negative effective empathy was not significantly different amongst the three groups, post-intervention or 12 months post-intervention. Morrison et al. (2019) found that CBGT's significant improvement of positive affective empathy versus MBSR was associated with greater reductions in social anxiety post-intervention. As with the majority of the other studies reviewed, the results from the mediation of post programme improvements did not meet the standards for testing empathy as a mechanism of action in SAD in this study, as both the mediator and outcome were measured at the same time. This study did however appropriately

temporally sequence their analysis at 12 month follow, where they tested the predictor, mediator and outcome in the proper sequence. In doing so, Morrison et al. (2019) found that significant improvement in positive affective empathy in CBGT versus MBSR was associated with lower social anxiety at 12-month follow-up. Morrison et al. (2019), like Kuyken et al. (2010) was the only other study, which met all eight of Alsubaie et al. (2017)'s criteria.

Risk of Bias in the RCTs

The risk of bias assessment using the Cochrane Risk of Bias tool is presented in Table 2. When appraising the quality of the retained studies, there was limited variation in terms of sample size, with a minimum of 45 and a maximum of 205 participants. Four of the eleven studies had small samples (n < 100), with the total number of participants being 1197 aged between 18 and 82. The majority of the studies comprised of more women than men. The risk of bias was low to high across the studies, but the source of bias varied. The blinding of participants, personnel and outcome assessment was at a high risk of bias in all of the studies (n = 11). The risk of bias in allocation concealment in the majority of the studies (n = 11)was low. There was low risk of bias in sequence generation in all studies, bar one, where it was not clearly stated (n = 10). The potential risk of bias due to selective reporting was low in 9 out of the 11 studies reviewed. However, 1 study had a moderate and another a high risk of bias. The eligibility criteria was specified in all 11 studies, with some level of programme compliance being clearly assessed in 10 out of the 11 studies. A power calculation was conducted in 8 out of the 11 studies. All of the 11 studies had valid data collection tools and accounted for all participants in their analyses. The studies reviewed used a range of validated questionnaires to assess the impact of the interventions on the proposed mediators and the same outcomes, e.g. depression (such as HAM-D, HADS-D, BDI-II), which further hinders direct comparison between studies.

Mechanistic Study Quality

The studies by Kuyken et al. (2010) and Morrison et al. (2019) were the only two studies which were successful in achieving all eight criteria of the Alsubaie et al. (2017) review framework. Kuyken et al. (2010) and Morrison et al. (2019) were the only studies which established the appropriate temporal sequence by measuring the mediator during the active treatment phase, and the outcomes subsequently (Kraemer et al., 2002). Haenen et al. (2016) and McManus et al. (2012) met 6 out of the 8 criteria, with limitations in in conducting mediation analysis on mediators and outcomes which were assessed at the same time-point and not using measurements which

reflected different perspectives. All of the other studies were only successful in 5 of the 8 criteria but had limitations in terms of relying on self-report measures, using only pre and post-intervention measurements and not showing appropriate temporal sequencing.

Did the Study Use a Theory?

Kazdin (2007) identified the importance of articulating how the mechanisms of a therapeutic intervention work using a theory or treatment rationale. All of the reviewed studies reported a theory underpinning their research question and analysis. There was limited testing of more integrative models of mindfulness mechanisms, which may be important to our understanding of how MBPs lead to beneficial mental health outcomes in clinical settings (Van der Velden et al., 2015).

Did the Study Use Process Measures that Assess the Constructs, if Necessary, from a Variety of Perspectives?

Kazdin (2007) identified the need to take into account different perspectives, including neuropsychological and experimental measures. All eleven studies used validated self-report measures; however, three studies (Kuyken et al., 2010; McManus et al., 2012; Morrison et al., 2019) used mechanistic measurements that took different triangulated perspectives into account. Kuyken et al. (2010) used a laboratory paradigm in order to measure cognitive reactivity after the induction of a sad mood. Morrison et al. (2019) used functional magnetic resonance imaging (fMRI) and an empathy task in order for participants to self-rate their feelings of empathy upon to watching a series of film clips in which people discussed emotional events in their lives. McManus et al. (2012) used a composite measure of health anxiety using an independent assessor (using visual analogue scales) and self-report measures. However, they relied on a self-report measure (FFMQ) to measure mindfulness, which was the hypothesised mediator in this study.

Did the Study Design Ensure the Hypotheses Can Be Addressed?

The nature of the inclusion and exclusion criteria for this study ensured that only RCT designs, which could assess changes over different time points and then assess potential changes in the hypothesised mediator's relationship with the outcomes versus a control group, were included (Kazdin, 2007). All studies thus used the gold standard for testing efficacy and effectiveness of either MBSR or MBCT; however, the majority of the studies (n=8) assessed potential mechanistic changes from pre to post-intervention only (Batink et al., 2013; Cladder-Micus et al., 2018; Goldin et al., 2016; Maddock et al., 2019b; McManus et al., 2012; Shahar et al., 2010; Van Aalderen et al., 2012; Vøllestad et al., 2011). This means that the temporal order of change, which is the first prerequisite for making inferences regarding the causal direction of an association, could not be examined (Snippe et al., 2015). As the proposed mediators and outcomes were assessed only twice at the same moment in time, alternative explanations for the significant mediations are still plausible e.g. the causal direction may be the reverse; other factors may change the outcome or the relationship may be reciprocal i.e. small increases in the mediator and outcome generating a positive feedback loop (Snippe et al., 2015). Haenen et al. (2016) measured their proposed mediators and outcomes at 4 time points, however they did not assess the temporal order of changes in the mediator and outcome as they conducted mediation analyses on both the mediator and outcome at the same time point on two separate occasions, once on changes from pre to post MBCT programme and then on changes from post programme to 6 months follow up. This prevented them from drawing conclusions on possible causality. Kuyken et al. (2010) attended to the temporal sequencing of their proposed mediator and outcome variables. They did this by conducting a mediation analysis on pre to post MBCT programme changes in their mediators and examined if these predicted changes in the proposed outcomes (residual depressive symptoms and depressive relapse risk) 15 months post programme. Kuyken et al. (2010) did not however measure all of the mediators and outcomes at all three points. This means that an alternative explanation for their significant mediated findings cannot be ruled out. In Kuyken et al. (2010) cognitive reactivity from pre to post MBCT programme was found to have a mediated effect on depressive symptoms and relapse rate at 15 month follow up. It could however be that changes in cognitive reactivity is a result of changes in depressive symptoms and that this change accounts for the reduced relapse rate. Morrison et al. (2019)'s tests of mediation of post treatment improvements in social anxiety did not meet the standards of testing empathy as a mechanism of treatment as the mediator and outcome were measured at the same time (Kazdin, 2009). Their tests of mediation of social anxiety at 12-month follow up did measure the predictor, mediator and outcome variable in the appropriate sequence. However one limitation of Morrison et al. (2019) is that they did not examine if the proposed mediator changed before the outcome by looking at change patterns across simultaneous outcomes. None of the reviewed studies assessed changes over several (4 or more) time points.

Did the Study Use Appropriate Statistical Analyses?

All studies used some form of appropriate mediation analysis (Kazdin, 2007, 2009; Kraemer et al., 2002). Nine of the eleven studies used a bootstrapping test of mediation, one used a

Sobel-Goodman test and another used the mediation and moderation statistical analytic framework recommended by Kraemer et al. (2002) for RCTs. The majority of the studies could not conduct full tests of mediation, due to the limited number of data collection time points.

Discussion

This study aimed to systematically review studies which conducted a controlled mediation analysis in order to examine the potential mechanisms which underlie MBCT, MBSR and MBRP's effects on anxiety, depression and psychological distress in any health or mental health population. The evidence from this review was evaluated using Alsubaie et al. (2017) framework for abstracting and interpreting the quality of findings relating to mechanisms of action of MBPs, which they derived from the recommendations made by Kazdin (2007, 2009). The results of the review are in line with those of the systematic reviews conducted by Gu et al. (2015), Van der Velden et al. (2015) and Alsubaie et al. (2017). There appears to be preliminary evidence that MBCT/MBSR may positively impact anxiety and/or depression, directly and/or through mediated relationships with hypothesised mechanisms, such as mindfulness, rumination, worry, self-compassion, cognitive reactivity, aversion, attention regulation skills and positive affect. This supports Kazdin (2009) assertion that single influences can produce multiple outcomes, and relatedly, similar outcomes may be reached through multiple paths activated by different experiences i.e. through participation in different MBPs. There are however significant limitations within the methodologies of the studies reviewed, which mitigate against the extent to which conclusions on causality in these relationships can be drawn. The lack of a consensually agreed theoretical framework of how MBPs impact anxiety and depression appear to have limited the extent to which integrative models of mindfulness mechanisms have been developed and tested in this research field (Van der Velden et al., 2015). Our findings provide insights into what the key mechanisms of such a model might be, which could be developed and tested in future RCTs with embedded mechanistic analyses. The current findings also have potential implications for the clinical application of MBPs, as they suggest that MBPs for anxiety and depression could be refined, or new MBPs developed and delivered as a standalone programme or as part of a sequential treatment programme. However further research with higher methodological quality, which includes all of Kazdin (2007, 2009) criteria, is required before more definitive conclusions can be drawn on whether focussing on one mediator is likely to improve the effects of MBPs on anxiety and depression in future.

This review found preliminary evidence that alterations in mindfulness, worry, cognitive reactivity, self-compassion and positive affect mediated MBCT's effect on the depressive symptoms of people with at least 3 prior episodes of depression, with more mixed evidence for rumination as a potential mediator. This review also found evidence that cognitive reactivity mediated depressive relapse after MBCT programme participation. These findings are in line with the findings of Van der Velden et al. (2015) which found evidence for mindfulness, worry, rumination and self-compassion and some preliminary evidence for positive affect being either associated with, predicting or mediating MBCT's effect on major depressive disorder. These findings are also in line with Gu et al. (2015) who in a broader analysis of MBSR and MBCTs effects on mental health outcomes more generally (including depression, anxiety, stress and mood states) found evidence for cognitive reactivity and moderate evidence for mindfulness, worry and rumination and partial preliminary evidence for self-compassion. These findings are also supported by Alsubaie et al. (2017) who found evidence that mindfulness, worry, cognitive reactivity, self-compassion and positive affect mediated the effects of MBCT on depression with mixed findings for rumination. The similarity in findings with Alsubaie et al. (2017) is not surprising, as this paper updates their review, whose systematic searches were completed in 2015. This means that our review and Alsubaie et al. (2017) reviewed five of the same papers. Maddock et al. (2019b), included in this review, provides a study with psoriasis patients against which these findings can be contrasted. Maddock et al. (2019b) tested the pre and post MBCT mediated relationships between significant changes in mindfulness, rumination, worry and self-compassion, along with other candidate mechanisms of action including acceptance, aversion, non-attachment and attention regulation and depressive symptoms. Maddock et al. (2019b) did not find any significant mediated relationships between any of these candidate mediators and depression. The likely difference between Maddock et al. (2019b) findings and the findings in this review - which contained samples with higher levels of depressive symptoms at baseline, is the potential floor effect in changes in depression which occurred due the participants in their study having lower levels of depression at baseline in their accompanying RCT (Maddock et al., 2019a). This indicates that for mediation studies to be able to examine mediated relationships between MBPs and mental health outcomes, that not only do they need to be powered sufficiently to be able to detect mechanistic effects, they also need to have sufficient levels of changes in the outcomes possible. This would avoid any potential floor effects in the data, impacting on the capacity for potentially statistically significant mechanistic relationships to be identified. We found only one paper, which examined if alterations in mindfulness due to MBSR might mediate depression, this paper, Vøllestad et al. (2011), did not find a mediated relationship between mindfulness skills and depression.

The preliminary evidence from this review indicates that increased mindfulness due to MBCT/MBSR participation may be universal mediator of change in anxiety and depressive symptoms across a range of different populations including people with recurrent depression, health anxiety, anxiety disorders and health conditions (including diabetes and psoriasis). These findings are largely consistent with the underlying theory which underpins both MBSR and MBCT, i.e. that the development of mindfulness skills leads to increased awareness of, and insight into maladaptive negative thinking, which may allow counter-productive thoughts, which contribute to and maintain anxiety and depression, to pass without further elaboration (Kabat-Zinn, 1982; Segal et al., 2002). Self-compassion and worry could also be candidates as universal mediators of change in anxiety and depression. This study found preliminary evidence that increased self-compassion and reduced worry could play a mediating role in reduced depressive symptoms in people with recurrent depression and reduced anxiety in people with psoriasis. The finding that self-compassion may be a universal mediator of change in anxiety and depression is supported by a number of studies that have found that increased selfcompassion is associated with decreased anxiety and depression (Neff & Dahm, 2015; Van Dam et al., 2011). The finding that changes in worry may be a universal mediator of in change in both anxiety and depression is supported by the work of Starcevic (1995), Papageorgiou and Wells (1999) and Watkins (2004). This study also found preliminary evidence that cognitive reactivity may be specific mediator of change in depressive symptoms and relapse rate in people with recurrent depression. One paper (Goldin et al., 2016) found that improved attention focussing and shifting, reappraisal frequency along with reduced safety behaviours and cognitive distortions mediated MBSR's effect on social anxiety. Maddock et al. (2019b) in a similar-sized study to Goldin et al. (2016) examined the relationship between attention regulation skills which contains facets of attention focussing and shifting and anxiety, both of which changed significantly post MBCT intervention, and did not find a mediated relationship. This indicates that though both MBSR and MBCT change attention regulation, but it may be that attention regulation is specific mechanism of change in social anxiety. This study, like the majority of the studies in this review, was only powered to detect large mediated effects, which means that for that small to mediated relationships may exist in this patient population, but this study may have been unable to detect them. Each of these hypotheses, on what the specific and universal

mechanisms of anxiety and depression might be, need to be tested more extensively in future research.

This review found no studies, which focused on psychological distress as an outcome or included a mediation analysis of the effectiveness of MBRP on depression or anxiety. MBRP, based on the content of MBCT, was designed to target negative mood along with craving in the substance use relapse process (Witkiewitz and Bowen 2010). This MBP was included in this review due to the fact that it met our inclusion criteria as an MBP for our initial search strategy. The authors also felt that because MBRP is over ten years old (Bowen et al., 2009) and that in the same way that MBSR was adapted from its initial focus, of reducing the stress of people with chronic health conditions to focus on depression and anxiety, that MBRP may also have developed an evidence base for these outcomes. We did find one study (Witkiewitz and Bowen 2010) that examined the effectiveness of MBRP on depression. However, the subsequent mechanism analysis, which was undertaken, explored depression as a mediating variable rather than an outcome, which meant it did not meet our inclusion criteria.

Quality of the Studies

It appears that the volume of research examining the potential mechanisms, which may underlie MBPs effects on the anxiety and depression levels of health or mental health populations, is increasing. It also appears that the quality of the methodologies contained within this research literature is improving. The increasing numbers of RCTs, which used a controlled mediation analysis, evidences this. In this review, we found 11 studies which met the inclusion criteria. This compares with Alsubaie et al. (2017) who only found only 5 studies of this nature. This increased amount of evidence along with the improved quality of statistical analyses being employed in the reviewed studies allows us to be more confident of our findings on the potential causal pathways between MBPs and reduced anxiety and depression. There is, however, room for further significant improvement in the studies reviewed. The majority of the studies relied on self-report measures, with four of the eleven studies having small sample sizes (n > n)100). The sample sizes ranged from 45 to 205 participants. This is significantly lower than the 462 participants that would be needed to control for Type II error using bias-corrected bootstrapping having 80% power to detect small effects (Fritz & Mackinnon, 2007). Thus, the majority of the studies in this review were underpowered to control for Type II error for small to medium effects. In order to ensure that all mechanistic relationships are detected and to allow other candidate mechanisms to be explored, triangulation of measurements e.g. neuroscience, experimental and self-report measures and larger sample sizes are needed in future studies. The results from the majority of these studies should thus be considered preliminary until replicated with larger samples. There were only three studies reviewed that used an active control comparison. This means that we cannot exclude that the changes in the mediator and outcomes scores based on MBP participation, when compared against non-active controls, were not due to non-group related factors e.g. expecting to improve or being in a supportive group context (Maddock et al., 2019a). The limited assessment and reporting of treatment fidelity in studies reviewed, or in the accompanying RCT studies, limits the validity and reliability of their results relating to changes in the predictor, mediating variables and anxiety and depression (Carroll et al., 2007; Leeuw et al., 2009). The studies reviewed contained motivated groups of participants who were randomly assigned to an MBP or control group. This self-selection may limit the external validity of these findings, as it is more difficult to establish how representative these groups were of people with anxiety or depression (Maddock et al., 2019a). The blinding of participants, personnel or outcome assessor bias was high risk in the majority of studies. However, due to the nature of the MBPs evaluated, it would not have been possible to blind the participants to treatment conditions in these studies (Davidson & Kaszniak, 2015). This means that detection or performance biases relating to the completion of the self-report outcome measures cannot be ruled out (Higgins et al., 2011). A number of validated self-report measures were used to test changes in the predictors, mediators and outcomes due to MBP participation. This means that common methods bias, which could have inflated the effects of MBPs on these variables, also cannot be ruled out (Podsakoff et al., 2003).

The reviewed studies varied in terms of specificity in the examination of potential mechanisms. Mediational analysis can determine whether there are important statistical relations between an MBP, a suggested mechanism and outcome but is limited in how precisely it can explain how the mediated change came about and it cannot establish causal specificity (Kazdin, 2009). The inclusion of an appropriate temporal sequence or temporal precedence measures (i.e. does the mediator change before the outcome) helps to improve the degree of causal specificity (Van der Velden et al., 2015). The best measure of temporal precedence includes measuring the proposed mediator and outcome at several time-points throughout the treatment process to access whether mediator changes before the outcome (Kazdin, 2007). In line with the systematic reviews of Gu et al. (2015), Van der Velden et al. (2015) and Alsubaie et al. (2017), the majority of the studies in the literature reviewed (n = 8) only conducted mediation analyses on changes in proposed mediators and outcomes from pre to post programme. This means that the temporal order of change, which is the first prerequisite for making inferences regarding the causal direction of an association, could not be examined (Snippe et al., 2015). Not taking temporality into account in this way means that the findings related to the role of the MBPs predictors and mediators in changes in anxiety and

depression in these studies are just preliminary (Kazdin, 2007). These studies do however help to narrow down what the potential mediators of influence on: depressive symptoms are for people with remitted depression; for subgroups of people with 3 or more previous episodes of major depressive disorder; the anxiety and depressive symptoms of people with anxiety disorders, health anxiety disorder and specific health populations (i.e. people with diabetes and psoriasis) (Kazdin, 2007). The quality of mechanistic studies of this nature does appear to be improving when compared to the literature that both Gu et al. (2015) and Alsubaie et al. (2017) reviewed. Three studies (Haenen et al., 2016; Kuyken et al., 2010; Morrison et al., 2019), two of which were conducted since Gu et al. (2015) and Alsubaie et al. (2017) all measured changes in both the mediating and outcome variables at multiple time points. Two studies (Kuyken et al., 2010; Morrison et al., 2019) employed recommendations which were in line with Kraemer et al. (2002) by ensuring that measurement of the proposed mediator temporally preceded the outcome. None of the studies included measures of temporal precedence as recommended by Kazdin (2007, 2009) where both the proposed mediator and outcome variables are measured at several time points during the MBP in order to identify if the proposed mediating variable changes prior to change in the outcome. It is also encouraging to see the increased use of more modern forms of recommended mediation analysis in these studies e.g. nine of the eleven studies used bootstrapping methods of mediation, rather than Baron and Kenny (1986) alone, which is now being actively discouraged in the mediation analysis literature (Rungtusanatham et al., 2014). Bootstrapping mediation tests are preferred over other mediation methods because they do not assume a normal sampling distribution of the indirect effects (Preacher & Hayes, 2008). Future research should continue to build on the improvements in methodological rigour shown in these studies. RCTs which examine the effectiveness of MBPs on anxiety, depression or psychological distress should design accompanying mechanism studies which can establish temporal precedence, as recommended by Kazdin (2007, 2009) by testing outcomes and candidate mechanisms at three or more time points in order to assess whether change in the mediator precedes changes in the outcome. These studies should also take into account other criteria recommended by Kazdin (2007, 2009) but not included in Alsubaie et al. (2017) to help demonstrate mediation e.g. showing a gradient in which greater activation of a proposed mediator is associated with increases or decreases in the outcome. It would also be useful if uniform measurements of outcome, predictor and mediating variables were used in order to facilitate the conducting of meta-analyses, which would indirectly result in larger sample sizes. It is also important that measurements of mediators that reflect different perspectives, e.g. neuroscientific measurements, are included.

Strengths and Limitations of the Current Review

The main strength of this study is that it fills a gap in the literature by being the only systematic review which has provided a narrative syntheses of mediation studies, which used a control condition as a moderating variable to explore the mechanisms underlying MBCT, MBSR and MBRP's effects on anxiety, depression and psychological distress. The narrow inclusion criteria and the fact that this study also only focused on MBCT, MBSR and MBRP rather than other studies that include mindfulness teachings, e.g. Acceptance and Commitment Therapy (Hayes and Wilson, 1994) minimised methodological heterogeneity across the studies reviewed and allowed relevant narrative synthesis to be developed. In line with Gu et al. (2015) recommendations, we improved the strength of this review, by including studies examining mechanisms without a strong theoretical basis. Kazdin's (2007) criteria requires a strong theoretical rationale for the testing of mediation, however limiting the inclusion criteria in this way, would have meant the overlooking of potentially important MBPs mechanisms of action which may inform both theoretical developments, future research and clinical practice (Alsubaie et al., 2017). We thus included Kazdin (2007) design requirement as a quality criterion in line with Alsubaie et al. (2017)'s framework. The use of this framework also strengthened this review by aiding comparability between Alsubaie et al. (2017)'s review and this review, while also allowing us to examine more recent literature and the evolution of this literature in the five years since their study searches were completed.

There are several limitations of this review. The aims of this study coupled with the use of the Alsubaie et al. (2017)framework for abstracting and interpreting mechanistic study quality limits the focus of this systematic review. The Alsubaie et al. (2017) framework is a useful tool, however future research should build on the development and use of this framework, by incorporating this framework in the development of a more comprehensive framework, which would include all of Kazdin (2007, 2009) criteria. The aims of this study meant that studies not employing RCT designs and using a control in their mediation analyses were excluded from the search. This meant that studies using other study designs e.g. case and observational studies, which could provide evidence on how and why MBPs lead to changes in anxiety or depression were discarded in the search process. An example of this is how the inclusion criteria meant that a dismantling trial of how MBCT may prevent depressive relapse versus cognitive psychoeducation, conducted by Williams et al. (2014) was omitted, as it did not test explicitly

measure mindfulness skills as a mediating variable. Farb et al. (2018), which used multilevel modelling to examine how linear increases in decentering (in an RCT of MBCT versus cognitive therapy) may impact relapse/recurrence in Major Depressive Disorder over a 26 month study also did not meet the inclusion criteria. This study also suffers from measurement heterogeneity due to the range of mechanisms and outcome measures used in the reviewed studies. These measures were all published in peer-reviewed journals and had at least good psychometric properties, which would mean that they were conceptually and empirically similar. The fact that we only reviewed studies published in peer-reviewed journals means that some publication bias may affect the findings from this study. This bias might be exacerbated by the fact that some RCTs of MBPs may include potential mechanism candidates but did not report mediation analyses unless evidence for mediation was found. This review also did not consider treatment fidelity or MBP implementation, which would likely influence the effect of these programmes on the mechanisms and mediators examined.

Conclusions

The current study is the first to systematically review mediation studies which used a control condition as a moderating variable in mediation analyses to identify and evaluate the strength and consistency of evidence for mechanisms underlying the effects of MBPs on different forms of anxiety, depression and psychological distress. The change processes involved in MBPs are complex, and MBP participation appears to enhance multiple potential mediators which may improve anxiety and depression in a range of health and mental health populations. This review provides preliminary evidence that MBCT/MBSR treatment effects on anxiety and depression may be mediated by hypothesised mechanisms, such as mindfulness, rumination, worry, self-compassion, cognitive reactivity, aversion, attention regulation skills and positive affect. Although the included studies using mediation analysis have key methodological shortcomings, which preclude strong conclusions regarding mediation, it is clear that this evidence base is increasing. The results from this study thus provide valuable insights into what the potential causal pathways connecting MBPs with improved anxiety and depression might be.

Data Availability Data sharing is not applicable to this article as no new data were created or analysed in this study.

Declarations

Ethics Statement The nature of the article (i.e. being a systematic review) meant that ethical approval was not needed for this research.

Informed Consent The nature of the article (i.e. being a systematic review) meant that informed consent was not needed for this research.

Conflict of Interest The author's declare no conflicts of interest.

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