MINDFULNESS

doi.org/10.1007/s12671-018-0942-z

Meditation and Secondary Prevention of Depression and Anxiety in Heart Disease: a Systematic Review

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Abstract

Heart disease is the leading cause of global mortality, accounting for 13.7 million deaths annually. Optimising depression and anxiety symptoms in adults with heart disease is an international priority. Heart disease secondary prevention is best achieved through implementation of sustainable pharmacological and non-pharmacological interventions, including meditation. Meditation is a means of generating self-awareness and has implications for enhanced self-management of depression and anxiety symptoms. This review aims to identify high-level quantitative evidence for meditation interventions designed to improve depression and/or anxiety symptoms among adults with heart disease and ascertain the most important elements of meditation interventions that facilitate positive depression and/or anxiety outcomes. This systematic review and narrative synthesis was completed in accordance with the PRISMA Statement and has adhered to the Cochrane Risk of Bias guideline. Six databases were searched between 1975 and 2017. Statistically significant outcomes were demonstrated in over half (5/9) of the phase II meditation studies for depression and/or anxiety and involved 477 participants. Meditation interventions that generated positive outcomes for depression and/or anxiety included elements such as focused attention to body parts (or body scan) (3/4 studies) and/or group meetings (4/5 studies). Meditation is a means of reframing heart disease outpatient services towards an integrated model of care. Future adequately powered phase III studies are needed to confirm which meditation elements are associated with reductions in depression and anxiety; and the differential effects between concentrative and mindfulness-based meditation types among adults with heart disease.

INTRODUCTION

Heart disease is the leading cause of death in both developed and developing countries (World Health Organisation, 2014; World Health Organization, 2014). Evidence targeting sustainable non-pharmacological interventions to optimise modifiable heart disease risk factors is an international priority (Mendis et al., 2005). The American Heart Association recommends the use of meditation as an adjunct to guideline-directed cardiovascular risk reduction (Levine et al., 2017). Calls for further research for meditation's effectiveness in large phase III trials are required to facilitate the implementation of mediation into heart disease clinical settings (Brook et al., 2013; Levine et al., 2017).

Depression is an independent risk factor for further cardiac events (Grippo & Johnson, 2002), whereas comorbid depression and anxiety are significantly associated with increased heart disease morbidity and mortality (Grippo & Johnson, 2002; Szekely et al., 2007). After an acute cardiac event or hospitalisation, rates of depression and anxiety are high, which persists on entry into cardiac rehabilitation programs (Milani & Lavie, 2007). It is essential that clinicians identify and work with patients post an acute cardiac event to ensure that those who have depression or anxiety are able to improve their chances of both mental and physical recovery. Specific psychological stressors for cardiac patients generally occur between the first few weeks after an acute cardiac hospitalisation up to six months post discharge. These can be in varied forms, such as existential anxiety, characterised by lingering fears of recurrence or progression of the disease, uncertainty and vulnerability (Simony, Pedersen, Dreyer, & Birkelund, 2015), high incidence of post-coronary bypass depression (Tully et al. 2012), as well as adjustment to reductions in physical function and quality of life (Fredericks, Lapum, & Lo, 2012). Whilst there are recommended pathways for referral of cardiac patients with depression and anxiety, depressive symptoms are often mistaken as cardiac in nature, and optimal treatment for these patients is often overlooked during the inpatient phase (Ceccarini, Manzoni, & Castelnuovo, 2014). How adults with heart disease can be best supported in this period of their heart disease trajectory is seldom explored outside an exercise based program (Taylor et al., 2014), leaving avenues for mind-body therapies such as meditation to address the unmet psychological support needs of these patients.

Meditation is a means of generating self-awareness and acceptance, which can facilitate adaptive affective regulation, behaviour change, and alleviation of depression and anxiety symptoms (Goyal et al., 2014). Skills attained through meditation such as grounding and centering provide opportunities for regeneration and allow the individual to integrate stressful experiences, such as hospitalisation and cardiac

interventions, thereby optimising self-management. Meditation may also lead to earlier detection of stress-ruminative thoughts and physiological arousal, enabling opportunities to engage in more effective coping responses (Toneatto & Nguyen, 2007). Whilst the predominant focus of secondary prevention has been towards the modification of physiological risk, meditation can empower individuals by identifying the role they play in addressing the emotional component of their illness (Schlitz, Amorok, & Micozzi, 2005).

Meditation can be defined as "…practices that self-regulate the body and mind, thereby affecting mental events by engaging a specific attentional set" (Cahn & Polich, 2006, p. 180). Meditation is commonly classified into two types, concentrative and mindfulness meditation. Concentrative meditation types, such as Transcendental Meditation, Benson's Relaxation Response or guided imagery, involve a focus on a specific mental or sensory activity, such as a repeated sound, visualised image(s) or specific body sensations such as breath (Cahn & Polich, 2006). Mindfulness encourages a present-moment awareness of thoughts, feelings, and sensations without attachment or analysis of mental contents (Cahn & Polich, 2006). There is overlap between the two approaches, as concentrative practices incorporate mindfulness by allowing thoughts to pass without attachment, returning attention to the object of concentrative awareness, whilst mindfulness encourages a return to an open, non-judgemental attentive set (Cahn & Polich, 2006). Whilst methods used to elicit state changes differ across practices, both approaches can mutually influence and enhance each other, producing similar changes towards an expanded awareness or consciousness (Cahn & Polich, 2006; Lutz, Slagter, Dunne, & Davidson, 2008).

Meditation and deep breathing are the two most commonly utilised mind-body therapies in cardiac rehabilitation programs for psychological and emotional well-being (Grant, Bin, Kiat, & Chang, 2012). Mindfulness meditation has demonstrated effectiveness in meta-analytic reviews in reducing risk for relapse in successfully treated depressed patients (Toneatto & Nguyen, 2007), and for coping with distress and disability across a broad range of chronic illnesses (Grossman, Niemann, Schmidt, & Walach, 2004), thereby supporting its use as an adjunct secondary prevention strategy. Meditation has also demonstrated capacity to improve a range of health outcomes in heart disease populations during hospitalisation and in the post-operative period, and there is strong evidence supporting the integration of mind-body therapies generally into cardiac rehabilitation programs (Astin, Shapiro, Eisenberg, & Forys, 2003; Casey et al., 2009; Chang, Casey, Dusek, & Benson, 2010; Hui, Wan, Chan, & Yung, 2006). However, the potential for meditation to be implemented in the outpatient cardiac rehabilitation setting, at a time when these adults desire additional support and are amenable to behaviour change is less clear. Implementing innovative

strategies to reduce depression and anxiety in heart disease populations is particularly important at this time point, as it occurs in the context of the patients psychosocial and socioeconomic circumstances; and is conducted in a setting that is supported by conventional medicine, which is likely to encourage participants and improve adherence (Linden, 2000) to meditation as an adjunct cardiac risk reduction strategy. This systematic review aims to: 1) identify high levels of evidence for adjunct meditation strategies designed to improve depression and anxiety symptoms among adults with heart disease, and 2) classify the elements of meditation interventions that facilitate improvements in depression or anxiety after a cardiac event.

METHOD

Study design

A systematic review of RCT and quasi-experimental studies conducted in accordance with the PRISMA Statement.

Eligibility criteria

The populations included in this review were adults with *modifiable risk factors* for heart disease, coronary heart disease, valvular disease, or heart failure (hypertension, angina, atrial fibrillation, or breathlessness), and/or *have undergone a surgical procedure* (cardiac bypass surgery-coronary, aortic or valvular; pacemaker or defibrillator insertion or pericardial window) and/or an *interventional procedure* (coronary angiogram, percutaneous coronary intervention, ablation or other procedure); who participated in a clinic or outpatient disease management program after a recent inpatient hospitalisation**.** Interventions included meditation techniques that fit the operational definition, as previously described (refer page 3). Guided imagery has been included as it is an inherent component of some meditation practices that incorporate aspects of spirituality (Delaney & Barrere, 2008), and is in alignment with the goals of some meditation practices to achieve heightened awareness (Cahn & Polich, 2006; Tusek, Cwynar, & Cosgrove, 1999). Comparison groups were identified as conventional cardiac rehabilitation programs offered in mainstream outpatient healthcare settings or clinic-based programs or interventions. Outcomes considered were depression and/or anxiety.

Exclusion criteria were interventions involving yoga, qigong, predominately exercise-based interventions and/or multicomponent interventions that did not discretely analyse the meditation component; relaxation interventions that did not include a meditation component (such as biofeedback, autogenic training, and progressive muscle relaxation), and paediatric populations. Visualisation or mental

rehearsal practices (for example, for peak performance) were excluded as they are a relaxation practice that is independent of meditation. Non-English articles and abstracts were excluded.

Information sources

This systematic review was completed in accordance with the PRISMA Statement. Databases searched included MEDLINE, AMED, CINAHL, Embase, PsycInfo and the Cochrane Database of Systematic Reviews between 1975 and 27th September 2017. Reference lists were also searched for additional articles.

Search Strategy

The keywords and search terms used in MEDLINE and CINAHL (Refer Supplementary Appendix S1).

Study Selection and data collection process

Titles and abstracts were screened for eligibility and all duplicates were removed (AR). Uncertainties around articles for inclusion were resolved by consensus (AR, LH & PN). The full-text article related to one abstract was obtained. Significant heterogeneity between intervention content, designs and outcomes precluded the use of meta-analysis and results were synthesised in a narrative review. To classify the elements of included interventions, each line of text describing the interventions were coded by one investigator (AR). Each element was listed in a table until all were included. Common elements were then identified and tallied across interventions.

Risk of Bias

A Cochrane Risk of Bias Table was used to report the risk of bias within and across studies (Higgins et al., 2011).

RESULTS

Study Selection

The initial search generated 780 articles, which after a process of review, elimination and hand searching, were reduced to nine articles for inclusion (Refer Figure 1).

Insert figure 1 here

Study Characteristics

Of these nine studies, four studies were phase II RCTs and five studies were pre and post-test designs. The majority of the 9 included studies were conducted in high-income countries (n=7) including the United States (n=6) and the Netherlands (n=1), whilst the remainder (n=2) were conducted in India

(n=1) and Iran (n=1), which are considered low-income countries. The mean number of participants was 53 (SD ± 33), with a mean age of 60 years (SD ± 6). Just over two-thirds of the participants were male (67%), with one study including only men (Parswani, Sharma, & Iyengar, 2013).

Concentrative meditation types were used in four studies, including guided imagery (Collins & Rice, 1997; Luskin, Reitz, Newell, Quinn, & Haskell, 2002; Mandel, 2007) and Transcendental Meditation (Paul-Labrador et al., 2006). Mindfulness-Based Stress Reduction or Mindfulness meditation were used in five studies (Delaney, Barrere, & Helming, 2011; Delui, Yari, Khouyinezhad, Amini, & Bayazi, 2013; Nyklíček, Dijksman, Lenders, Fonteijn, & Koolen, 2014; Parswani et al., 2013; Salmoirago-Blotcher et al., 2013), with one of these studies categorising participants into mindfulness only or combined mindfulness and concentrative meditation techniques according to Spirituality Scale scores (Delaney et al., 2011). The mean frequency of group meditation interventions was 11 sessions (SD ± 7; n = 5 studies), and the mean duration of these sessions was 68 minutes (SD ± 27; n = 5 studies). Four studies did not utilise group meditation practices. The average amount of personal instruction received across studies was 3 sessions (SD ± 3; n = 5 studies), with a mean duration of 45 minutes (SD ± 27; n = 4 studies). Home practice was utilised at an average of 1.3 sessions (SD ± 0.8; n = 9 studies); with a mean duration of 23 minutes (SD ± 9; n = 6 studies). The mean intervention period across studies was 9.5 weeks (SD ± 4.8; n = 8 studies). In one study the intervention period was unclear (Delui et al., 2013) (refer Table 1). Time since the patients' cardiac event ranged between 1 week and 12 months. Individual data around time since admission or cardiac event was not reported in any of the included studies.

Setting

Interventions took place across a number of settings, including a university medical centre (tertiary care) (Salmoirago-Blotcher et al., 2013), an outpatient clinic (Parswani et al., 2013), or in an outpatient cardiac rehabilitation centre (Collins & Rice, 1997; Delaney et al., 2011; Delui et al., 2013; Mandel, 2007). The setting was not clearly defined in three studies (Luskin et al., 2002; Nyklíček et al., 2014; Paul-Labrador et al., 2006).

Intervention delivery

A variety of methods were used for intervention delivery that included an intial session delivered by the researcher (Paul-Labrador et al., 2006), followed by self administered home practice with an audiotape or CD (Delaney et al., 2011; Paul-Labrador et al., 2006; Salmoirago-Blotcher et al., 2013); investigator delivered (who was also a registered nurse) (Collins & Rice, 1997); use of professional health educators

(Paul-Labrador et al., 2006), phone delivery of sessions by health care professionals and graduates of a mindfulness training program (Salmoirago-Blotcher et al., 2013); use of a certified clinical psychologist with 10 years expereince in mindfulness/vipassana meditation and 5 years supervision experience (Nyklíček et al., 2014); a licensed psychotherapist (Luskin et al., 2002); a music therapist trained and supervised by the study investigator, who has extensive experience eliciting the relaxation response (Mandel, 2007); or was not specified (Delui et al., 2013; Parswani et al., 2013).

Control and/or Comparison Groups

Usual care was clearly defined in seven of the nine studies. Usual care was described as a conventional cardiac rehabilitation program in one study that included exercise and peer support (Collins & Rice, 1997), or was not specified (Delui et al., 2013). Usual care also included one month follow-up with a cardiologist (Parswani et al., 2013). In one study, a waitlist control was used where participants were offered relaxation or meditation training at the end of the study (Luskin et al., 2002). Comparison groups included a 10 minute phone call regarding defibrillator concerns (Salmoirago-Blotcher et al., 2013); a self-help booklet based on group psycho-education sessions (Nyklíček et al., 2014), maintenance of a regular diet as suggested by the medical team, 30 minutes of regular exercise, and a single (Parswani et al., 2013), or weekly health education class for heart disease risk factor modification (Paul-Labrador et al., 2006). Two studies did not include a control or comparison group (Delaney et al., 2011; Mandel, 2007).

Insert Table 1 here

Risk of Bias Assessment

All nine meditation studies have an inherently high risk of bias due to the inability to blind study participants and intervention delivery personnel (n=9). Apart from this unavoidable risk other identified reasons for bias included incomplete or no randomisation in quasi-experimental designs (n= 3) (Delaney et al., 2011; Luskin et al., 2002; Mandel, 2007); lack of allocation concealment procedures (n=3) (Delaney et al., 2011; Luskin et al., 2002; Mandel, 2007); blinding of outcome assessors for patient reported outcomes (n= 3) (Collins & Rice, 1997; Delaney et al., 2011; Mandel, 2007); and/or incomplete outcome data for measures taken at greater than 6 weeks (n= 3) (Mandel, 2007; Parswani et al., 2013; Paul-Labrador et al., 2006) (refer Table 2).

Insert Table 2 here

Outcomes

Whilst none of these studies were adequately powered, significant improvements in depression and/or anxiety were demonstrated over half (5/9) of the identified phase II meditation studies. Populations with significant improvements in depression and/or anxiety included adults with congestive heart failure (n=33), coronary heart disease or cardiovascular disease (n=85), metabolic syndrome with comorbid CHD (n= 103), CVD with comorbid depression (n=45), recipients of a percutaneous coronary intervention (n= 114), or male recipients of an automatic implantable cardioverter defibrillator (AICD) (n= 52). Significant interventions included guided imagery (2 studies), Mindfulness-Based Stress Reduction (2 studies), or Mindfulness meditation (1 study) (refer Table 1).

Depression

Four studies demonstrated statistically significant between-group differences in depression. A further three studies did not show improvements in depression after using meditation, and two studies did not assess depression outcomes. Three of the studies that generated significant between-group differences in depression utilised a mindfulness meditation approach such as MBSR (Delui et al., 2013; Parswani et al., 2013), or an adapted version of MBSR (Nyklíček et al., 2014), whilst one other successful study used concentrative meditation techniques, including guided imagery (Luskin et al., 2002).

Anxiety

The results for state anxiety were equivocal. One out of two studies evaluating meditation's effectiveness for state anxiety generated statistically significant within-group differences using guided imagery (Mandel, 2007). None of the two studies that utilised concentrative meditation approaches such as guided imagery (Mandel, 2007) or Transcendental Meditation (Paul-Labrador et al., 2006) were successful in demonstrating improvements within or between groups in trait anxiety. Two studies that generated statistically significant improvements in overall anxiety between groups both used either MBSR (Parswani et al., 2013) or an adapted version of MBSR (Nyklíček et al., 2014). However, a further five studies that utilised either an adapted version of MBSR (Salmoirago-Blotcher et al., 2013), mindfulness (Delaney et al., 2011; Delui et al., 2013) or guided imagery (Collins & Rice, 1997; Luskin et al., 2002) did not demonstrate improvements in overall anxiety within or between groups.

Elements of meditation interventions

The elements of meditation interventions that facilitate improvements in depression and/or anxiety outcomes are highlighted in Supplementary Appendix S2. All included studies advised participants to adhere to daily home meditation practice. Three out of four studies that included focused attention to body

parts or a ‘body scan’ generated significant results in depression, anxiety (Nyklíček et al., 2014; Parswani et al., 2013) and state anxiety (Mandel, 2007). However, one of these studies did not produce significant results for trait anxiety (Mandel, 2007). Four out of five studies that utilised group meetings demonstrated statistically significant improvements in depression (Delui et al., 2013; Luskin et al., 2002; Nyklíček et al., 2014; Parswani et al., 2013) and/or anxiety (Nyklíček et al., 2014; Parswani et al., 2013). However, two of these studies did not generate significant improvements in anxiety (Delui et al., 2013; Luskin et al., 2002).

Mindfulness as a potential mediator of meditation efficacy for depression and anxiety symptoms

Interestingly, two studies that used adapted mindfulness meditation also generated statistically significant improvements in mindfulness (Nyklíček et al., 2014; Salmoirago-Blotcher et al., 2013). In one of these two studies, increases in mindfulness were found to mediate the improvements in depression in anxiety symptoms between the intervention and comparison group in adults <60 years (Nyklíček et al., 2014).

DISCUSSION

There were no phase III randomised controlled trials to determine the effectiveness of meditation for the secondary prevention of depression and anxiety for adults who have recently experienced a cardiac event or hospitalisation. Based on the results of this review, there is evidence to suggest that meditation can improve depression and anxiety in patients with heart disease. Whilst there is no definitive evidence, common elements of effective meditation interventions that may influence depression and/or anxiety outcomes include: focused attention to body parts or ‘body scan’, and group meetings (particularly with depressed patients).

This review identified that 67% of participants were male, and there were no meditation studies specifically designed for women. These results are consistent with the AHA consensus statement, reflecting the underrepresentation of women with heart disease in clinical trials and reduced referral rates to outpatient secondary prevention programs (Mehta et al., 2016). This is significant given that women have higher rates of heart disease morbidity and mortality compared to men (Benjamin et al., 2017) and experience poorer outcomes after a cardiac event (Udell et al., 2017). Collaborative group-based approaches such as meditation may also address the unique psychosocial support needs of women alongside conventional exercise-based programs (Davidson et al., 2008).

Findings of this review are consistent with previous systematic reviews of meditation that have demonstrated small, consistent improvements in anxiety, stress and depression in clinical (Goyal et al., 2014) and chronic illness populations (Gotink et al., 2015); vascular disease (Abbott et al., 2014); and

quality of life in heart failure patients (Kwekkeboom & Bratzke, 2015). However, it is difficult to determine meditation efficacy given an unknown dose-response relationship, mechanism of effect and significant heterogeneity within and between study designs (Delaney et al., 2011). Measures of self-efficacy have also been recommended to determine the degree to which participants can adapt and integrate new relaxation strategies into their lifestyle and identify areas where further training is required (Gordon, 2007).

One study found mindfulness to be a mechanism of change, which could indicate that mindfulness practices positively affect anxiety by improving cognitive flexibility (Lee & Orsillo, 2014). Focusing on the breath, an element common to a variety of meditation practices, involves aspects of cognitive flexibility such as maintaining *attention* to the breath, *inhibiting* focus to other thoughts when the mind wanders and *switching* attention back to the breath (Lee & Orsillo, 2014). Thus, focusing on the breath and the 'body scan', which again draws *attention* to the sensation of different body parts, is likely to assist in the development of practices that enhance cognitive flexibility and are challenging skills for adults with generalised anxiety disorder to develop (Lee & Orsillo, 2014).

Risk of bias in meditation studies is frequently high given the inability to blind the participant or practitioner (Astin et al., 2003). There will always be an element of provider-participant interaction that contributes to a risk of bias, however, this should not overshadow positive findings of robust study designs and the potential for translation of findings into practice. One way around bias appraisal has been to implement a modified Jadad scale with a maximum score of 4 rather than 5, with no points assigned to information provided with regards to participant blinding (Canter & Ernst, 2004). Controlled trial designs may require minimising therapeutic interaction between participant and provider to accurately assess meditation efficacy, however, this may reduce ecological validity and thereby reduce the potential treatment effect (Mandel, 2007). Various factors, such as levels of anxiety, depression, stress, recent life events and personality (Fava & Sonino, 2010), may also determine which elements of meditation (for example guided imagery vs mindfulness) might be most suitable in initiating meditation practice, which requires exploration in future qualitative or mixed methods designs.

A few studies have explored the effect of age as a covariate for meditation effects. One study determined that younger patients (<60 years) benefited most from meditation (Nyklíček et al., 2014). Such differences in outcome measures could be a floor effect, that is, older adults with CVD are more likely to report higher baseline quality of life compared to younger adults, and lower levels of psychological distress (Gordon, 2007). Younger females, in particular, are likely to benefit from meditation as an adjunct

secondary prevention strategy given increased openness to complementary therapies and higher baseline levels of psychological distress (Gordon, 2007; Lavie & Milani, 2006; Rabito & Kaye, 2013).

A floor effect was also identified in one study as a reason for non-significant within-group changes in depression post-intervention (Delaney et al., 2011). Baseline state anxiety in two studies (Collins & Rice, 1997; Delaney et al., 2011) was also lower than the suggested 39-40 STAI-S cut-off score for clinically significant symptoms (Julian, 2011). Baseline mean scores in two other non-significant studies indicated mild trait anxiety on the STAI-T (Paul-Labrador et al., 2006), and less than clinically significant anxiety on the HADS (Bunevicius et al., 2013; Salmoirago-Blotcher et al., 2013) which may have contributed to non-significant results in these studies. The capacity of meditation interventions to capture changes in trait anxiety using the STAI may be limited given that the purpose of the trait subscale is to determine anxiety as a longstanding characteristic, and is less responsive to change (Julian, 2011). Meditation interventions delivered over longer periods of time, with longer follow-up periods may be required to capture changes in trait anxiety, such as heightened sensory awareness and shifts in the relationship between thoughts, feelings, and sense of self that are often seen in experienced meditators (Cahn & Polich, 2006).

Implications for practice

Utilising a novel approach such as meditation addresses a clearly identified need to reframe cardiac rehabilitation service provision from a conventional prescriptive approach to an integrated disease management model (Davidson, 2015). Small group meditation instruction also provides an opportunity for peer support and trust building, provides a safe environment for relaxation and promotes positive interaction between care provider and participant, which is vital to maintain health behaviour change (Clark, Whelan, Barbour, & MacIntyre, 2005).

Meditation also has the potential to reduce health care utilisation and costs (Rutledge et al., 1999), however formal cost-benefit analyses are required for confirmation, and to ensure effective resource utilisation (Krisanaprakornkit, Krisanaprakornkit, Piyavhatkul, & Laopaiboon, 2006). It is also important to consider patient preferences and determine the specific demographic and clinical characteristics of cardiac rehabilitation participants that are most likely to adhere to and benefit from a meditation intervention.

Implications for research

Future well designed, methodologically rigorous studies with sufficient detail around intervention content and setting are required to allow for replication, and reporting of these studies should adhere to the CONSORT statement. Consensus processes are required to develop a standardised taxonomy for the

reporting of meditation intervention elements to better identify which elements are most effective in reducing cardiovascular risk (Hickman et al., 2015). The inclusion of data such as time since admission or cardiac event and stratification of depression and anxiety rates by gender and type of cardiac procedure is required in the reporting of future studies to shed light on which cardiac populations would most benefit from a meditation intervention. Gender differences in receptivity to meditation and its effectiveness also needs to be considered in future research. Multicomponent interventions need to discretely analyse the meditation component of their intervention. Research designs targeted to patients with a minimum of mild depression or anxiety symptoms may lead to better outcomes attributable to meditation interventions. Strategies to control for secondary relaxation effects associated with meditation and practitioner interaction effects (Lee & Orsillo, 2014), such as a relaxation comparison group, are required in future phase III meditation intervention designs.

Limitations

This review is limited by the small number of methodologically strong studies, and lack of availability of any phase III RCT's that were solely evaluating meditation effects. Some of the included meditation intervention descriptions were brief, limiting conclusions drawn around the optimal elements of meditation interventions that may improve outcomes, as well as replication and generalisability of the findings. The authors acknowledge the potential for confounding factors to affect the results of individual studies included in the review.

Compliance with ethical standards

The manuscript does not contain clinical studies or patient data.

Conflicts of interest

The authors declare there are no conflicts of interest.

Authors Contributions

AR designed and executed the study, analysed the data and wrote the paper. MD collaborated in the writing and editing of the final manuscript. PJN collaborated with the design and writing of the study. JLP collaborated in the writing and editing of the final manuscript. LH collaborated with the design, data analysis and writing of the study.

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Table 1: Summary Table of Meditation Interventions

Author	P	Age mean (SD)	M/ F (%)	O	Measure	N	Intervention	Comparison	Frequency Duration	IP	Before mean (SD):	After mean (SD), or differences between groups over time	Results
(Paul-Labrador et al., 2006) US	Metabolic syndrome Stable CHD	67.4 (0.42)	84 (82)/ 19 (18)	D, TA	CES-D STAI	103 52 IG 51 CG	**Transcendental meditation** mental procedure; sitting comfortably with eyes closed. Calming of ordinary thinking processes, towards a psychophysiological state of restful alertness (Schneider et al., 2001). Introductory lecture, personal interview, group meetings, daily home practice.	Health education, daily home assignment	F: 2x daily HP; 2 x IL; PI x 1; Pin x 1; 3 x GM; then GM 2 x weekly/ 4 weeks; then GM weekly/ 12 weeks D: HP not stated; 90 mins IL; 10-15 min	16 weeks	CES-D IG: 6.8 (7.1) CES-D CG: 12.2 (10.7) STAI (T): IG: 14.4 (10.1) STAI (T): CG: 17.8 (11.7)	CES-D: IG 7.1 (6.9) CES-D: CG: 11.2 (10.0) STAI (T): IG: 12.8 (7.9) STAI (T): CG: 15.8 (11.4)	No significant reduction in depression (p= 0.053) or trait anxiety (p= 0.31) between groups at 16 weeks

									PI; 60-90 min Pin; 90 min GM.				
Salmoirago-Blotcher et al. (2013) US	ICD out-patients	64.6 (2.40)	31 (69)/ 14 (31)	A	HADS	46 24 IG 22 CG	Adapted **Mindfulness based stress reduction**: 1) **body scan** –attention to bodily sensations and cognitions; 2) training in **breathing awareness. sitting meditation** with **mindful** eating, drinking, attention to sounds, visual objects, thoughts & emotions); daily HP with CD	10 minute scripted weekly phone call addressing possible defibrillator concerns	F: weekly phone call; daily HP D: 30 mins phone call; 20 mins HP	8 weeks	HADS IG: 5.5 (4.1) HADS CG: 6.4 (4.1)	HADS: beta=-1.15 (95% CI: 0.046, -2.344)	No significant reduction in anxiety between groups (p=0.059) at 8 weeks
Parswani et al. (2013)	Male CHD out-patients	48.93 (2.35)	30 (100) male	A, D	HADS	30 15 IG 15 CG	**Mindfulness based stress reduction (body scan, sitting meditation, mindful** walking, eating, **3 minute**	Treatment as usual with one health	F: weekly GM; daily HP	8 weeks	HADS A IG:7.87 (3.11) HADS A CG:7.67(3.65)	HADS A IG: 3.27 (1.27) HADS A CG: 7.53 (3.33)	Reduced anxiety (p=0.001), depression (p=0.01)

India							**breathing space** –resting awareness of inner experience, focus and **awareness of the breath**, body)	education session; maintain diet and 30 mins regular exercise	D: 60-90 mins GM; 30 mins HP		HADS D IG: 6.13(2.03) HADS D CG: 4.93(2.49)	HADS D IG: 3.33 (1.59) HADS D CG: 5.47 (2.39) Between groups/ time: HADS-A: t=-4.63; HADS-D: t=-2.9	between groups at 8 weeks.
Nyklíček et al. (2014) Netherlands	PCI	55.85 (0.64)	88 (82) / 19 (18)	A, D	SAD-4	114 57 IG 57 CG	Adapted **Mindfulness Based Stress Reduction**, (mindfulness of bodily sensations, emotions and thoughts in an upright position, discussion of experiences during home practice), **psycho-education** (role of behaviour, bodily sensations, emotions, thoughts in psychological distress, role of	Self-help booklet based on group training	F: weekly GM; daily HP D: 90-120 mins GM; 30 mins HP	6 weeks	SAD-4: IG: 4.03 (0.49) SAD-4: CG: 3.01(0.49)	SAD-4: IG: 2.42 (0.41) SAD-4: CG: 2.80 (0.42) Between groups/ time t (102)= 3.46	Improved depression and anxiety between groups at 6 weeks ($p<0.01$); Younger adults more likely to have greater decreases in anxiety/ depression vs older adults ($p=0.001$).

							mindfulness and non-judgemental acceptance of thoughts and emotions in stress reduction)						
Collins and Rice (1997) US	CVD (MI and/or CABG)	59.17 (0.35)	39 (78)/ 11 (22)	SA, D, A	STAI	50 24 IG 26 CG	Progressive muscle relaxation and **guided imagery** (mental journey to a pleasant relaxing setting using the senses; think of the heart as healed and strong); daily home practice with audiotape	CR, monitored supervised exercise training, CHD risk factor modification education, peer support	F: Pin x 1 (initial study visit); daily HP D: Pin not stated; HP not stated	6 weeks	STAI (S) IG: 33.50 (8.41) STAI (S) CG: 32.78 (9.85)	STAI (S) IG: 32.05 (9.34) STAI (S) CG: 31.48 (8.59) Between groups/ time: STAI (S): t(42)= 0.21	No significant reduction in state anxiety (p>0.05), or anxiety between groups at 6 weeks (p>0.05).
Luskin et al. (2002) US	NYHA class I-III	66 (9)	13 (39)/ 20 (61)	D, A	GDS STAI	33 14 IG 15 CG	**Guided imagery** (conscious shifting of attention from stressful experiences to an area around one's heart),	Waitlist. Invited to attend 1 day training	F: 8 weekly GM; daily HP x 4	10 weeks	GDS IG: 8.3 (6.0) GDS CG: 5.3 (6.3) STAI IG: 40.2 (8.0) STAI CG: 36.4 (9.9)	GDS IG: 5.5 (3.0) GDS CG: 6.0 (6.8) STAI: IG: 35.9 (7.1) STAI: CG:36.6 (11.1)	Reduced depression between groups at 10 weeks (p=0.02). No significant reduction in

	heart failure						**visualisation** of positive emotion or memory, holding of that feeling/emotion within the heart; **stress education** (discussion of secondary gain, practice of **deep breathing,** pausing before making a decision, review of stress management research	at end of study.	weeks; then 2x daily HP x 4 weeks D: 75 mins GM; 15 mins HP				anxiety between groups at 10 weeks (p>0.05).
Mandel (2007) US	CR patients	58	9 (60)/ 6 (40)	D, A	CES-D STAI	15	**Deep breathing, guided imagery** (comfortable place), **visualisation** for muscle relaxation, comforting word or phrase, positive affirmations	n/a	F: 1 x Pin; daily HP D: 60 mins Pin; 31.5 mins HP	4 months	STAI (S): 44.14 (14.35) STAI (T): 40.27 (11.79) CES-D: 18.33 (12.5)	Post Pin: STAI (S): 35.36 (12.06) 2 weeks: CES-D: 15.5 (12.31) STAI (T): 35.75 (11.95) 4 months: CES-D: 11.0 (10.42) STAI (T): 34.00 (9.97)	Within group differences: Improved state anxiety post Pin (p=0.002). No significant reductions in depression (p=0.67/0.07) or trait anxiety (p=0.31/0.44) at 2 weeks/ 4 months

Delaney et al. (2011) US	CVD	64.4 (11.4)	15 (37)/ 26 (63)	D, A	CES-D STAI	41	**Mindfulness meditation,** present moment awareness, setting aside worrisome thoughts, **attention to breathing, guided visualisation** of a small circle of light from the head to the heart and chest area, recall a situation of feeling loved or loving, connecting to a higher power, sending and receiving of loving energy, **prayer/reflection** in a **perceived healing environment**	n/a	F: Pin x 1; PI x 1 at 2 weeks; 3 x week HP D: 15 mins Pin; 12-60 min HP	1 month	CES-D: 19.49 (5.3) STAI (S): 24.03 (2.4)	CES-D: 18.75 (4.2) STAI (S): 24.90 (3.2)	Within group differences: No significant reductions in depression (p=0.33) or anxiety (p=0.19) at 1 month.
(Delui et al., 2013) Iran	CVD and comorbid	45-60 years not	27 (60)/ 18 (40)	D, A	BDI Zung Self Rating	45 15 IG 15 PMR	**Mindfulness meditation** (details not stated); routine CR.	Jacobsen's PMR or no intervention CG	F: 10 sessions after CR;	Not stated	BDI IG: 21.93±7.226 BDI: PMR: 21.60±7.491	BDI IG v PMR: 7.60 (1.64) BDI IG v CG: 5.73 (1.64)	Significantly reduced depression v PMR (p<0.001) and v CG

	depression referred to CR	stated			Anxiety Scale	15 CG			3 x week HPD: 25 mins after CR; HP not stated		BDI: CG: 23.27±6.984 Zung: IG: 36.87±6.323 Zung: PMR: 36.33±7.326 Zung: CG: 35.73±6.193	Zung IG v PMR: 3.07 (1.95) Zung IG v CG: 3.13 (1.95)	(p=0.03) post intervention; No significant reductions in anxiety vs PMR (p=0.27) or CG (0.25) post intervention

Key: P, Population; SD, Standard Deviation; *, Where reported; M, Male; F, Female; O, Outcome; N, Number; IP, Intervention period; US, United States; RCT, Randomised controlled trial; CHD, Coronary Heart Disease; D, Depression, TA, Trait Anxiety; CES-D, Centre for Epidemiological Studies Depression Scale; STAI, State Trait Anxiety Inventory; IG, Intervention Group; CG, Control Group; F, Frequency; HP, Home Practice; IL, Introductory Lecture; PI, Personal instruction; Pin, Personal interview; GM, Group Meeting; D, Duration; min, Minutes; STAI (T), Trait anxiety; ICD, Implantable Cardioverter Defibrillator; A, Anxiety; HADS, Hospital Anxiety and Depression Scale; v, Versus, HADS A, Hospital Anxiety and Depression Scale Anxiety Subscale; HADS-D, Hospital Anxiety and Depression Scale Depression Subscale; PCI, Percutaneous Coronary Intervention; SAD-4, Symptom Anxiety Depression Index- 4; CR, Cardiac Rehabilitation; CVD, Cardiovascular Disease, MI, Myocardial infarction, CABG, Coronary artery bypass graft; STAI (S), State anxiety; n/s, not significant; NYHA, New York Heart Association; GDS, Geriatric Depression Scale; n/a, not applicable; BDI, Beck Depression Inventory.

Table 2: Assessment of Risk of Bias

Author/Year	Selection Bias		Performance Bias	Detection Bias		Attrition Bias		Reporting Bias
	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessors pt. reported	Blinding of outcome: mortality	Incomplete outcome data short term outcomes 2-6 weeks	Incomplete outcome data>6 weeks long term	Selective reporting
Collins and Rice (1997)	Low risk Prospective quasi experimental Random assignment within sites	Unclear risk No information provided	High risk Unable to blind participant or practitioner	High risk Individually instructed by investigator during initial study visit.	n/a	Low risk 5% IG; 4% CG	n/a	Low risk
Luskin et al. (2002)	High risk “incomplete randomisation”	High risk Not considered	High risk Unable to blind participant or practitioner	Unclear risk Not reported	n/a	Low risk 12% overall attrition	n/a	Low risk

						Equal attrition between groups (6%)		
(Paul-Labrador et al., 2006)	Low risk Block randomisation via a computerised program'	Unclear risk No information provided	High risk Unable to blind participants or interventionists. Study personnel blinded	Low risk "…outcome data collected and analysed by personnel blinded to treatment status"	n/a	n/a	High risk 18% overall attrition 13% IG; 23% CG	Low risk
Mandel (2007)	High risk Non-randomised design	High risk Not considered in study design	High risk No binding used	High risk No blinding used. Author did not interact with patients during the intervention.	n/a	n/a	High risk 42% attrition	Low risk
Delaney et al. (2011)	High risk Quasi-experimental study. No randomisation	High risk Not considered in study design	High risk No blinding used	High risk No blinding used	n/a	Low risk 34.2% attrition. Attrition analysis: no significant differences between study	n/a	Low risk

						completers and non-completers.		
Salmoirago-Blotcher et al. (2013)	Low risk "…sequence of group assignments randomly permuted in blocks of several sizes"	Low risk "A programmer will generate random allocation sequence and upload table containing sequence of group assignments to an Access database".	High risk No blinding used	Low risk "… research coordinator administered study questionnaires, experienced instructors blinded to study outcomes conducted intervention"	n/a	n/a	Low risk 4% attrition from intervention group, retention rate 93%	Low risk
Parswani et al. (2013)	Low risk 'Randomly assigned… using computer	Unclear risk No information provided	High risk; Unable to blind participants or interventionists; no	Unclear risk No information provided	n/a	n/a	High risk >20% attrition 20% IG;	Low risk

	generated random tables'		information provided for study personnel				33% CG at 3 month follow up	
(Delui et al., 2013)	Unclear risk 'randomly selected using medical records at our centre'	Unclear risk No information provided	High risk Unable to blind participant or practitioner	Low risk Unclear if rehabilitation nurses BP blinded to group assignment. 'Post-test measures conducted by individual blinded to treatment condition'.	n/a	Unclear risk Data seems complete (n=45). Numbers eligible, recruited, dropped out not specified	n/a	Low risk
Nyklíček et al. (2014)	Unclear risk "randomised"	Unclear risk No information provided	High risk; Unable to blind participants or interventionists; no information provided for study personnel	Unclear risk No information provided	n/a	Low risk <20% attrition 12% IG; 14% CG Missing data imputed	n/a	Low risk
Total	4 low risk 2 unclear risk 3 high risk	1 low risk 5 unclear risk 3 high risk	9 high risk	3 low risk 3 unclear risk 3 high risk	9 n/a	4 low risk 1 unclear risk 4 n/a	3 high risk 1 low 5 n/a	9 low risk

Key: IG, Intervention group; CG, Control Group, ; n/a, Not Applicable; n, Number

Figure 1: PRISMA 2009 Flow Diagram