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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 nonpharmacological 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 \pm 33), with a mean age of 60 years (SD \pm 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 \pm 7; n = 5 studies), and the mean duration of these sessions was 68 minutes (SD \pm 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 \pm 3; n = 5 studies), with a mean duration of 45 minutes (SD \pm 27; n = 4 studies). Home practice was utilised at an average of 1.3 sessions (SD \pm 0.8; n = 9 studies); with a mean duration of 23 minutes (SD \pm 9; n = 6 studies). The mean intervention period across studies was 9.5 weeks (SD \pm 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, 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). Aside 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 it is too early to definitively determine, 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 reflect the AHA consensus statement which has identified the general 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).

These findings 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 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 for 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 due to their higher perceived 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 cut-off score for clinically significant symptoms (Julian, 2011). Baseline mean scores in two other included non-significant studies indicated mild trait anxiety (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 | Р | Age | M/F | 0 | Measure | N | Intervention | Comparison | Frequency | IP | Before mean (SD): | After mean (SD), or | Results |
|-------------|-----------|--------|-------|----|---------|-------|--------------------------------------|------------|---------------|------|---------------------------|---------------------------|----------------------------|
| | | mean | (%) | | | | | | Duration | | | differences between | |
| | | (SD) | | | | | | | | | | groups over time | |
| (Paul- | Metabolic | 67.4 | 84 | D, | CES-D | 103 | Transcendental meditation | Health | F: 2x daily | 16 | CES-D IG: 6.8 (7.1) | CES-D: IG 7.1 (6.9) | No significant reduction |
| Labrador et | syndrome | (0.42) | (82)/ | TA | STAI | 52 IG | mental procedure; sitting | education, | HP; 2 x IL; | week | CES-D CG: 12.2 (10.7) | CES-D: CG: 11.2 (10.0) | in depression (p= 0.053) |
| al., 2006) | Stable | | 19 | | | 51 CG | comfortably with eyes closed. | daily home | PI x 1; Pin x | S | STAI (T): IG: 14.4 (10.1) | STAI (T): IG: 12.8 (7.9) | or trait anxiety (p= 0.31) |
| | CHD | | (18) | | | | Calming of ordinary thinking | assignment | 1; 3 x GM; | | STAI (T): CG: 17.8 | STAI (T): CG: 15.8 (11.4) | between groups at 16 |
| US | | | | | | | processes, towards a | | then GM 2 | | (11.7) | | weeks |
| | | | | | | | psychophysiological state of | | x weekly/ 4 | | | | |
| | | | | | | | restful alertness (Schneider et al., | | weeks; | | | | |
| | | | | | | | 2001). Introductory lecture, | | then GM | | | | |
| | | | | | | | personal interview, group | | weekly/ 12 | | | | |
| | | | | | | | meetings, daily home practice. | | weeks | | | | |
| | | | | | | | | | D: HP not | | | | |
| | | | | | | | | | stated; 90 | | | | |
| | | | | | | | | | mins IL; 10- | | | | |
| | | | | | | | | | 15 min PI; | | | | |

| | | | | | | | | | 60-90 min | | | | |
|-------------|----------|--------|-------|----|------|-------|----------------------------------|---------------|-------------|------|-----------------------|------------------------|--------------------------|
| | | | | | | | | | Pin; 90 min | | | | |
| | | | | | | | | | GM. | | | | |
| Salmoirago- | ICD out- | 64.6 | 31 | Α | HADS | 46 | Adapted Mindfulness based | 10 minute | F: weekly | 8 | HADS IG: 5.5 (4.1) | HADS: beta=-1.15 (95% | No significant reduction |
| Blotcher et | patients | (2.40) | (69)/ | | | 24 IG | stress reduction: 1) body scan – | scripted | phone call; | week | HADS CG: 6.4 (4.1) | CI: 0.046, -2.344) | in anxiety between |
| al. (2013) | | | 14 | | | 22 CG | attention to bodily sensations | weekly | daily HP | s | | | groups (p=0.059) at 8 |
| US | | | (31) | | | | and cognitions; 2) training in | phone call | D: 30 mins | | | | weeks |
| | | | | | | | breathing awareness. sitting | addressing | phone call; | | | | |
| | | | | | | | meditation with mindful eating, | possible | 20 mins HP | | | | |
| | | | | | | | drinking, attention to sounds, | defibrillator | | | | | |
| | | | | | | | visual objects, thoughts & | concerns | | | | | |
| | | | | | | | emotions); daily HP with CD | | | | | | |
| Parswani et | Male | 48.93 | 30 | Α, | HADS | 30 | Mindfulness based stress | Treatment | F: weekly | 8 | HADS A IG:7.87 (3.11) | HADS A IG: 3.27 (1.27) | Reduced anxiety |
| al. (2013) | CHD out- | (2.35) | (100) | D | | 15 IG | reduction (body scan, sitting | as usual with | GM; daily | week | HADS A CG:7.67(3.65) | HADS A CG: 7.53 (3.33) | (p=0.001), depression |
| | patients | | male | | | 15 CG | meditation, mindful walking, | one health | НР | s | HADS D IG: 6.13(2.03) | HADS D IG: 3.33 (1.59) | (p=0.01) between |
| India | | | | | | | eating, 3 minute breathing | education | D: 60-90 | | HADS D CG: 4.93(2.49) | HADS D CG: 5.47 (2.39) | groups at 8 weeks. |
| | | | | | | | space –resting awareness of | session; | mins GM; | | | Between groups/ time: | |
| | | | | | | | | maintain | 30 mins HP | | | HADS-A: t=-4.63; | |

| | | | | | | | inner experience, focus and | diet and 30 | | | | HADS-D: t=-2.9 | |
|-------------|-----|--------|-------|----|-------|-------|-----------------------------------|--------------|------------|------|------------------------|------------------------|------------------------|
| | | | | | | | awareness of the breath, body) | mins regular | | | | | |
| | | | | | | | | exercise | | | | | |
| Nyklíček et | PCI | 55.85 | 88 | Α, | SAD-4 | 114 | Adapted Mindfulness Based | Self-help | F: weekly | 6 | SAD-4: IG: 4.03 (0.49) | SAD-4: IG: 2.42 (0.41) | Improved depression |
| al. (2014) | | (0.64) | (82)/ | D | | 57 IG | Stress Reduction, (mindfulness of | booklet | GM; daily | week | SAD-4: CG: 3.01(0.49) | SAD-4: CG: 2.80 (0.42) | and anxiety between |
| | | | 19 | | | 57 CG | bodily sensations, emotions and | based on | НР | S | | Between groups/ time | groups at 6 weeks |
| Netherlands | | | (18) | | | | thoughts in an upright position, | group | D: 90-120 | | | t <u>(1</u> 02)= 3.46 | (p<0.01); |
| | | | | | | | discussion of experiences during | training | mins GM; | | | | Younger adults more |
| | | | | | | | home practice), psycho - | | 30 mins HP | | | | likely to have greater |
| | | | | | | | education (role of behaviour, | | | | | | decreases in anxiety/ |
| | | | | | | | bodily sensations, emotions, | | | | | | depression vs older |
| | | | | | | | thoughts in psychological | | | | | | adults (p=0.001). |
| | | | | | | | distress, role of mindfulness and | | | | | | |
| | | | | | | | non-judgemental acceptance of | | | | | | |
| | | | | | | | thoughts and emotions in stress | | | | | | |
| | | | | | | | reduction) | | | | | | |

| Collins and | CVD (MI | 59.17 | 39 | SA, | STAI 5 | 50 | Progressive muscle relaxation | CR, | F: Pin x 1 | 6 | STAI (S) IG: 33.50 (8.41) | STAI (S) IG: 32.05 (9.34) | No significant reduction |
|---------------|----------|--------|-------|-----|--------|-------|------------------------------------|---------------|---------------|------|---------------------------|---------------------------|--------------------------|
| Rice (1997) | and/or | (0.35) | (78)/ | D,A | 2 | 24 IG | and guided imagery (mental | monitored | (initial | week | STAI (S) CG: 32.78 | STAI (S) CG: 31.48 (8.59) | in state anxiety |
| | CABG) | | 11 | | 2 | 26 CG | journey to a pleasant relaxing | supervised | study | s | (9.85) | Between groups/ time: | (p>0.05), or anxiety |
| US | | | (22) | | | | setting using the senses; think of | exercise | visit); daily | | | STAI (S): t(42)= 0.21 | between groups at 6 |
| | | | | | | | the heart as healed and strong); | training, | НР | | | | weeks (p>0.05). |
| | | | | | | | daily home practice with | CHD risk | D: Pin not | | | | |
| | | | | | | | audiotape | factor | stated; HP | | | | |
| | | | | | | | | modification | not stated | | | | |
| | | | | | | | | education, | | | | | |
| | | | | | | | | peer support | | | | | |
| Luskin et al. | NYHA | 66 (9) | 13 | D, | GDS 3 | 33 | Guided imagery (conscious | Waitlist. | F: 8 weekly | 10 | GDS IG: 8.3 (6.0) | GDS IG: 5.5 (3.0) | Reduced depression |
| (2002) | class I- | | (39)/ | Α | STAI 1 | 14 IG | shifting of attention from | Invited to | GM; daily | week | GDS CG: 5.3 (6.3) | GDS CG: 6.0 (6.8) | between groups at 10 |
| | III | | 20 | | 1 | 15 CG | stressful experiences to an area | attend 1 day | HP x 4 | S | STAI IG: 40.2 (8.0) | STAI: IG: 35.9 (7.1) | weeks (p=0.02). No |
| US | heart | | (61) | | | | around one's heart), | training at | weeks; | | STAI CG: 36.4 (9.9) | STAI: CG:36.6 (11.1) | significant reduction in |
| | failure | | | | | | visualisation of positive emotion | end of study. | then 2x | | | | anxiety between groups |
| | | | | | | | or memory, holding of that | | daily HP x | | | | at 10 weeks (p>0.05). |
| | | | | | | | feeling/emotion within the heart; | | 4 weeks | | | | |
| | | | | | | | stress education (discussion of | | | | | | |

| | | | | | | | secondary gain, practice of deep | | D: 75 mins | | | | |
|------------|----------|--------|--------|----|-------|----|---|-----|-------------|--------|-------------------------|-------------------------|---------------------------|
| | | | | | | | breathing, pausing before | | GM; 15 | | | | |
| | | | | | | | making a decision, review of | | mins HP | | | | |
| | | | | | | | stress management research | | | | | | |
| Mandel | CR | 58 | 9 | D, | CES-D | 15 | Deep breathing, guided imagery | n/a | F: 1 x Pin; | 4 | STAI (S): 44.14 (14.35) | Post Pin: | Within group |
| (2007) | patients | | (60)/ | Α | STAI | | (comfortable place), visualisation | | daily HP | months | STAI (T): 40.27 (11.79) | STAI (S): 35.36 (12.06) | differences: |
| | | | 6 (40) | | | | for muscle relaxation, comforting | | D: 60 mins | | CES-D: 18.33 (12.5) | 2 weeks: | Improved state anxiety |
| US | | | | | | | word or phrase, positive | | Pin; 31.5 | | | CES-D: 15.5 (12.31) | post Pin (p=0.002). No |
| | | | | | | | affirmations | | mins HP | | | STAI (T): 35.75 (11.95) | significant reductions in |
| | | | | | | | | | | | | 4 months: | depression |
| | | | | | | | | | | | | CES-D: 11.0 (10.42) | (p=0.67/0.07) or trait |
| | | | | | | | | | | | | STAI (T): 34.00 (9.97) | anxiety (p=0.31/0.44) at |
| | | | | | | | | | | | | | 2 weeks/ 4 months |
| Delaney et | CVD | 64.4 | 15 | D, | CES-D | 41 | Mindfulness meditation, present | n/a | F: Pin x | 1 | CES-D: 19.49 (5.3) | CES-D: 18.75 (4.2) | Within group |
| al. (2011) | | (11.4) | (37)/ | Α | STAI | | moment awareness, setting aside | | 1; PI x 1 | month | STAI (S): 24.03 (2.4) | STAI (S): 24.90 (3.2) | differences: |
| | | | 26 | | | | worrisome thoughts, attention to | | at 2 | | | | No significant |
| US | | | (63) | | | | breathing, guided visualisation | | weeks; 3 | | | | reductions in |
| | | | | | | | of a small circle of light from the | | | | | | depression (p=0.33) or |

| | | | | | | | head to the heart and chest area, | | x week | | | | anxiety (p=0.19) at 1 |
|----------------|-----------|--------|-------|----|---------|-------|-------------------------------------|--------------|-------------|-------|-----------------------|---------------------------|--------------------------|
| | | | | | | | recall a situation of feeling loved | | НР | | | | month. |
| | | | | | | | or loving, connecting to a higher | | D: 15 mins | | | | |
| | | | | | | | power, sending and receiving of | | Pin; 12-60 | | | | |
| | | | | | | | loving energy, prayer/reflection | | min HP | | | | |
| | | | | | | | in a perceived healing | | | | | | |
| | | | | | | | environment | | | | | | |
| (Delui et al., | CVD and | 45-60 | 27 | D, | BDI | 45 | Mindfulness meditation (details | Jacobsen's | F: 10 | Not | BDI IG: 21.93±7.226 | BDI IG v PMR: 7.60 (1.64) | Significantly reduced |
| 2013) | comorbid | years | (60)/ | Α | Zung | 15 IG | not stated); routine CR. | PMR or no | sessions | state | BDI: PMR: 21.60±7.491 | BDI IG v CG: 5.73 (1.64) | depression v PMR |
| | depressio | not | 18 | | Self | 15 | | intervention | after CR; 3 | d | BDI: CG: 23.27±6.984 | Zung IG v PMR: 3.07 | (p<0.001) and v CG |
| Iran | n | stated | (40) | | Rating | PMR | | CG | x week HP | | Zung: IG: 36.87±6.323 | (1.95) | (p=0.03) post |
| | referred | | | | Anxiety | 15 CG | | | D: 25 mins | | Zung: PMR: | Zung IG v CG: 3.13 (1.95) | intervention; |
| | to CR | | | | Scale | | | | after CR; | | 36.33±7.326 | | No significant |
| | | | | | | | | | HP not | | Zung: CG: 35.73±6.193 | | reductions in anxiety vs |
| | | | | | | | | | stated | | | | 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 | Allocation | Blinding of participants | Blinding of outcome | Blinding of | Incomplete outcome | Incomplete | Selective |
| | generation | concealment | and personnel | assessors pt. reported | outcome: | data short term | outcome data>6 | reporting |
| | | | | | mortality | outcomes 2-6 weeks | weeks long term | |
| Collins and | Low risk | Unclear risk | High risk | High risk | n/a | Low risk | n/a | Low risk |
| Rice (1997) | Prospective quasi | No | Unable to blind | Individually instructed by | | 5% IG; 4% CG | | |
| | experimental | information | participant or | investigator during initial | | | | |
| | Random | provided | practitioner | study visit. | | | | |
| | assignment within | | | | | | | |
| | sites | | | | | | | |
| Luskin et al. | High risk | High risk | High risk | Unclear risk | n/a | Low risk | n/a | Low risk |
| (2002) | "incomplete | Not | Unable to blind | Not reported | | 12% overall | | |
| | randomisation" | considered | participant or | | | attrition | | |
| | | | practitioner | | | Equal attrition | | |
| | | | | | | between groups | | |
| | | | | | | (6%) | | |

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

| Salmoirago- | Low risk | Low risk | High risk | Low risk | n/a | n/a | Low risk | Low risk |
|-------------|--------------------|----------------|----------------------|---------------------------|-----|-----|-------------------|----------|
| Blotcher et | "sequence of | "A programmer | No blinding used | " research coordinator | | | 4% attrition from | |
| al. (2013) | group assignments | will generate | | administered study | | | intervention | |
| | randomly | random | | questionnaires, | | | group, retention | |
| | permuted in blocks | allocation | | experienced instructors | | | rate 93% | |
| | of several sizes" | sequence and | | blinded to study outcomes | | | | |
| | | upload table | | conducted intervention" | | | | |
| | | containing | | | | | | |
| | | sequence of | | | | | | |
| | | group | | | | | | |
| | | assignments to | | | | | | |
| | | an Access | | | | | | |
| | | database". | | | | | | |
| Parswani et | Low risk | Unclear risk | High risk; | Unclear risk | n/a | n/a | High risk | Low risk |
| al. (2013) | 'Randomly | No | Unable to blind | No information provided | | | >20% attrition | |
| | assigned using | information | participants or | | | | 20% IG; | |
| | computer | provided | interventionists; no | | | | 33% CG at 3 | |
| | | | | | | | month follow up | |

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

| 3 high risk | 3 high risk | 3 high risk | 4 n/a | 5 n/a | |
|-------------|-------------|-------------|-------|-------|--|
| | | | | | |

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

Figure 1: PRISMA 2009 Flow Diagram

