

# Meditation and Cardiovascular Risk Reduction

## A Scientific Statement From the American Heart Association

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**Abstract**—Despite numerous advances in the prevention and treatment of atherosclerosis, cardiovascular disease remains a leading cause of morbidity and mortality. Novel and inexpensive interventions that can contribute to the primary and secondary prevention of cardiovascular disease are of interest. Numerous studies have reported on the benefits of meditation. Meditation instruction and practice is widely accessible and inexpensive and may thus be a potential attractive cost-effective adjunct to more traditional medical therapies. Accordingly, this American Heart Association scientific statement systematically reviewed the data on the potential benefits of meditation on cardiovascular risk. Neurophysiological and neuroanatomical studies demonstrate that meditation can have long-standing effects on the brain, which provide some biological plausibility for beneficial consequences on the physiological basal state and on cardiovascular risk. Studies of the effects of meditation on cardiovascular risk have included those investigating physiological response to stress, smoking cessation, blood pressure reduction, insulin resistance and metabolic syndrome, endothelial function, inducible myocardial ischemia, and primary and secondary prevention of cardiovascular disease. Overall, studies of meditation suggest a possible benefit on cardiovascular risk, although the overall quality and, in some cases, quantity of study data are modest. Given the low costs and low risks of this intervention, meditation may be considered as an adjunct to guideline-directed cardiovascular risk reduction by those interested in this lifestyle modification, with the understanding that the benefits of such intervention remain to be better established. Further research on meditation and cardiovascular risk is warranted. Such studies, to the degree possible, should utilize randomized study design, be adequately powered to meet the primary study outcome, strive to achieve low drop-out rates, include long-term follow-up, and be performed by those without inherent bias in outcome. (*J Am Heart Assoc.* 2017;6:e002218. DOI: 10.1161/JAHA.117.002218.)

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Despite numerous advances in the prevention and treatment of atherosclerosis, cardiovascular disease (CVD) remains a leading cause of morbidity and mortality in the United States<sup>1,2</sup> and the developed world.<sup>3–5</sup> Although educational, lifestyle modifying, and pharmacological interventions

have lowered the prevalence of cardiovascular risk factors, most Americans still have at least 1 major risk factor.<sup>6,7</sup> More than \$200 billion are spent on care of patients with CVD in the United States annually, and this is expected to increase 2- to 3-fold over the next several decades.<sup>2,8</sup> Accordingly, novel and

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Accompanying Tables S1 through S9 are available at <http://jaha.ahajournals.org/content/6/10/e002218/DC1/embed/inline-supplementary-material-1.pdf>

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inexpensive interventions that are of benefit to patients and can contribute to the primary and secondary prevention of CVD are of interest.

Dozens of studies have reported on the health benefits of meditation. According to the National Health Interview Survey, 8% of US adults practice some form of meditation.<sup>9</sup> Up to 14% to 24% of patients with CVD have been reported to use or to have used some form of mind-body therapy, and 2% to 3% use or have used some form of meditation.<sup>10–13</sup> In addition, half of CVD patients are interested in participating in a clinical trial of alternative therapies, and 17% are interested in participating in a clinical trial of meditation.<sup>10–13</sup> Many forms of meditation can be learned from publications, the internet, and audio media. Many meditation courses are available for a modest fee or voluntary contribution. Hence, meditation may be an attractive cost-effective adjunct to more traditional medical therapies. Accordingly, the American Heart Association commissioned this scientific statement to systematically and scientifically review the data on the potential benefits of meditation related to CVD.

## Methodology

Studies on meditation and cardiovascular risk reduction were searched for on PubMed using search terms including meditation, stress, blood pressure, hypertension, smoking, tobacco use, insulin resistance, metabolic syndrome, atherosclerosis, endothelial function, myocardial ischemia, primary prevention, and secondary prevention. Additional searches were performed on Google and Google Scholar, because some articles on meditation are not listed in PubMed.

Practices such as tai chi, qigong, and yoga, although involving inner focus and a concentration on breathing, consist of both mental and physical practices. Regular physical activity and exercise has itself been associated with cardiovascular risk reduction,<sup>14,15</sup> and thus findings from such studies would be confounded. Therefore, this review was restricted to practices of sitting meditation.

For all sections examining the effects of meditation on aspects of cardiovascular risk, a primary author without relationships with industry and a secondary reviewer drafted the initial text and conclusions. All sections, tables, and conclusions were then reviewed by all writing group members and the manuscript revised based on this review. The manuscript was then reviewed by 4 external reviewers and revised accordingly. The finalized manuscript was approved by all writing group members.

## Meditation

The practice of meditation dates as far back as 5000 BC.<sup>16</sup> Although associated with Eastern philosophies and religion,

including Buddhism and Hinduism, references or inferences regarding meditation and the meditative process can be found in Christianity, Judaism, and Islam.<sup>16</sup> Over the past several decades, meditation is increasingly practiced as a secular and therapeutic activity.

In the traditional context, meditation refers to a family of mental practices that are designed to improve concentration, increase awareness of the present moment, and familiarize a person with the nature of their own mind.<sup>16</sup> In a more general and contemporary context, meditation can be categorized as primarily focused attention, mindfulness, loving kindness and compassion, or mantra repetition, although there is usually overlap between the focuses.<sup>17–19</sup> With focused attention (“samatha” meditation), the practitioner may focus on the breath or on an object, sound, sensation, visualization, thought, or repeated word or phrase (“mantra”). When the mind wanders, the meditator notices the mind wandering and learns to bring the mind back to the present moment or the object of meditation. In mindful meditation, the individual strives to be in the present moment and aware of internal sensations, thoughts, and external stimuli, without becoming engrossed in or distracted by them. Mindfulness-based stress reduction is a program based primarily on mindful meditation, as well as yoga; other mindfulness-based programs are similarly based on mindful meditation. Insight (“vipassana”) meditation can be considered a form of mindful meditation. In loving kindness and compassion, the meditator cultivates a feeling of benevolence toward oneself and others. In Vedic or transcendental meditation, repeated thought of a word is used to relax and clear the mind. The “relaxation response” technique similarly uses focused silent repetition of a word, sound, or phase. These practices may be used to: (1) increase concentration, insight, or awareness of the present moment; (2) promote relaxation; (3) reduce stress; (4) settle the mind; (5) achieve a state of increased consciousness; and (6) reduce perceived suffering and increase happiness.

Table 1 provides a summary of common types of meditation. Most forms of meditation are practiced  $\geq 20$  minutes or once or twice daily. Although meditation was first practiced millennia ago as part of Buddhist and Hindu religions, it has recently been introduced in the West as a stand-alone secular activity.

## Neurophysiology and Neuroanatomy of Meditation

Almost 2 decades of scientific studies, conducted at  $\geq 20$  universities, have identified the effects of meditation on the brain.<sup>18</sup> Most forms of meditation engage regions in the brain that regulate attention and emotion.<sup>29</sup> The adult brain can undergo changes through a process called neuroplasticity, which may include development of new circuits (“rewiring”) and/or neurons.<sup>30</sup> The different psychological targets of

**Table 1.** Common Types of Meditation

Meditation	Description	Origins and Well-Known Teachers in the West
Samatha meditation	Samatha is translated to mean “calm” and samatha meditation is often referred to as calm, abiding meditation. Samatha meditation is the practice of calming the mind by practicing single-pointed meditation through mindful concentration focusing on the breath, image, or object.	Buddhist practice, dating to the time of the Buddha or even before
Vipassana meditation (insight meditation)	Vipassana is translated to mean, “to see things as they really are.” Vipassana emphasizes awareness of the breath, tuning into the air passing in and out through the nose. Vipassana teaches one to label thoughts and experiences as they arise, taking mental notes as one identifies objects that grab one’s attention. Vipassana meditation is often taught at 10-day retreats.	Traditional Buddhist and Indian meditation. Well-known teachers include Mahasi Sayadaw, S.N. Goenka, Sharon Salzberg, Joseph Goldstein, Jack Kornfield, and Michael Stone
Mindful meditation	An umbrella term for the category of techniques used to create awareness and insight by practicing focused attention, observing, and accepting all that arises without judgment. This type of meditation is also referred to as “open monitoring,” in which one allows one’s attention to flow freely without judgment or attachment.	Origins come from Buddhist teaching. Well-known Western teachers include Jon-Kabat Zinn, Tara Brach, Sharon Salzberg, Joseph Goldstein, Jack Kornfield, and Pema Chodron
Zen meditation (zazen)	A type of meditation where one focuses one’s awareness on one’s breath and observes thoughts and experiences as they pass through the mind and environment. In some senses similar to Vipassana meditation, but with an emphasis on a focus of the breath at the level of the belly and on posture while sitting.	Buddhist meditation from Japan. Well-known teachers include Thich Nhat Hanh and Joan Halifax Roshi
Raja yoga meditation	Referred to also as “mental yoga,” “yoga of the mind,” or Kriya yoga. A practice of concentration to calm the mind and bring it to one point of focus. Includes a combination of mantra, breathing techniques, and meditation on the chakras/spinal cord focus points.	Hindu practice dating back thousands of years. Introduced to the West in 1893 by Swami Vivekananda. Further clarified and taught by Paramhansa Yogananda for the Western audience
Loving-kindness (metta) meditation	Loving-kindness meditation involves sending loving kindness to oneself, then continuing to send it to a friend or loved one, to someone who is neutral in your life, to a difficult person, and then out to the universe. Through this practice, the meditator cultivates a feeling of benevolence toward oneself and others.	Originates from Buddhist teachings, mainly Tibetan Buddhism. Well-known instructors include Sharon Salzberg and Pema Chodron
Transcendental meditation	Mantra-based meditation technique in which each practitioner is given a personal mantra that is used to help settle the mind inward. Transcendental meditation is taught by certified teachers through a standard 4-day course of instruction. Transcendental meditation is practiced for 20 minutes twice daily.	Origins in ancient Vedic traditions of India. Popularized in the West by the Maharishi Mahesh Yogi and now taught in the United States by the Maharishi Foundation
Relaxation response	A multifaceted practice that can involve awareness and tracking of breaths or repetition of a word, short phrase, or prayer	A term and practice pioneered by Dr Herbert Benson in the 1970s, based in part of the practice of transcendental meditation

There is no definitive definition of most types of meditation. These descriptions represent a synthesis of numerous sources and are best viewed as a general overview of the techniques. Initial table concept from references 20 and 21. Additional data from references 16–19 and 22–28. Table adapted with permission from Rinkel,<sup>21</sup> *Integrative Medicine*, 3rd ed. Copyright Elsevier 2012.

meditation are instantiated in distributed neural circuits that include different sectors of the prefrontal cortex and anterior cingulate cortex, the insula, and the midline regions that are important in default mode function.<sup>31</sup> In addition, studies of loving-kindness and/or compassion meditation practices often lead to alterations in subcortical circuits directly implicated in emotional processing, such as the amygdala and ventral striatum.<sup>29,32,33</sup>

Studies of the effects on meditation on the brain include those using electroencephalography, magnetic resonance

imaging, and functional magnetic resonance imaging. Whereas numerous studies have reported on the acute neurophysiological effects of meditation, more relevant to this scientific statement are long-term neurophysiological and neuroanatomical changes. In 1 of the first reports on the long-term effects of meditation on the brain, a 2-month mindfulness meditation program resulted in increased left-sided anterior brain electrical activation, a pattern associated with positive affect and emotion, whereas no such changes occurred in a wait-listed control group.<sup>34</sup> A study of long-

standing Buddhist meditation practitioners demonstrated durable electroencephalographic changes, suggesting that the resting state of the brain may be altered by long-term meditative practices.<sup>35</sup> A brain magnetic resonance imaging study of experienced meditators found, when compared with age-matched controls, higher gray matter density in lower brainstem regions involved in the autonomic system and cardiorespiratory control.<sup>36</sup> Some, though not all, longitudinal studies of 1 to 3 months of mindful meditation have demonstrated changes in brain structure and function not observed in control participants.<sup>37</sup> A meta-analysis of 21 neuroimaging studies examining ≈300 meditation practitioners found 8 brain regions consistently altered in meditators, including areas key to meta-awareness, body awareness, and self- and emotion regulation.<sup>38</sup> Anatomical changes have been reported in the cerebral cortex, subcortical gray and white matter, brainstem, and cerebellum of meditators.<sup>37</sup>

Neurophysiological and neuroanatomical studies suggest that meditation can have long-standing effects on the brain, which may have beneficial consequences on the physiological basal state, physiological responses, and cardiovascular risk. However, these studies generally were nonrandomized and involved modest numbers of participants, some of whom were highly experienced (>10 000 hours) meditators. Additionally, different forms of meditation (eg, focused attention, mindfulness, and loving kindness) will have different psychological and neurological effects. Thus, the neurophysiological and neuroanatomical findings associated with 1 type of meditation cannot be extrapolated to all forms. Extrapolation of the findings in the aforementioned studies to the general population who engage in meditation must be done with caution.

## Meditation and Cardiovascular Risk Reduction

A summary of the findings on meditation and cardiovascular risk reduction is provided in Table 2. Summaries of the individual studies, as well as their limitations, evaluated in this scientific statement are provided in Tables S1 through S9. These summary tables are not all-inclusive but summarize the findings of those studies deemed most relevant to this scientific statement. Findings on the effects of meditation on specific aspects of cardiovascular health are given in the following sections.

### Effects of Meditation on Psychological, Psychosocial, and Physiological Responses to Stress

Numerous studies, across both healthy and disease-based populations, have explored the effects of meditation on psychological and psychosocial outcomes. Most published

studies report some improvements in levels of perceived stress, mood, anxiety, depression, quality of sleep, or overall well-being<sup>39–45</sup> (Table S1). A review by the Agency for Healthcare Research and Quality restricted to randomized, controlled trials with an active control concluded—with low strength of evidence—that mindfulness meditation programs show modest improvements in stress/distress and negative affect.<sup>46</sup>

Few studies have focused on patients with CVD. In a study of 60 patients recruited from a private cardiology clinic, those randomized to 8 weeks of mindfulness-based stress reduction (primarily using meditation techniques) had significantly lower perceived stress and anger<sup>47</sup> than a comparison control group. Similarly, a study of 59 elderly participants with stage I hypertension randomized to Zen meditation (20 minutes twice daily for 3 months) or a wait list found that meditation significantly improved psychological facets of and overall quality of life.<sup>48</sup>

A growing body of research has examined the mechanisms by which meditation alters the physiological response to stress, with salivary cortisol the most commonly studied biomarker and a few exploring salivary amylase,<sup>49</sup> proinflammatory cytokines (ie, interleukin-6), or telomerase activity. Overall, findings from these studies have been mixed, with some demonstrating improvements in physiological parameters with meditation and others finding no changes.<sup>39,43,44,50–56</sup>

Several recent studies have focused on the impact of meditation on proteomic and genomic regulators of the physiological stress response.<sup>51,57,58</sup> Although unique gene expression profiles have been noted with meditation, their association with established physiological parameters is unknown.<sup>59</sup> One study of 40 patients reported that mindfulness-based stress reduction downregulated proinflammatory nuclear factor kappa B gene expression profile compared to wait-list control, with a trend—but no statistically significant reduction—in C-reactive protein levels.<sup>57</sup>

Overall, many, though not all, studies have reported that meditation is associated with improved psychological and psychosocial indices. Differences in study populations, control of potential confounders, and type and length of meditation evaluated may account for discrepant findings. Furthermore, small sample sizes and lack of randomization are common study limitations. Further study is needed on how meditation influences physiological processes associated with stress.

### Effects of Meditation on Blood Pressure

Few high-quality, randomized trials of meditation and lowering of blood pressure have been published (Table S2). The efficacy of mindfulness meditation for blood pressure reduction has been evaluated in a few studies.<sup>48,60–62</sup> The HARMONY (Hypertension Analysis of Stress Reduction Using Mindfulness Meditation and Yoga) trial assessed 24-hour ambulatory blood

**Table 2.** Summary of Findings on Studies of Meditations and Cardiovascular Risk Reduction\*

Topic	Findings
Neurophysiology and neuroanatomy	<ul style="list-style-type: none"> <li>Neurophysiological and neuroanatomical studies suggest that meditation can have long-standing effects on brain physiology and anatomy</li> <li>Studies generally are nonrandomized and involve modest numbers of participants, sometimes performed under the direction of extremely experienced (&gt;10 000 hours) meditators</li> <li>Different forms of meditation have different psychological and neurological effects, and thus the neurophysiological and neuroanatomic findings of 1 type of meditation cannot be extrapolated to other forms of meditation</li> </ul>
Psychological, psychosocial, and physiological response to stress	<ul style="list-style-type: none"> <li>Many, although not all, studies report that meditation is associated with improved psychological and psychosocial indices</li> <li>Differences in populations, control of potential confounders, and type and length of meditation evaluated may account for discrepant findings. Small sample sizes and lack of randomization are common study limitations</li> <li>Further study is needed on how meditation influences physiological processes associated with the stress response</li> </ul>
Blood pressure	<ul style="list-style-type: none"> <li>Magnitude of reductions of systolic blood pressure varies widely</li> <li>Study limitations including the methods of blood pressure measurements and bias in data ascertainment, high dropout rates, and different populations studied</li> </ul>
Smoking and tobacco use	<ul style="list-style-type: none"> <li>Some randomized data show that mindful meditation instruction improves smoking cessation rates</li> </ul>
Insulin resistance and metabolic syndrome	<ul style="list-style-type: none"> <li>Limited data on the effects of meditation on insulin resistance and metabolic syndrome</li> </ul>
Subclinical atherosclerosis	<ul style="list-style-type: none"> <li>A few suboptimal studies of meditation and lifestyle intervention suggest the potential for benefit on atherosclerosis regression</li> <li>Studies limited by multimodality approach, attrition, and incomplete follow-up</li> <li>No firm conclusions can be drawn on the effects of meditation on atherosclerosis</li> </ul>
Endothelial function	<ul style="list-style-type: none"> <li>Three studies showed no benefit of meditation on brachial reactivity in the overall cohorts, although 1 study suggested a benefit in a subgroup of patients with coronary artery disease</li> <li>No conclusions can be drawn on the effects of meditation on endothelial function</li> </ul>
Inducible myocardial ischemia	<ul style="list-style-type: none"> <li>Limited older studies suggest that meditation can lead to improvement in exercise duration and decreased myocardial ischemia</li> <li>No contemporary studies have evaluated effects of meditation on myocardial blood flow or ischemia with advanced imaging techniques</li> </ul>
Primary prevention of CVD	<ul style="list-style-type: none"> <li>Two studies of short-term intervention report surprising mortality reductions, and thus these findings need to be reproduced in larger, multicenter studies</li> <li>Overall, because of the limited evidence to date, no conclusions can be drawn as to the effectiveness of meditation for the primary prevention of CVD</li> </ul>
Secondary prevention of CVD	<ul style="list-style-type: none"> <li>Data on the potential benefits of meditation in patients with established coronary artery disease can best be characterized as generally of modest quality and as suggesting, but not definitely establishing, benefit</li> <li>Because of generally limited follow-up time, there are more data on reduction of cardiac risk factors and psychological indices than on hard end points (eg, death, myocardial infarction)</li> </ul>

\*Summaries of the individual studies, as well as their limitations, evaluated in this scientific statement are provided in Tables S1 through S9. CVD indicates cardiovascular disease.

pressure measurements in patients with stage I hypertension randomized to an 8-week mindfulness-based stress reduction program or wait-list control and found no benefit of meditation.<sup>63</sup> In contrast, in a pilot study of 83 predominantly hypertensive blacks randomized to a mindful meditation program or control social support group, an 11/4 mm Hg decrease in systolic/diastolic blood pressure was observed in

those randomized to 8 weeks of treatment and an analysis-adjusted 22/17 mm Hg difference in blood pressure between the 2 groups at follow-up.<sup>64</sup> Of note, this trial had 100% data ascertainment, over 80% compliance at each clinic visit, and measured blood pressure with an unattended manual device (a rigorous protocol with measurements 7–15 mm Hg lower than typical office readings). Other mind-body interventions that

involve both a physical and mental component have been associated with significant reductions in blood pressure,<sup>65–69</sup> but the specific contribution of meditation and meditation-like practices of inner focus and a concentration on the breath cannot be determined.

The effects of transcendental meditation on blood pressure have also been reported.<sup>70–73</sup> A study of 298 university students randomized to transcendental meditation or wait-list control found at 3-month follow-up no significant changes in systolic or diastolic blood pressure, although significant reductions in blood pressure (5/3 mm Hg, respectively) did occur in those at high risk of the development of hypertension.<sup>71</sup> In a randomized study of stress reduction in 201 black men and women with angiographically documented coronary artery disease randomized to transcendental meditation or health education, 5.4-year follow-up found a 4.9 mm Hg lower systolic blood pressure, 1 of numerous secondary study end points, in those randomized to transcendental meditation than in those randomized to health education, primarily because of an increase in blood pressure in the health education group.<sup>70</sup>

Numerous systematic reviews have been conducted on the effects of meditation on blood pressure. One 2007 systematic review assessed several methods of stress reduction in patients with hypertension and found modest benefit (ie, 5/3 mm Hg systolic/diastolic blood pressure reduction) with transcendental meditation; other popular types of meditation were not assessed.<sup>74</sup> Numerous meta-analyses in a 2007 Agency for Healthcare Research and Quality report on meditation and health generally found modest to no significant benefit with different meditation techniques when compared with active control groups (eg, health education), though the report also stated that meta-analyses based on low-quality studies and small numbers of hypertensive participants showed that transcendental meditation and Zen Buddhist meditation significantly reduced blood pressure.<sup>75</sup> A 2013 American Heart Association scientific statement on alternate approaches to lowering blood pressure concluded that transcendental meditation modestly lowers blood pressure and that its use may be considered.<sup>75</sup> The writing group also concluded at that time that there were insufficient high-quality studies assessing the benefit of other forms of meditative techniques to recommend them for blood pressure lowering. A 2015 analysis of 12 randomized, clinical trials of transcendental meditation involving a total of 996 predominantly black patients with or without hypertension found a mean reduction in blood pressure of 4/2 mm Hg (systolic/diastolic) over the study duration of 2 to 60 months (mean 4 months) when compared with control participants.<sup>72</sup> Benefit in systolic blood pressure reduction seemed to persist up to 12 months.<sup>70–73,76</sup> Of note, the completion rate (percentage of patients who completed all training and post-test) in these studies was a modest 63%.

The mechanism(s) whereby meditation lowers blood pressure when it occurs has not been fully elucidated.<sup>77</sup> Possibly, the long-term neurophysiological changes that occur with meditation<sup>35–37,78</sup> may lead to autonomic nervous system–mediated changes in blood pressure. One study of 15 participants with hypertension and chronic kidney disease reported a decrease in muscle sympathetic nerve activity and blood pressure during mindfulness meditation,<sup>79</sup> but no such long-term data exist. The impact of stress reduction on blood pressure remains to be better defined.

Reported reductions of systolic blood pressure with meditation vary widely. The heterogeneity in results reflects the various study populations, study designs, data ascertainment protocols, study duration, baseline blood pressure, and blood pressure measurement techniques used. Limitations to clinical interpretation include high drop-out rates, bias in data ascertainment, and lack of attention to statistical power, control participants, and methods of blood pressure measurements.<sup>46,80</sup> The ability to generalize the findings is limited by the lack of reproducibility of results.

## Effects of Meditation on Smoking and Tobacco Use

Cigarette smoking is the leading cause of preventable disease and deaths in the United States, accounting for >480 000 deaths every year, or 1 of every 5 deaths.<sup>81,82</sup> Two thirds of American adults want to quit smoking, and yet only ≈6% achieve this goal annually.<sup>83</sup> Several types of meditation have been studied as interventions to facilitate smoking cessation (Table S3). Small studies<sup>84–89</sup> have shown that mindfulness training, a form of meditation, increases abstinence rates when compared with more traditional intervention programs. In 1 study of volunteers wishing to reduce stress, half of whom were smokers, who were randomized to either a 2-week program of integrative body-mind technique—a form of mindfulness meditation—or relaxation training, a 60% reduction in smoking was observed among those instructed in integrative body-mind technique, with no reduction in those instructed in relaxation training. In this study, resting-state brain scans before and after intervention showed increased activity in the anterior cingulate and prefrontal cortex—areas of the brain that are related to self-control—for the meditation group, but not the relaxation training group.<sup>90</sup> A meta-analysis of 4 randomized, controlled trials of mindfulness training involving a total of 474 patients found that it was more effective than group counseling, with 25% of mindfulness training participants remaining abstinent from smoking for >4 months, compared with 14% of those receiving more-traditional cessation instruction.<sup>91</sup> One study of transcendental meditation in 295 college students found no significant reduction in cigarette smoking at 3-month follow-up between

those randomized to transcendental meditation and those in a wait-list control group.<sup>92</sup>

Thus, some randomized data show that mindful meditation instruction improves smoking cessation rates. Potential mechanisms include management of cravings and decreasing negative affect, which has been shown to be a potent stimulus for drug-seeking behavior and smoking relapse. Meditation may also affect smoking behavior through changes in urge intensity<sup>87</sup> and improved self-control.<sup>90</sup>

## Effects of Meditation on Insulin Resistance and Metabolic Syndrome

Metabolic syndrome, a cluster of conditions including hypertension, dyslipidemia, elevated fasting blood glucose, and abdominal obesity, is a risk factor for diabetes mellitus and CVD.<sup>93–95</sup> Data on the effects of meditation on insulin resistance and metabolic syndrome are sparse (Table S4). In a study of 103 patients with coronary artery disease randomized to transcendental meditation or active control (health education), transcendental meditation improved insulin resistance.<sup>96</sup> A study of the effects of meditation, yoga, and a vegetarian diet on parameters of metabolic syndrome<sup>97</sup> was too confounded by the multimodality approach to draw meaningful conclusions.

The relaxation response—the counterpart of the stress response—can be evoked by meditation. In 1 novel study,<sup>98</sup> 20 minutes of listening to a relaxation response instructional CD reduced expression of genes linked to inflammatory response and the stress-related pathway—mechanisms that contribute to metabolic syndrome<sup>99,100</sup>—and enhanced expression of genes associated with energy metabolism, mitochondrial function, and insulin secretion. Changes in gene expression were more pronounced in experienced practitioners of relaxation techniques than in novices who had recently undergone 8 weeks of relaxation response training. The clinical effects of these changes in gene expression, if any, remain unknown.

A comprehensive review of metabolic syndrome and mind-body therapies identified only 3 relevant clinical trials, 2 of which are discussed above and the third of which involved restorative yoga as the primary intervention.<sup>101</sup> In summary, data on the effects of meditation on insulin resistance and metabolic syndrome are limited.

## Effects of Meditation on Subclinical Atherosclerosis

Limited evidence exists for the effects of meditation on subclinical atherosclerosis (Table S5). Only 1 randomized, controlled trial was identified that studied the effects of a

meditation intervention on atherosclerosis progression.<sup>102</sup> In this study, carotid intimal thickness was assessed in 138 hypertensive blacks randomized to a transcendental meditation or control health education program and followed for a mean of 7 months. Attrition was high, with 57% of participants not completing follow-up. Among completers of the study, carotid intimal thickness regression was noted in the meditation group, whereas progression occurred in controls, with the difference between the 2 groups being statistically significant. In another randomized study, 57 healthy adults aged  $\geq 65$  years were randomized to 1 of 3 interventions: a transcendental meditation program that also included diet, exercise, and vitamin treatment; a diet/exercise/vitamin arm without the meditation component; or a usual care arm.<sup>103</sup> At 1 year, the meditation intervention group showed reduction in carotid intimal thickness that was not observed in the other groups.

Other studies on subclinical atherosclerosis evaluated more comprehensive multimodality lifestyle interventions that generally included components of dietary changes, exercise, and stress management (including components of meditative practice).<sup>104–107</sup> Study end points included changes in coronary artery atherosclerosis as assessed by quantitative coronary angiography<sup>104–106</sup> and ankle-brachial indices.<sup>107</sup> Although these studies showed favorable effects of lifestyle intervention on atherosclerosis regression, given the multimodality approach, it is difficult to discern the effects of the meditation component alone. Study result interpretation is also limited by attrition and incomplete follow-up. In summary, although a few studies of meditation and lifestyle intervention suggest the potential for benefit on atherosclerosis progression, no firm conclusions can be made on the effects of meditation alone on atherosclerosis.

## Effects of Meditation on Endothelial Function

Endothelial function can be indirectly assessed by evaluating brachial artery endothelial vasomotor response. In a pilot study of 41 participants (33 of whom completed the study), a 6-week combined yoga and meditation intervention failed to significantly improve endothelial function, although there was improvement in the cohort of 10 patients with coronary artery disease.<sup>108</sup> In a trial of 103 patients with coronary artery disease (84 of whom completed follow-up) randomized to 16 weeks of transcendental meditation or control health education, meditation had no significant effect on brachial artery reactivity testing.<sup>96</sup> In a trial of 68 black Americans with metabolic syndrome risk factors, consciously resting meditation improved flow-mediated dilation at 12-month follow-up, but compared with changes in the control

health-education group, this improvement was not significantly different.<sup>109</sup> Only 38 participants (56%) completed the 12-month follow-up.

Limitations of these studies variably include modest sample size, relatively short durations of intervention, high attrition rates, and incomplete follow-up (Table S6). Given these factors, as well as the different patient populations studied and variable findings in those with established coronary artery disease, no definitive conclusions on the effects of meditation on endothelial function can be made.

## Effects of Meditation on Inducible Myocardial Ischemia

A paucity of studies has examined the effects of meditation on inducible myocardial ischemia (Table S7). In a 1996 study of 21 participants with coronary artery disease, 7.6 months of transcendental meditation led to significant increases in exercise duration (15%) and maximal workload (12%) compared with wait-listed controls, as well as lower rate-pressure products at given workloads and significantly delayed onset of ST depression.<sup>110</sup> In a 1983 study of 46 patients with ischemic heart disease that combined stress management (meditation and stretching/relaxation exercises) and a vegan-based diet, after 24 days those randomized to the lifestyle-intervention group had a 44% increase in exercise duration, 55% increase in total work, and improved exercise ejection fraction and regional wall motion, whereas no significant changes occurred in those randomized to the control group.<sup>111</sup>

No contemporary studies have evaluated the impact of meditation on myocardial blood flow or ischemia with techniques such as stress echocardiography, single-photon emission computed tomography, cardiac positron emission tomography, or cardiac magnetic resonance imaging. Larger, randomized, clinical studies that evaluate the impact of meditation-based interventions on inducible myocardial ischemia, ideally using more sophisticated modalities to assess and quantify ischemia, are needed.

## Meditation and Primary Prevention of CVD

Although studies have assessed the effect of meditation on cardiovascular risk factors, recent Cochrane reviews<sup>112–115</sup> have concluded that no properly conducted randomized, controlled trials have assessed its role in the primary prevention of cardiovascular mortality or nonfatal primary end points. This is largely because the relevant studies are small, with short-term follow-up and carried out in predominantly healthy participants.

One study<sup>116</sup> measured survival rate in 73 elderly participants randomly assigned to 3 months of transcendental meditation, mindfulness training, mental relaxation, or a no-treatment control group. The survival rate after 3 years for the transcendental meditation group was significantly better; 100% compared with 65% to 87% for other groups. In a second study, mortality and cause of death were assessed from vital statistics over 8 years of follow-up in 109 older black patients who had participated in a hypertension study. Participants were randomly assigned to 2 stress reduction approaches—either transcendental meditation or progressive muscle relaxation—or to a health education (ie, control) group for 3 months. The adjusted relative risk for CVD mortality was significantly reduced by 81% in the transcendental meditation group when compared with the control group.<sup>117</sup> In both studies, mortality was assessed 3 to 8 years after the intervention period, so the results may not be attributed to transcendental meditation. This and other methodological issues raise concerns about the validity of their findings.

When patient data from the abovementioned 2 randomized, controlled trials were combined in a post-hoc analysis,<sup>8</sup> the transcendental meditation group reportedly showed a 23% reduction in all-cause mortality compared with the control patients, a 30% reduction in cardiovascular mortality, and a nonstatistically significant 51% reduction in rate of cancer mortality (Table S8). These studies of short-term intervention applied to a limited number of participants report surprising mortality reductions that are on par with, or greater than, those observed in long-term intervention, large-scale, primary prevention studies of cholesterol therapy<sup>118</sup> and of blood pressure reduction.<sup>119,120</sup> Accordingly, these findings need to be reproduced in larger, multicenter studies.

In summary, data regarding the effectiveness of meditation for primary prevention of CVD are lacking, and because of the limited evidence to date, no conclusions can be drawn as to the effectiveness of meditation for the primary prevention of CVD.

## Meditation and Secondary Prevention of CVD

Limited and limited-quality data are available from studies of meditation for secondary prevention of CVD (Table S9). Such studies, which generally have enrolled patients with stable coronary artery disease, have variably reported reductions in systolic blood pressure, insulin resistance, serum lipids, clinical symptoms, and anxiety and stress.<sup>70,96,106,110,121–127</sup> Most, although not all, studies randomized patients to either meditation or some type of “usual care.” These studies are generally limited by modest sample size and limited duration



follow-up, and a few assessed multifactorial interventions that combined meditation with other interventions (ie, yoga, diet). A systematic review and meta-analysis of randomized, controlled trials of mind-body practices, including meditation but other interventions as well, found that such interventions were associated with improvements in physical and mental quality of life, depression and anxiety, and systolic and diastolic blood pressure, but rated the overall quality of the studies as low.<sup>128</sup>

One commonly cited study involves 201 patients with angiographically documented coronary artery disease randomized to transcendental meditation or health education.<sup>70</sup> After a mean of 5.4 years, the primary composite end point of all-cause mortality, nonfatal myocardial infarction, or nonfatal stroke was significantly lower in the meditation group (adjusted hazard ratio, 0.52). Post-hoc analysis found greater benefit (hazard ratio, 0.34) in those with high adherence. There was a nonsignificant 24% reduction in the broader secondary composite endpoint, which also included coronary revascularization or hospitalization for cardiac causes. The study, though, was conducted in 2 phases after a 1-year hiatus with 58 patients not participating in phase 2 of the study, and some concerns about analysis of the data have been raised.<sup>129,130</sup>

Overall, data on the potential benefits of meditation in patients with established coronary artery disease can best be characterized as of modest quality and suggesting, but not definitely establishing, benefit in secondary prevention. Because of the generally limited follow-up time, more data on reduction of cardiac risk factors and psychological indices (eg, stress, anxiety, and depression) exist than on hard end points (eg, death or myocardial infarction).

## Summary

Studies of meditation to date suggest a *possible*, though not definitively established, benefit of meditation on cardiovascular risk reduction. A 2008 review of >400 trials of meditation and health care rated the methodological quality of clinical trials as poor, but noted that the quality of these trials had significantly improved over time.<sup>80</sup> Methodological issues in research to date include modest study size, limited and often incomplete follow-up, high drop-out rates, lack of randomization and/or appropriate control group, and unavoidable patient non-blinded study design. As with many other novel interventions, there is the possibility of publication bias toward positive studies of the beneficial effects of meditation.<sup>37,38</sup> Many investigators who conducted studies of meditation may have a strong belief in the benefits of meditation and may be enthusiastic meditators themselves,<sup>37</sup> thereby introducing the possibility of unintended

**Table 3.** Summary of Findings and Suggestions on Meditation and Cardiovascular Risk Reduction

- Studies of meditation suggest a *possible* benefit on cardiovascular risk, although the overall quality and, in some cases, quantity of study data is modest
- The mainstay for primary and secondary prevention of CVD is ACC/AHA guideline-directed interventions
- Meditation may be considered as an adjunct to guideline-directed cardiovascular risk reduction by those interested in this lifestyle modification with the understanding that the benefits of such intervention remain to be better established
- Further research on meditation and cardiovascular risk is warranted. Such studies, to the degree possible, should meet the following criteria:
  - Utilize a randomized study design
  - Blinded adjudication of end points
  - Adequate power to meet the primary study outcome(s)
  - Include long-term follow-up
  - Have <20% dropout rate
  - Have >85% follow-up data
  - Be performed by investigators without inherent financial or intellectual bias in outcome

ACC indicates American College of Cardiology; AHA, American Heart Association; CVD, cardiovascular disease.

bias. Many studies of meditation techniques are performed by the same groups of researchers, so there is a need for independent verification of reported positive findings. Whereas these studies are important in that they serve to suggest that meditation may reduce cardiovascular risk, these limitations prevent definitive conclusions regarding efficacy of meditation on cardiovascular risk reduction.

Currently, the mainstay for primary and secondary prevention of CVD is American College of Cardiology/American Heart Association guideline-directed interventions. However, considering the generally low costs and risks associated with meditation, meditation may be considered as a reasonable adjunct to guideline-directed cardiovascular risk reduction by those so interested in this lifestyle modification, with the understanding that the benefits of such intervention remain to be better established.

Further research on meditation and cardiovascular risk is warranted. Such studies, to the degree possible, should utilize randomized study design, be adequately powered to detect clinically meaningful benefit, include long-term follow-up, and be performed by those without inherent bias in outcome. One such example is the ongoing Yoga-CaRe study for secondary prevention of myocardial infarction.<sup>131</sup> A summary of findings on meditation and cardiovascular risk reduction and on suggested methodology for future research are given in Table 3.

## Disclosures

## Writing Group Disclosures

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\*Modest.

†Significant.

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\*Significant.

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**Supplementary Study Summary Table 1. Effects of meditation on psychological, psychosocial, and physiological response to stress**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Momeni, J, J Am Soc Hypertension, 2016 (1)	<ul style="list-style-type: none"> <li>Single-blind randomized controlled trial to that assessed blood pressure, perceived stress, and anger in 60 cardiac patients.</li> <li>Experimental group (N=30) received 8 weeks MBSR training while those in control group received no psychological training (wait-listed control group N=30).</li> </ul>	<ul style="list-style-type: none"> <li>Systolic blood pressure, perceived stress, and anger were significantly improved (p&lt;.01) in MBSR group as compared to control group.</li> </ul>	<ul style="list-style-type: none"> <li>Wait-listed control group</li> <li>Small sample size</li> </ul>
Epel ES, Transl Psychiatry, 2016 (2)	<ul style="list-style-type: none"> <li>97 Healthy women aged 30–60 entered into 1 week spa retreat: 30 regular meditators and 64 non meditators (31 vacation only and 33 vacation + meditation) with post intervention 1 and 10 month follow up</li> </ul>	<ul style="list-style-type: none"> <li>Regular meditators had lower telomerase at baseline, and a significant increase in peripheral blood cell telomerase activity post treatment not observed in the other two groups.</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> <li>Quasi controlled design (confounding of vacation with meditation)</li> </ul>
Koncz, R, J Occup Environ Med, 2016 (3)	<ul style="list-style-type: none"> <li>University employees were randomized to a 6-week mindfulness-based stress release program (SRP) (N=50) or a waitlist control group (N=29)</li> <li>SRP program is a structured program consisting of “practices using body, breath, and cognitive strategies and reflective activities to enhance professional and personal life” and is considered to be less intensive than MBSR</li> <li>Perceived stress, workplace well-being, and engagement were measured at baseline and at completion of the program</li> </ul>	<ul style="list-style-type: none"> <li>Participants in SRP group had significant improvements in level of distress [-3.0 (95% CI -5.5 to -0.6 p=0.02], university workplace wellbeing (2.5, 95% CI 0.5 to 4.5, p=0.02), and vigor (0.39, 95% CI 0.65 to 3.07; p &lt;0.01) at follow-up compared with baseline. No improvements were observed in control group.</li> </ul>	<ul style="list-style-type: none"> <li>Wait-listed control group</li> <li>Attendance at sessions and practice time not assessed.</li> </ul>
Himashree, G., et al. Altern Ther Health Med 2016 (4)	<ul style="list-style-type: none"> <li>200 soldiers fully acclimatized to high altitude were randomized to routine physical training activities vs. comprehensive yoga package (physical asanas, pranayama, and meditation)</li> </ul>	<ul style="list-style-type: none"> <li>The yoga group had lower body fat %, respiratory rate, DBPs, and anxiety scores. They had higher EtCO<sub>2</sub>, forced vital capacity, forced expiratory volume in the first second (FEV<sub>1</sub>), and VO<sub>2</sub>Max. Also, the yoga group showed a significant reduction in serum cholesterol, LDL, and triglycerides.</li> </ul>	<ul style="list-style-type: none"> <li>Greatest benefit in those markedly hypertensive (SBP&gt;160 mmHg)</li> <li>No long-term f/u of durability of benefit</li> </ul>

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<p>Bharshankar JR, et al. Indian J Physiol Pharmacol. 2015 (5) <sup>4</sup></p>	<ul style="list-style-type: none"> <li>• Case control study of 50 Raja-yoga meditators practicing meditation for 5 years and 50 age matched non-meditators.</li> </ul>	<ul style="list-style-type: none"> <li>• Mean resting HR, SBP and DBP were less in meditators. Galvanic Skin Response in meditators was significantly more (<math>p &lt; 0.001</math>). Mean increase BP response to Hand Grip Test and Cold Pressor Test was significantly less in meditators than non-meditators. (<math>p &lt; 0.001</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Results, suggest a shifting of the autonomic balance to parasympathetic side in Raja-yoga meditators, which suggests meditation combat the ill effects of stress.</li> <li>• Case control design</li> </ul>
<p>Black, DS, JAMA Intern Med, 2015 (6)</p>	<ul style="list-style-type: none"> <li>• Randomized clinical trial</li> <li>• Participants (older adults with sleep disturbances) randomized to a standardized mindful awareness practice (MAP) intervention (N=24) or sleep hygiene education (SHE) intervention (N=25).</li> <li>• Each group met for 2 hours per week for 6 weeks with assigned homework</li> </ul>	<ul style="list-style-type: none"> <li>• Participants in the MAP group had better improvements in sleep than the SHE group.</li> <li>• MAP group participants reported significant improvements relative to the SHE group in health outcomes, depressive symptoms, and levels of fatigue.</li> <li>• NF-kappa B concentrations significantly declined over time for both groups</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> </ul>
<p>Bower, JF, Cancer, 2015 (7)</p>	<ul style="list-style-type: none"> <li>• Randomized trial that examined brief mindfulness-based intervention for younger female breast cancer survivors.</li> <li>• Women diagnosed with early stage breast cancer at or before age 50 who had completed cancer treatment were randomly assigned to a 6-week Mindful Awareness Practices (MAPs) intervention group (n = 39) or to a wait-list control group (n = 32).</li> <li>• Participants completed questionnaires before and after the intervention to assess stress and depressive symptoms (primary outcomes) as well as physical symptoms, cancer-related distress, and positive outcomes. Blood samples were collected to examine genomic and circulating markers of inflammation. Participants also completed questionnaires at a 3-month follow-up assessment.</li> </ul>	<ul style="list-style-type: none"> <li>• Perceived stress reduced (<math>p = .004</math>) post intervention,</li> <li>• Decreased pro-inflammatory gene expression (<math>P = .009</math>) and inflammatory signaling (<math>P = .001</math>) at post intervention.</li> <li>• Intervention effects on psychological and behavioral measures not maintained at 3 month follow up.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Use of wait-list control group</li> </ul>



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Schutte, NS, Psychoneuro-endocrinology, 2016 (8)	<ul style="list-style-type: none"> <li>• Meta-analysis of 4 clinical trials (total N=191) examining telomerase activity in association with meditation.</li> </ul>	<ul style="list-style-type: none"> <li>• A meta-analytic effect size of <math>d = 0.46</math> indicated that mindfulness meditation leads to increased telomerase activity in peripheral blood mononuclear cells. These results</li> </ul>	<ul style="list-style-type: none"> <li>• Small number of studies included in analysis.</li> </ul>
Younge, JO, PLoS One, 2015 (9)	<ul style="list-style-type: none"> <li>• Randomized controlled single-blind trial that examined the physiological and psychological outcomes of a 12 weeks online mindfulness training program (N=215) as compared to usual care (N=109) in patients with cardiac disease</li> <li>• Primary outcome was exercise capacity as measured by a 6 min walk test. Other outcomes included heart rate, blood pressure, respiratory rate, NT-proBNP, subjective health status, perceived stress, psychological well-being, social support, and a composite end-point (all-cause mortality, heart failure, symptomatic arrhythmia, cardiac surgery, and percutaneous cardiac intervention).</li> </ul>	<ul style="list-style-type: none"> <li>• Compared to the control group, participants in the online MBSR program demonstrated improved exercise capacity (effect size: 13.2, 95% CI: -0.02-26.4, <math>p=0.050</math>).</li> <li>• Participants in the MBSR group also had a lower heart rate (effect size, beats per minute; -2.8, 95% CI: -5.4;0.2, <math>p=0.033</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• No control group</li> </ul>
Azam, MA, Int J Psychophysiology, 2015 (10)	<ul style="list-style-type: none"> <li>• Stratified-randomized trial</li> <li>• Following a laboratory cognitive stressor, participants (maladaptive perfectionists – N=21, and controls – N=39, were randomly assigned to a 10 min audio instructed mindfulness meditation condition or a 10 min rest condition with audio description of mindfulness meditation.</li> </ul>	<ul style="list-style-type: none"> <li>• Significant elevated heart rate variability (HRV) during meditation for controls but not for maladaptive perfectionists</li> <li>• Findings suggest that mindfulness meditation promotes relaxation following cognitive stress but the maladaptive perfectionist personality hinders relaxation possibly due to decreased cardiac vagal tone</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• 10 minutes of audiotaped guided meditation may not be sufficient</li> </ul>
de Fátima Rosas Marchiori M, et al. Geriatric Gerontol Int., 2015 (11)	<ul style="list-style-type: none"> <li>• 59 volunteers, aged <math>\geq 60</math> years with SBP 130-159 mmHg and DBP 85-99 mmHg, were randomly divided into meditation twice a day for 20 min for 3 months vs. control wait-list control</li> </ul>	<ul style="list-style-type: none"> <li>• SBP, CRP and IL-6 levels did not differ between groups</li> <li>• QOL improved in psychological aspects (e.g. loneliness) and overall in the meditation group vs. control.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• No change in physiologic parameters</li> </ul>

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<p>Carlson, LE, Cancer, 2015 (12)</p>	<ul style="list-style-type: none"> <li>• Randomized controlled trial comparing Mindfulness Based Cancer Recovery program to a supportive-expressive group. A one day stress management seminar was used for the control group.</li> <li>• 88 distressed cancer survivors with a diagnosis of stage 1 or stage 11 cancer who completed treatment at least three months prior participated.</li> </ul>	<ul style="list-style-type: none"> <li>• No differences were found in regards to telomere length between the mindfulness group and the supportive expressive group – but a trend was observed in the combined intervention group as compared to the control group (F(1,84) 3.82, p=.054, <math>\eta^2=.043</math>).</li> <li>• No associations were found between changes in telomere length and changes in mood or stress scores over time.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Control group consisted only of a one-day stress management seminar.</li> </ul>
<p>Cash, E, Ann Behav Med, 2015 (13)</p>	<ul style="list-style-type: none"> <li>• Randomized clinical trial of MBSR in women with fibromyalgia</li> <li>• Examined pain, perceived stress, sleep quality, fatigue, symptom severity, and salivary cortisol at baseline, post-program, and 2 month follow up</li> <li>• 51 women in treatment group, 40 in wait-list control group</li> </ul>	<ul style="list-style-type: none"> <li>• MBSR significantly reduced perceived stress, symptom severity, and sleep disturbances with changes sustained at follow up.</li> <li>• MBSR did not change level of pain, physical functioning, or cortisol profile.</li> <li>• Frequency of home MBSR practice significantly associated with greater symptom relief.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• High attrition rate (attendance fell over 33% from first session to fourth session)</li> </ul>
<p>Creswell, JD, Psychoneuro-endocrinology, 2014 (14)</p>	<ul style="list-style-type: none"> <li>• Examined the extent to which a brief mindfulness training intervention buffered self-reported psychological and cortisol responses to TSST in 66 young adults.</li> <li>• Participants were randomly assigned to either a 3 day (25 min per day) mindfulness meditation training or an analytic cognitive training control program.</li> <li>• Controlled for treatment expectancies.</li> </ul>	<ul style="list-style-type: none"> <li>• Perceived stress was reduced in brief mindfulness training group however demonstrated increased cortisol reactivity to TSST as compared to the control group.</li> <li>• No changes were observed in systolic or diastolic blood pressure between the two groups.</li> </ul>	<ul style="list-style-type: none"> <li>• Did not include a validated state mindfulness measure</li> <li>• Since blood pressures were not taken continuously during/after the TSST, BP reactivity may not have been fully captured.</li> </ul>

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<p>Arch, JI,          Psychoneuro-          endocrinology,          2014 (15)</p>	<ul style="list-style-type: none"> <li>• Examined the extent to which a brief self-compassion training program (consisting of 10 min. recordings listened to daily for 3 days) moderated biophysiological responses to the Trier Social Stress Test in women (N=105).</li> <li>• Compared intervention to attention and no training control conditions</li> <li>• Collect salivary cortisol, salivary alpha amylase, and heart rate variability in response to Trier Social Stress Test</li> </ul>	<ul style="list-style-type: none"> <li>• Brief self-compassion training attenuated sympathetic, cardiac parasympathetic, and subjective anxiety to Trier Social Stress test as compared to attention and no training control conditions</li> <li>• No differences were noted in cortisol response to the TSST between the self-compassion group and the control groups.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> </ul>
<p>Kaliman, P.          Psychoneuro-          endocrinology,          2014 (16)</p>	<ul style="list-style-type: none"> <li>• Examined impact of a day of intensive mindfulness meditation in experienced individuals (N=19) on expression of circadian, chromatin modulatory, and inflammatory genes in peripheral blood mononuclear cells compared to a control group (N=21) of individuals with no meditation experience who engaged in leisure activities in the same environment as intervention group</li> <li>• Blood was collected before and after the intervention for analysis of gene expression. In addition, individuals underwent the Trier Social Stress Test (TSST).</li> </ul>	<ul style="list-style-type: none"> <li>• Core clock gene expression at baseline was similar between groups and their rhythmicity was not influenced by meditation.</li> <li>• Epigenetic regulatory enzymes and inflammatory genes were similar at baseline for the two groups.</li> <li>• Reduced expression of histone deacetylase genes (HDAC 2, 3, and 9), alterations in global modification of histones (H4ac;H3Lme3), and decreased expression of pro-inflammatory genes (RIPK2 and COX2 were found in meditators as compared to controls.</li> <li>• Faster recovery of cortisol levels after the TSST was associated with lower gene expression levels of <i>RIPK2</i> and <i>HDAC2</i></li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> </ul>
<p>Lengacher CA,          Biol Res          Nursing 2014          (17)</p>	<ul style="list-style-type: none"> <li>• 162 breast cancer survivors were randomized or wait-listed. 6 week Mindfulness-based stress reduction (MBSR) on telomere length (TL) and telomerase activity (TA) at 6 and 12 weeks.</li> </ul>	<ul style="list-style-type: none"> <li>• MBSR led to increased telomerase activity but no increase in telomere length</li> </ul>	<ul style="list-style-type: none"> <li>• Small-moderate sample size</li> <li>• Mindfulness-based stress reduction influenced telomerase activity in women with breast cancer</li> </ul>

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<p>Lipschitz, DL, Psychoneuro-endocrinology, 2013 (18)</p>	<ul style="list-style-type: none"> <li>• Randomized controlled trial of 57 cancer survivors with sleep disturbances. Participants were randomized into either a sleep hygiene education control group (n=18) or a Mind-Body Bridging program (N=19) or a Mindfulness Meditation program (N=20).</li> <li>• The Mind-Body Bridge program is a program that teaches individuals how to become aware of dysfunctional mind-body states.</li> <li>• Each intervention consisted of one session per week for three consecutive weeks.</li> <li>• Saliva cortisol and serum alpha amylase (sAA) measured at baseline and one week after last session.</li> </ul>	<ul style="list-style-type: none"> <li>• Mean sAA upon awakening levels declined in the Mind-Body Bridge group as compared to the Sleep Hygiene Education group.</li> <li>• Self-reported sleep improved in all three interventions with largest improvements demonstrated in Mind-Body Bridge group.</li> <li>• Cortisol levels were not altered by any of the interventions.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Saliva samples were collected over the course of a single day rather than 2 or 3 consecutive days</li> <li>• Intervention was only three weeks long.</li> </ul>
<p>Malarkey, WB, Brain Behav Immun, 2013 (19)</p>	<ul style="list-style-type: none"> <li>• Controlled randomized of university faculty and staff at risk for cardiovascular disease (N=186) comparing a low dose Mindfulness Based Intervention group to an active control group receiving lifestyle education program.</li> <li>• Low dose Mindfulness Based Intervention (MBI-l) consisted of one hour sessions for 8 consecutive weeks. Participants were expected to practice 20 minutes per day.</li> </ul>	<ul style="list-style-type: none"> <li>• The low dose Mindfulness Based Intervention significantly improved mindfulness post intervention and this change was sustained 1 year later as compared to the education group.</li> <li>• No significant changes were found between groups in regards to cortisol, IL-5, or self-reported measures of stress, depression, or sleep quality.</li> </ul>	<ul style="list-style-type: none"> <li>• Did not compare low dose MBSR to traditional MBSR program</li> </ul>

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<p>Bhasin MK, PLOS ONE 2013 (20)</p>	<ul style="list-style-type: none"> <li>• Prospective study of 26 healthy subjects who had no prior relaxation response training (RR; diaphragmatic breathing, mantra repetition, and mindfulness meditation)- eliciting experience (Novices, N1) who underwent 8 weeks of RR-eliciting training (Short-term Practitioners, N2).</li> <li>• Parallel cross-sectional study of another 26 healthy subjects with significant prior RR- practice (4– 20 years; Long-Term Practitioners, M) and compared with novices either before or after their 8-week RR training.</li> </ul>	<ul style="list-style-type: none"> <li>• Both short-term and long-term practitioners evoked significant temporal gene expression changes with greater significance in the long-term practitioners as compared to novices. RR practice enhanced gene expression related to energy metabolism, mitochondrial function, insulin secretion and telomere maintenance, and reduced expression of genes linked to inflammatory response and stress-related pathways.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Quasi-experimental design</li> <li>• Relaxation response induces temporal transcriptome changes in energy metabolism, insulin secretion and inflammatory pathways. Some genes were modified only in long-term practitioners, whereas others were modified in both short- and long-term practitioners with a greater intensity in the latter.</li> </ul>
<p>Rosenkranz, MA, Brain Behav Immun, 2013 (21)</p>	<ul style="list-style-type: none"> <li>• Randomized controlled trial (N=49) comparing 8 weeks MBSR program to Health Enhancement Program (HEP)</li> <li>• Psychological stress and endocrine response were measured before and after the Trier Social Stress Test.</li> <li>• Inflammation was measured by using capsaicin topical cream to induce inflammation before and after intervention</li> </ul>	<ul style="list-style-type: none"> <li>• Cortisol responses to TSSST were similar between MBSR and HEP groups.</li> <li>• Reduction in psychological distress and symptoms in response to TSSST were similar between groups</li> <li>• Those randomized to MBSR group had significantly smaller post-stress inflammatory response as compare to HEP.</li> </ul>	<ul style="list-style-type: none"> <li>• Generalizability to populations with chronic illness</li> <li>• Unable to determine interaction between stress and inflammation because, due to potential participant burden, stress condition was not employed in the absence of inflammation and an inflammation condition was not tested in the absence of stress.</li> </ul>
<p>Qu S, PLOS ONE 2013 (22)</p>	<ul style="list-style-type: none"> <li>• Ten health adults did two courses of 4 consecutive days of a comprehensive yoga program, at the same time of the day (6:30 am – 8:30 am) or yoga and related practices or nature walk with relaxing music.</li> </ul>	<ul style="list-style-type: none"> <li>• Gene expression changes were noted as early as 2 hours. 97 unique genes were affected by yoga and related practices vs. 24 by the control regimen. 36% of the control group genes were also influenced by the yoga regimen, suggesting overlap in effect on biological processes.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Intervention is poorly described</li> <li>• Rapid gene expression changes in peripheral blood lymphocytes upon practice of a comprehensive yoga program</li> </ul>

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<p>Nyklicek, L, Health Psychol, 2013 (23)</p>	<ul style="list-style-type: none"> <li>• 88 community-dwelling volunteers reporting elevated levels of perceived stress were randomly assigned to a MBSR program or waitlist control group.</li> <li>• Participants underwent a social stressor consisting of mental math and making a speech before and after the intervention.</li> <li>• Measurements before, during and after the social stressor included heart rate variability, blood pressure, and salivary cortisol.</li> </ul>	<ul style="list-style-type: none"> <li>• Controlling for age, body mass index, and beta blockers, participants in the MBSR group demonstrated larger decreases in systolic blood pressure, diastolic blood pressure.</li> <li>• No effect was obtained for other physiological measures.</li> </ul>	<ul style="list-style-type: none"> <li>• Absence of critical committee during TSST could have reduced cortisol response to stressor.</li> <li>• Recovery period after social stressor was only 10 minutes which may have limited the ability to capture changes during recovery.</li> </ul>
<p>Carlson, J Clin Oncol, 2013 (12)</p>	<ul style="list-style-type: none"> <li>• Randomized controlled trial to compare mindfulness–based cancer recovery (MBCR) program to supportive-expressive group therapy (SET) in distressed survivors of stage 1 to III breast cancer (N=271)</li> <li>• 1-day stress management class was used as a control condition</li> <li>• Measures (mood, diurnal salivary cortisol, stress, quality of life, and social support) were collected at baseline and after the intervention by evaluators blinded to the study condition.</li> </ul>	<ul style="list-style-type: none"> <li>• Cortisol slopes were maintained in MBCR (p=.011) and SET group (p=.002) participants in comparison to those in the control group whose cortisol slopes became flatter.</li> <li>• Stress symptoms were improved in MBCR group compared to SET (p=.009) and control (p=.024) groups.</li> <li>• Those participating in the MBCR group demonstrated greater improvements in quality of life compared to the control group (p=.005) and social support compared to those in the SET group (p=.012).</li> </ul>	<ul style="list-style-type: none"> <li>• Only breast cancer patients in study –findings may not be generalizable.</li> <li>• High attrition (34.5% in MBCR group).</li> </ul>
<p>Jacobs, TL, Health Psychol, 2013 (24)</p>	<ul style="list-style-type: none"> <li>• Observational study examining self-reported mindfulness and evening cortisol at the beginning and after a 3 month Shamatha meditation retreat (N=57)</li> <li>• The group met 2x/day for 1-hr sessions to engage in guided meditations and dialogue but primarily practiced solitary meditation for much of the day (M = 6.3 hr/day, SD = 1.34).</li> </ul>	<ul style="list-style-type: none"> <li>• Mindfulness increased from pre-retreat (M = 5.16, SD = .77) to post-retreat (M = 5.76, SD = .72), <math>F(1, 56) = 36.20, p = .001</math></li> <li>• Cortisol levels did not change</li> <li>• Mindfulness was inversely related to cortisol levels both pre and post retreat.</li> </ul>	<ul style="list-style-type: none"> <li>• To allow for acclimatization, cortisol measures were taken 2 weeks after arrival to the retreat site, which meant that participants had already been meditating for up to 9 days before the initial cortisol measure was obtained</li> </ul>

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<p>Jensen, J Exp Psychol Gen, 2012 (25)</p>	<ul style="list-style-type: none"> <li>Blinded design - 48 young, healthy meditation novices were randomly assigned to MBSR, non-MBSR, or inactive control group.</li> <li>At posttest, those in the inactive control group were randomly split into incentive and non-incentive controls</li> <li>Attention, self-report of mindfulness, perceived stress, and salivary cortisol were measured at pre and post intervention.</li> </ul>	<ul style="list-style-type: none"> <li>Attentional effects of MBSR, non-MBSR, and the financial incentive were comparable or significantly larger in the incentive group.</li> <li>Selective attention improved significantly more in the MBSR group than non-MBSR and inactive control group. <math>F(6, 84)=2.30, p=.052</math>.</li> <li>Conscious perception and visual working memory capacity were only improved in the MBSR group <math>F(1, 22)= 7.31, p=.05</math></li> <li>MBSR participants had significant reduction of perceived stress (<math>p=.04</math>) and improvement in salivary cortisol levels (<math>p&lt;.05</math>).</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> <li>Use of inactive control group</li> </ul>
<p>Creswell JD, Brain Behav Immun 2012 (14)</p>	<ul style="list-style-type: none"> <li>40 healthy older adults (mean age 65 years) in a 8 week randomized controlled trial, Mindfulness-Based Stress Reduction (MBSR) program vs. wait-list control</li> </ul>	<ul style="list-style-type: none"> <li>MBSR downregulated NF-<math>\kappa</math>B gene expression profile &amp; a trend to reduce C Reactive Protein</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> <li>MBSR training reduced loneliness and proinflammatory gene expression in older adults</li> </ul>
<p>Matousek, RH, Complement Ther Clin Pract 2011 (26)</p>	<ul style="list-style-type: none"> <li>33 women who had completed treatment for breast cancer participated in the study'</li> <li>MBSR group met weekly for 2.5 hours for 8 consecutive weeks</li> <li>Cortisol Awakening Response (CAR) was assessed at three days prior to the MBSR program and three days after.</li> <li>Depressive symptoms, perceived stress, and medical symptoms were measured pre and post intervention.</li> </ul>	<ul style="list-style-type: none"> <li>Cortisol levels demonstrated a prolonged increase after awakening at the post MBSR assessment. This was accompanied by significant improvements in self-reported stress, depressive symptoms, and medical symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> <li>No control or comparison group</li> </ul>

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<p>Jacobs TL, Psychoneuro-endocrinology 2011; 36: 664–681 (27) (27)</p>	<ul style="list-style-type: none"> <li>• 3-month meditation retreat (concentrative meditation techniques and complementary practices used to cultivate benevolent states of mind: 30 active and 30 matched waitlist) on telomerase activity and two measures of stress: Perceived Control and Neuroticism</li> </ul>	<ul style="list-style-type: none"> <li>• Telomerase activity was significantly greater in retreat participants than in controls at the end of the retreat</li> <li>• Retreat group: increases in Perceived Control, decreases in Neuroticism, and increases in both Mindfulness and Purpose in Life were greater in the</li> </ul>	<ul style="list-style-type: none"> <li>• Intensive meditation training, immune cell telomerase activity, and psychological mediators</li> <li>• Small sample size but lengthy intervention with control.</li> </ul>
<p>Klatt, MD, Health Educ Behav, 2009 (28)</p>	<ul style="list-style-type: none"> <li>• University employees and staff randomized to a low dose MBSR program (N=24 or wait list control group (N=24).</li> <li>• Low dose MBSR program consisted of 1 hour weekly sessions for 6 consecutive weeks with 20 minutes of daily practice.</li> <li>• Perceived stress, sleep quality and mindfulness assessed at baseline and at end of 6 weeks intervention.</li> <li>• Salivary cortisol was collected three times a day for 2 consecutive days every week for the duration of the intervention.</li> </ul>	<ul style="list-style-type: none"> <li>• Participants in the low dose MBSR group had significant reduction of perceived stress (p=.0025) and increase in mindfulness (p=.0149).</li> <li>• No changes in average daily salivary cortisol levels over time for participants in both groups and no differences from the pretest to the posttest were found.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Psychological measures (i.e. perceived stress) only measured at baseline and end of intervention.</li> <li>• Wait list control group</li> </ul>
<p>Pace, TW, Psychoneuro-endocrinology, 2009 (29)</p>	<ul style="list-style-type: none"> <li>• Examined the effect of compassion meditation on innate immune, neuroendocrine, and behavioral responses to psychosocial stress and examined the degree to which meditation practice influenced stress reactivity in 61 healthy adults randomized to 6 weeks of training in compassion meditation (N=33) or in a health discussion control group (N=28).</li> <li>• Response to TSST was measured by repeated measures of interleukin -6 (IL-6), cortisol and total distress scores on the Profile of Mood States (POMS).</li> </ul>	<ul style="list-style-type: none"> <li>• No main effect of group assignment on TSST responses was found for IL-6, cortisol, or POMS scores.</li> <li>• Increase meditation practice was correlated with decreased TSST-induced IL-6 (p=.0008) and POMS distress scores (p=.014).</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Did not perform TSST prior to intervention – may be possible that individuals who had reduced inflammatory response to social stress may have been more willing or able to engage in meditation practice.</li> <li>• Those randomized to the meditation group may have had higher expectations of outcomes than those randomized to the control group.</li> </ul>



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<p>Witek-Janusek, Brain Behav Immun, 2008 (30)</p>	<ul style="list-style-type: none"> <li>• Non randomized controlled design to evaluate the effect of MBSR on immune function, quality of life, and coping in women recently diagnosed with breast cancer</li> <li>• Participants self-selected into the MBSR group (N=44) or control group (usual care) (N=31).</li> <li>• Data was collected from a cancer free group of women (N=30) for comparison of immune measures.</li> </ul>	<ul style="list-style-type: none"> <li>• Over time, women in MBSR group re-established NKCA and cytokine production levels while women in the usual care group demonstrated continued reductions in NKCA and IFN-gamma. IL4, IL-6, and IL-10 increased.</li> <li>• Women in MBSR group had reduced cortisol levels and improved QOL and coping effectiveness compared to those in the usual care group.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Non-randomization of participants</li> </ul>
<p>Carlson, LE, Brain Behav Immun, 2007 (31)</p>	<ul style="list-style-type: none"> <li>• 49 women with breast cancer and 10 men with prostate cancer were enrolled in an 8 weeks MBSR program.</li> <li>• Health behaviors, quality of life, mood, stress, salivary cortisol levels, immune cell counts, intracellular cytokine production, blood pressure and heart rate were assessed at baseline, post-intervention, and 6 and 12 months post intervention.</li> </ul>	<ul style="list-style-type: none"> <li>• Symptoms and stress were significantly improved after the intervention and improvements were maintained at 12 months post intervention.</li> <li>• Cortisol and proinflammatory cytokines decreased over follow up period</li> <li>• Blood pressure significantly decreased from baseline to post intervention.</li> </ul>	<ul style="list-style-type: none"> <li>• No control or comparison group</li> <li>• Multiple statistical comparisons</li> </ul>
<p>Tang, YF, Proc Natl Acad Sci USA, 2007 (32)</p>	<ul style="list-style-type: none"> <li>• Randomly assigned undergraduate Chinese students to 5 days of meditation practice with integrative body–mind training (20 minutes per day) (N=40) or 5 days of relaxation training (20 minutes per day) (N=40).</li> </ul>	<ul style="list-style-type: none"> <li>• Those in meditation practice group demonstrated improved attention (p&lt;.01), lower anxiety (p&lt;.01), depression (p&lt;.05), anger (p&lt;.05), and fatigue (p&lt;.01).</li> <li>• Cortisol response to 3 min of mental arithmetic was significantly lower in the meditation group than the relaxation group (p&lt;.01) after 20 minutes of practice.</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> </ul>

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<p>Jain, S. Annals of Behavioral Medicine, 2007 (33)</p>	<ul style="list-style-type: none"> <li>• Randomized controlled trial examining the effects of a 1-month mindfulness meditation to a somatic relaxation training to a control group in 83 students.</li> </ul>	<ul style="list-style-type: none"> <li>• Both meditation and relaxation groups demonstrated improvements in mood and decreases in distress when controlling for social desirability as compared to the control group (<math>p &gt; .05</math>).</li> <li>• Meditation group demonstrated significant pre-post decreases in distractive and ruminative thoughts compared to control group (<math>p &lt; .04</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> </ul>
<p>Robert MacComb, JJ, J Altern Complement Med, 2004 (34)</p>	<ul style="list-style-type: none"> <li>• Women with documented histories of cardiovascular disease were randomly assigned to a MBSR group (N=9) or control group (N=9).</li> <li>• Pre-post hormonal measures and physical functioning were collected</li> <li>• Submaximal exercise responses were measured after the 8 weeks intervention.</li> </ul>	<ul style="list-style-type: none"> <li>• No significant main effects or interaction for resting levels of stress hormones or physical functioning, or submaximal exercise responses</li> <li>• Significant differences in breathing patterns (<math>p &lt; .01</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> </ul>
<p>Speca, M. Psychosomatic Medicine, 2000 (35)</p>	<ul style="list-style-type: none"> <li>• 90 outpatient cancer patients were randomized to a weekly meditation group lasting 1.5 hours or 7 weeks with home meditation practice or a wait-list control group.</li> <li>• Participants completed the Profile of Mood States and the Symptoms of Stress Inventory before and after the intervention</li> </ul>	<ul style="list-style-type: none"> <li>• Participants in meditation group reported significantly lower total mood disturbance and fewer overall symptoms of stress (<math>p &lt; .05</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• Wait list control group</li> </ul>

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**Supplementary Study Summary Table 2. Effects of meditation on blood pressure**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Bai Z, J Human Hypertension, 2015	<ul style="list-style-type: none"> <li>MA of 12 RTC's of TM versus control for effect on blood pressure</li> <li>Total 996 patients</li> </ul>	<ul style="list-style-type: none"> <li>TM improved BP 4.26/2.33 mmHg when compared to control P&lt;.05</li> </ul>	<ul style="list-style-type: none"> <li>The completion rate was &lt;75% in 6 of 11 studies. Dropouts might have enhanced tendency to favor TM</li> <li>Only one study reported on all primary and secondary outcomes with intention-to-treat analysis,</li> <li>The efficacy of TM on BP tended to decrease with the study durations</li> </ul>
de Fátima Rosas Marchiori M, Geriatr Gerontol Int., 2015	<ul style="list-style-type: none"> <li>RCT of twice-daily meditation for 20 min for 3 months vs. wait-list control</li> <li>59 volunteers, aged ≥60 years with SBP 130-159 mmHg and DBP 85-99 mmHg</li> </ul>	<ul style="list-style-type: none"> <li>At one month SBP was lower in meditation group but at 3 months BP did not differ</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> <li>No change in physiologic parameters at end of study</li> </ul>
Blom, Am J Hypertension, 2014	<ul style="list-style-type: none"> <li>RTC of 8 weeks of mindfulness meditation on 24 hour BP control</li> <li>101 subjects (38% male)</li> </ul>	<ul style="list-style-type: none"> <li>Decrease in 24 hour BP of 0.4 mmHg in both treatment and control (wait list group)</li> <li>No significant between group reductions in blood pressure</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> </ul>
Hughes JW, Psychosomatic medicine. 2013	<ul style="list-style-type: none"> <li>RCT of mindfulness-based stress reduction (MBSR) vs progressive muscle relaxation (PMR) over 8 weeks</li> <li>56 pre-hypertensive adults (50.3 years of age, on no BP meds). Clinic BP was the primary outcome.</li> </ul>	<ul style="list-style-type: none"> <li>In an intention to treat, clinic SBP fell 4.8 mmHg with MBSR vs 0.7 mmHg with PMR (P=0.016)</li> </ul>	<ul style="list-style-type: none"> <li>Small sample size</li> </ul>
Schneider RH, Circ Cardiovasc Qual Outcomes. 2012	<ul style="list-style-type: none"> <li>RCT 201 adults with coronary artery disease treated with a TM program or health education</li> </ul>	<ul style="list-style-type: none"> <li>Systolic blood pressure fell 4.9 mmHg in TM vs. control (P=0.01)</li> </ul>	<ul style="list-style-type: none"> <li>Blood pressure reduction was a secondary outcome</li> </ul>

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<p>Palta P, J Urban Health, 2012</p>	<ul style="list-style-type: none"> <li>• 8 week RTC on mindfulness meditation versus social support on BP control</li> <li>• 12 intervention and 8 control subjects</li> </ul>	<ul style="list-style-type: none"> <li>• there was a 11/4 mmHg decrease in systolic/diastolic blood pressure in those randomized to 8 weeks of treatment</li> <li>• there was a analysis adjusted significant 22/17 mmHg difference in blood pressure between the two groups at follow-up</li> </ul>	<ul style="list-style-type: none"> <li>• Small number of patients studied</li> </ul>
<p>Gregoski MJ, et al. J Adolesc Health. 2011</p>	<ul style="list-style-type: none"> <li>• Randomized trial - breathing awareness meditation (BAM), Botvin Life Skills Training (LST), and health education control (HEC)</li> <li>• Study population consisted of 166 normotensive African American adolescents</li> </ul>	<ul style="list-style-type: none"> <li>• BAM had greatest reduction in SBP and SBP, DBP and HR over the 24-hour period, overnight and during school hours. (Bonferroni adjusted, <math>p &lt; 0.05</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Hypertension risk subgroup was a secondary analysis</li> </ul>
<p>Nidich SJ, Am J Hypertens. 2009</p>	<ul style="list-style-type: none"> <li>• Randomized trial in 298 university students treated with a transcendental meditation program or wait-list control.</li> <li>• 3 month intervention</li> </ul>	<ul style="list-style-type: none"> <li>• Overall no difference in SBP &amp; DBP between groups.</li> <li>• In hypertension risk subgroup (<math>n=112</math>), SBP fell 5 mmHg with TM compared to increased 1.3 mmHg for control (<math>P=0.014</math>)</li> </ul>	<ul style="list-style-type: none"> <li>• Hypertension risk subgroup was a secondary analysis</li> </ul>
<p>Anderson, JV, Am J Cardiol, 2008</p>	<ul style="list-style-type: none"> <li>• MA of RTC of TM that randomly assigned individuals to different target BP levels</li> </ul>	<ul style="list-style-type: none"> <li>• Transcendental Meditation, compared to control, was associated with the following changes: -4.7 mm Hg (95% confidence interval (CI), -7.4 to -1.9 mm Hg) and -3.2 mm Hg (95% CI, -5.4 to -1.3 mm Hg)</li> </ul>	<p>Study designs and BP methods of blood pressure measurement, as well as dropout rates, limit the extrapolation of results</p>
<p>Manikonda JP, J Hum Hypertens. 2008</p>	<ul style="list-style-type: none"> <li>• 8 week pilot study of either contemplative meditation combined with breathing techniques (CMBT) or no intervention in this</li> <li>• observer-blind design</li> </ul>	<ul style="list-style-type: none"> <li>• SBP after 8 weeks of meditation fell 15 mm Hg (vs 3 mm Hg in controls (<math>P &lt; 0.0001</math>))</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Short duration</li> </ul>

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<p>Rainforth MV,          Curr Hypertens          Rep, 2007</p>	<ul style="list-style-type: none"> <li>• Systematic review and MA of stress reduction therapies</li> <li>• Seventeen trials of 960 participants with elevated BP</li> </ul>	<ul style="list-style-type: none"> <li>• Reductions in blood pressure with Transcendental Meditation were 5.0/2.8 mmHg (systolic/diastolic); p=0.002 (systolic) and p=0.02 (diastolic)</li> <li>• No significant reductions in blood pressure with biofeedback, relaxation-assisted biofeedback, progressive muscle relaxation, and stress management training.</li> <li>• program, -5.0/-2.8 mm Hg (P = 0.002/0.02)</li> </ul>	<ul style="list-style-type: none"> <li>• Review did not study other forms of meditation</li> </ul>
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**Supplementary Study Summary Table 3. Effects of meditation on smoking and tobacco use**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Oikonomou, Journal of health Psychology, 2016 (36)	<ul style="list-style-type: none"> <li>• Meta-analysis of 4 randomized controlled trials</li> <li>• Studies between 2011-2014, included 474 patients</li> <li>• Included studies examined smoking abstinence in short (4–6 weeks) and long term (17–24 weeks) comparing mindfulness training for smokers to a control group</li> </ul>	<ul style="list-style-type: none"> <li>• 25.2% of participants in the mindfulness group remained abstinent in the long term (17-24 weeks) compared to 13.6% of those who received usual care therapy (RR: 1.88; 95% confidence interval, 1.04-3.40)</li> </ul>	<ul style="list-style-type: none"> <li>• No significant differences were found in the short term (4-6 weeks) (RR: 1.52; 95% CI, 0.95–2.45)</li> <li>• Small number of studies included in the meta-analysis (4), of which 3 are conducted by the same author</li> </ul>
Ruscio, Nicotine & Tobacco Research, 2016 (37)	<ul style="list-style-type: none"> <li>• Randomized controlled trial of a brief mindfulness practice (Brief-MP) intervention on self-reported smoking behavior delivered to smokers on a Personal Digital Assistant (PDA) in the field</li> <li>• Participants carried a PDA for 2 weeks and were instructed to initiate 20 minutes of meditation (or control) training on the PDA daily (n=24 (MP) vs. n=20 (control))</li> </ul>	<ul style="list-style-type: none"> <li>• Brief-MP (vs. Control) reduced overall negative effect, reduced craving immediately post-meditation and reduced cigarettes smoked per day over time</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• 27% of the participants did not complete the study (12 of 44)</li> <li>• The study advertisements mentioned meditation, which could have appealed to individuals who were more educated, more interested in meditation, or more motivated to quit smoking, and reduces the generalizability of the findings</li> </ul>

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<p>Davis JM, BMC Complement Altern Med, 2015 (38)</p>	<ul style="list-style-type: none"> <li>• Prospective observational study</li> <li>• Participants (n=26) were asked to watch eight classes of web-based video instruction describing mindfulness skills and how to use these skills to overcome various core challenges in tobacco dependence</li> <li>• Participants received eight weekly phone calls from a smoking cessation coach who provided general support and answered questions about the videos</li> </ul>	<ul style="list-style-type: none"> <li>• 7-day point prevalence smoking abstinence at 4 and 6-months post-quit of 23.1% and 15.4% respectively</li> <li>• Participants showed a significant pre- to post-intervention increase in mindfulness as measured by the Five-Factor Mindfulness Questionnaire</li> <li>• Participants also demonstrated a significant pre- to post-intervention decrease in the Anxiety Sub-scale of the Depression Anxiety and Stress Scale</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Lack of control group</li> <li>• Possible selection bias as participants were required to have internet access</li> </ul>
<p>Davis JM, J Subst Abuse Treat, 2014 (39)</p>	<ul style="list-style-type: none"> <li>• Randomized controlled trial comparing mindfulness training to a matched control based on the American Lung Association's Freedom From Smoking program</li> <li>• 135 low socioeconomic status smokers were randomized to Mindfulness Training for Smokers (MTS) or Freedom from smoking-enhanced (FFS-E)</li> <li>• Participants in the MT and FFS-E groups received 24 hours of instruction in each group</li> </ul>	<ul style="list-style-type: none"> <li>• Intent-to-treat analysis of 7-day point prevalence abstinence between two groups was almost identical at 4 weeks (MTS = 35.3%; FFS-E = 34.3%; <math>p = 1.00</math>, OR = 1.04, CI = 0.51-2.19)</li> <li>• At 24 weeks, MTS compared to FFS-E showed higher numerical abstinence rates (MTS = 25.0%; FFS-E = 17.9%; <math>p = 0.35</math>, OR = 1.53, CI = 0.67-3.51), but failed to reach statistical significance</li> <li>• Mindfulness training was associated with decreased urges, increased mindfulness, and decreased stress and experiential avoidance</li> </ul>	<ul style="list-style-type: none"> <li>• Participants were not blinded to their respective treatments</li> <li>• Intervention attrition was 32.4% in the MTS group and 26.9% in the FFS-E group</li> </ul>

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<p>Davis JM, Subst Use Misuse, 2014 (40)</p>	<ul style="list-style-type: none"> <li>• Randomized trial comparing mindfulness training for smokers (MTS) to a usual care therapy (Controls), which included the availability of a tobacco quit line and nicotine patches</li> <li>• 198 low socioeconomic status smokers were randomized to MTS or Quit Line</li> </ul>	<ul style="list-style-type: none"> <li>• Primary outcome measure of the study (7-day point-prevalence abstinence at 4 and 24- weeks post-quit) did not reach statistical significance in an intent-to-treat analysis</li> <li>• Did reach statistical significance comparing treatment initiators at 4-weeks (MTS = 45.8%, Controls = 25.4%) and at 24-weeks (MTS = 38.7%, Controls = 20.6%, OR = 2.33 p = .05)</li> </ul>	<ul style="list-style-type: none"> <li>• The study showed high pre-intervention attrition and high 24-week assessment visit attrition</li> <li>• Participants not blinded to their respective interventions</li> <li>• Compares MTS to a less intensive usual-care therapy and as such lacks a time/intensity matched control</li> </ul>
<p>Tang YV, Proc Natl Acad Sci USA, 2013 (41)</p>	<ul style="list-style-type: none"> <li>• Healthy college students recruited through campus advertisements for learning meditation/relaxation to reduce stress and improve cognitive performance</li> <li>• Randomized to Integrated body-mind (IBMT) technique for meditation (15 smokers and 18 non-smokers) vs. Relaxation (RT) technique (12 smokers and 15 non-smokers)</li> <li>• The participants received 30-min of IBMT or RT group practice every night for 10 consecutive sessions, for a total of 5 h of training</li> </ul>	<ul style="list-style-type: none"> <li>• Among smokers, meditation training produced a significant reduction in smoking of 60%; no reduction was found in the relaxation control</li> <li>• Resting-state brain scans showed increased activity for the meditation group in the anterior cingulate and prefrontal cortex, brain areas related to self-control</li> </ul>	<ul style="list-style-type: none"> <li>• Small study</li> <li>• Recruitment via advertisements, so possible selection bias</li> <li>• Participants with the goal of quitting smoking were not included</li> </ul>



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<p>Brewer, Drug Alcohol Depend, 2011 (42)</p>	<ul style="list-style-type: none"> <li>• 88 smokers were randomly assigned to receive Mindfulness Training (MT) or the American Lung Association's Freedom From Smoking (FFS) treatment</li> <li>• Both treatments were delivered twice weekly over four weeks (eight sessions total) in a group format</li> </ul>	<ul style="list-style-type: none"> <li>• 88% of individuals who received MT and 84% of individuals who received FFS completed treatment</li> <li>• Compared to those randomized to the FFS intervention, individuals who received MT showed a greater rate of reduction in cigarette use during treatment and maintained these gains during follow-up</li> <li>• They also exhibited a trend toward greater point prevalence abstinence rate at the end of treatment (36% vs. 15%, <math>p = .063</math>), which was significant at the 17-week follow-up (31% vs. 6%, <math>p = .012</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• First randomized clinical trial to evaluate the efficacy of Mindfulness Training as a stand-alone treatment for smoking cessation compared to an active, empirically-supported control condition</li> <li>• Exclusion of individuals using psychoactive medications</li> <li>• Single site study</li> </ul>
<p>Davis JM, BMC Complement Altern Med, 2007 (43)</p>	<ul style="list-style-type: none"> <li>• Pilot study designed to test the feasibility of using Mindfulness Based Stress Reduction (MBSR) as a smoking intervention</li> </ul>	<ul style="list-style-type: none"> <li>• At the 6-week post-quit visit, 10 of 18 subjects (56%) achieved biologically confirmed 7-day point-prevalent smoking abstinence</li> </ul>	<ul style="list-style-type: none"> <li>• Small sample size</li> <li>• Short follow-up</li> <li>• Lack of control group</li> <li>• 28% (5 of 18 subjects) attrition rate</li> <li>• No concurrent use of pharmacotherapy for smoking cessation</li> </ul>

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**Supplementary Study Summary Table 4. Effects of meditation on insulin resistance and metabolic syndrome.**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Paul Labrador, Archives of Internal Medicine, 2006 (44)	<ul style="list-style-type: none"> <li>Randomized control trial with 103 subjects diagnosed with coronary artery disease randomized to health education versus transcendental meditation for 16 weeks.</li> </ul>	<ul style="list-style-type: none"> <li>At study end, compared to changes in the control group, in the transcendental meditation group there were significant reductions in systolic blood pressure and insulin resistance, and a trend towards improved heart rate variability</li> <li>There were no significant changes in diastolic blood pressure, lipoprotein levels, C-reactive protein, BMI, or brachial artery reactivity</li> </ul>	<ul style="list-style-type: none"> <li>Limitations of this trial included its numerous endpoints, relatively small size and short duration.</li> </ul>
Khatri, Diabetes Research and Clinical Practice, 2007 (45)	<ul style="list-style-type: none"> <li>Randomized control trial of 101 subjects diagnosed with metabolic syndrome.</li> <li>Usual care versus usual care plus yoga for 12 weeks</li> </ul>	<ul style="list-style-type: none"> <li>Significant improvement in waist circumference, blood pressure, blood glucose, HbA1c, triglycerides, and HDL-C in Yoga Group</li> </ul>	<ul style="list-style-type: none"> <li>Limited description of study population, methods and intervention time and frequency of meditation/ Yoga</li> </ul>
Vaccarino, Psychosomatic Medicine, 2013 (46)	<ul style="list-style-type: none"> <li>Randomized control in 68 black Americans with metabolic syndrome.</li> <li>Comparing the effect of consciously resting meditation (CRM), a sound (mantra)-based meditation, with a control intervention of health education (HE) on endothelial function in the setting of metabolic syndrome as primary endpoint and metabolic risk factors, psychosocial and behavioral variables were secondary endpoints</li> </ul>	<ul style="list-style-type: none"> <li>CRM, did not improve endothelial function significantly more than a control intervention of HE (p=0.51)</li> <li>Improved metabolic syndrome parameters like Diastolic BP, Weight, lipid profile and metabolic risk factors score.</li> </ul>	<ul style="list-style-type: none"> <li>Study is limited by small number and high attrition rate</li> </ul>

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<p>Bijani RL, The journal of alternative and complimentary medicine, 2005 (47)</p>	<ul style="list-style-type: none"> <li>• Single group with 98 subjects with hypertension, coronary artery disease, diabetes mellitus, and multiple comorbidities.</li> <li>• The intervention consisted of yoga, breathing exercises, meditation, stress management, diet, and health education.</li> </ul>	<ul style="list-style-type: none"> <li>• Improved lipid profile at the end of the study. The changes were more marked in subjects with hyperglycemia or hypercholesterolemia</li> </ul>	<ul style="list-style-type: none"> <li>• Subjects were too heterogeneous and study is limited by meagre intervention period of 9 days</li> </ul>
<p>Sivasankaran, Clinical Cardiology, 2006 (48)</p>	<ul style="list-style-type: none"> <li>• Prospective Cohort study with 2 cohort of subjects with and without established CAD.</li> <li>• 6 weeks of yoga and meditation on hemodynamic and laboratory parameters as well as on endothelial function were studied.</li> </ul>	<ul style="list-style-type: none"> <li>• Significant reductions in blood pressure, heart rate, and BMI in the total cohort with yoga.</li> <li>• None of the laboratory parameters changed significantly with yoga.</li> <li>• Improved endothelial function in patients with CAD is demonstrated 69% (6.38-10.78%, p = 0.09).</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited with small group of subjects and 20 % of patients failed to complete some portion of the study protocol</li> </ul>
<p>Young, Psychosomatic Medicine, 2015 (49)</p>	<ul style="list-style-type: none"> <li>• Cross sectional study with 2579 subjects free of Cardiovascular disease from Rotterdam, Netherlands were interviewed for mind body practices (prayer, meditation, yoga, tai chi, qi-gong, breathing exercises, or any other form of mind-body related relaxation techniques).</li> <li>• Cardiomtabolic risk factors (body mass index, blood pressure, and fasting blood levels of cholesterol, triglycerides, and glucose) and presence of metabolic syndrome were recorded.</li> <li>• Age, gender, Daily activities, Diet, Alcohol consumption and smoking habits were documented and analyzed statistically.</li> </ul>	<ul style="list-style-type: none"> <li>• Fifteen percent of the participants engaged in a form of mind-body practice of which only (n = 97 ) were meditating.</li> <li>• Population which did mind-body practices had significantly lower body mass index (<math>\beta = -0.84 \text{ kg/m}^2</math>, 95% confidence interval [CI] = <math>-1.30</math> to <math>-0.38</math>, <math>p &lt; .001</math>), log transformed triglyceride levels (<math>\beta = -0.02</math>, 95% CI = <math>-0.04</math> to <math>-0.001</math>, <math>p = .037</math>), and log-transformed fasting glucose levels (<math>\beta = -0.01</math>, 95%CI = <math>-0.02</math> to <math>-0.004</math>, <math>p = .004</math>).</li> <li>• Metabolic syndrome was less common among individuals who engaged in mind-body practices (odds ratio = 0.71, 95% CI = 0.54-0.95, <math>p = .019</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• Observational cross section study where conclusions cannot be drawn for causality.</li> <li>• Low number of subjects practicing Meditation.</li> <li>• Findings may be subjected to confounding factors like more health conscious lifestyle among mind body practicing subjects.</li> </ul>

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**Supplementary Table 5. Studies of meditation on subclinical atherosclerosis:**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Zhang Y et al. Res Sports Med 2013 (50) <sup>7</sup>	<ul style="list-style-type: none"> <li>● Design: Within group change (no comparator intervention)</li> <li>● Population: 20 female hypertensive patients (mean age 57 ±3.5 years)</li> <li>● Intervention: Program of traditional Chinese mental and physical exercises performed for 60 minutes twice a week x 24 weeks. One of the mental exercises, “Tu-Na-Yang-Sheng” included breathing and meditation</li> <li>● Outcome: ABI (as well as SBP, DBP, and PP)</li> <li>● Follow-up: 24 weeks</li> </ul>	<ul style="list-style-type: none"> <li>● Right ABI increased from 1.06 ± 0.08 to 1.12 ±0.08, p=0.041</li> <li>● Left ABI increased from 1.06 ± 0.09 to 1.11 ± 0.09, p=0.100</li> <li>● Also improvements in SBP, DBP, PP</li> </ul>	<ul style="list-style-type: none"> <li>● A program of physical and mental Chinese exercises (which includes a meditative component) may improve ABI (only statistically significant in right ABI noted but sample is small).</li> <li>● Multi-modality, so unable to discern the effects of the meditative components vs. the other stretching and postural components.</li> <li>● Small sample</li> <li>● Hypertensive women only</li> <li>● No comparator group (each participant was their own control)</li> <li>● By nature, intervention was noted blinded.</li> <li>● Mean ABI was normal to begin with – did not look at a group with PAD.</li> </ul>

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<p>Gupta SK, et al. Indian Heart Journal 2011 (51)</p>	<ul style="list-style-type: none"> <li>• Design: Pre-post (within group change)</li> <li>• Population: 123 individuals with angiographically-documented moderate to severe CAD.</li> <li>• Intervention: Rajyoga meditation for stress management, healthy diet (low fat, high fiber vegetarian diet), moderate aerobic exercise. Patients first spent 7 days in-house training, with retraining at 6 month</li> <li>• Outcome: Change in CAD severity by angiography</li> <li>• Follow-up: 2 years for angiographic change in coronary stenosis; 6.48 years for cardiac events</li> </ul>	<ul style="list-style-type: none"> <li>• Decline in absolute % diameter of coronary stenosis and cardiac events were correlated with percent adherence to intervention.</li> <li>• In patients with highest adherence, percent diameter stenosis regressed by 18.2 ±12.0 absolute percentage points (29% relative improvement, p&lt;0.0001).</li> <li>• Least adherence had a progression of 10.6 ± 13.2 absolute percentage points (23% relative worsening, p&lt;0.0001)</li> <li>• 91% patients showed a trend towards regression and 51.4% lesions regressed by more than 10 absolute percentage points.</li> <li>• Cardiac events were 11 in group with most adherence, and 38 in least adherence. (risk ratio of least vs most; 4.32; 95% CI: 1.69-11.71; p&lt;0.002).</li> </ul>	<ul style="list-style-type: none"> <li>• A lifestyle intervention that associated meditation was associated with regression in CAD relative to adherence</li> <li>• By nature, intervention not blinded. Also intervention required a 7 day in-house “sojourn”.</li> <li>• Only 76% of patients completed 2 year follow-up angiography</li> <li>• No comparison group; patients served as their own control and compared by adherence scores</li> <li>• Intervention could not be blinded</li> <li>• Multimodality intervention including meditation, diet, exercise – unable to discern the effects of meditation alone</li> </ul>
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<p>Fields JZ et al.          Am J Cardiol          2002 (52)</p>	<ul style="list-style-type: none"> <li>• Design: RCT</li> <li>• Population: 57 healthy older adults older than 65 years (mean age 74 years), of which 46 completed post-test ultrasound</li> <li>• Intervention (3 arms):            1. Maharishi Vedic Medicine (MVVM) which is Transcendental Meditation practiced 20 min twice daily. This group also got herbal supplements high in antioxidants, were instructed on a Vedic medicine diet (low in fat, high in fruits &amp; vegetables), incorporated Vedic exercises (yoga poses and walking), and attended monthly f/u meetings. 2. "Modern Medicine" arm that included a conventional diet, exercise, and multivitamin approach.            3. Usual care (no added therapy)</li> <li>• Outcome: cIMT by B-mode U/S</li> <li>• Follow-up: 1 yr</li> </ul>	<ul style="list-style-type: none"> <li>• Significant within change in MVVM arm (-0.15 +/- 0.21, p=0.004). No significant within change in other treatment groups.</li> <li>• Among high risk subjects with multiple CAD risk factors, cIMT decreased more in MVVM group (-0.32 ± 0.23 mm) than in the usual care (+0.022 ± 0.085; p=0.009) or modern medicine (-0.082 ± 0.095, p=0.10) groups.</li> <li>• cIMT decreased in a larger fraction of MVVM subjects (16 out of 20) than in modern (5 out of 9) or usual care groups (7 of 14).</li> <li>• Trend for more cIMT decrease among those with better adherence (r= -0.34, p=0.08)</li> </ul>	<ul style="list-style-type: none"> <li>• MVVM (which is TM) reduced carotid atherosclerosis among older adults</li> <li>• Reductions in cIMT were greater than the Castillo-Richmond study suggesting benefit for multimodality approach with MVVM.</li> <li>• By nature, intervention not blinded.</li> <li>• Small sample size</li> <li>• Multi-modality approach. The MVVM arm also included an herbal supplement, counseling on healthy diet and incorporated exercise which limits the ability to discern the effect of MVVM alone.</li> <li>• Older adults only were included.</li> </ul>
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<p>Castillo-Richmond et al. Stroke 2000 (53)</p>	<ul style="list-style-type: none"> <li>• Design: RCT</li> <li>• Population: 138 hypertensive African Americans enrolled but only 60 completed post-test carotid ultrasound.</li> <li>• Intervention: Transcendental Meditation vs a Health Education program. TM is a mental technique practiced twice a day for 20 minutes. Initial teaching instructions conducted in both groups within 1 week, follow-up meetings 1 week later, then every 2 weeks for 2 months, and once a month for 3 months.</li> <li>• Outcome: carotid intimal medial thickness (cIMT) by B-mode U/S.</li> <li>• Follow-up: 6-9 months (mean 6.8±1.3 months)</li> </ul>	<ul style="list-style-type: none"> <li>• TM group showed a significant decrease of -0.098 mm (95% CI -0.198 to 0.003 mm) in cIMT compared with an increase of 0.054 mm (95% CI -0.05 to 0.158 mm) in the control group (P=0.038 for between group difference).</li> <li>• Correlation between attendance rates of meetings and change in cIMT scores was significant for TM group but not health education group</li> <li>• TM group also had statistically significant within-group changes in SBP, DBP, pulse and pulse pressure while health education group improved only SBP and DBP.</li> </ul>	<ul style="list-style-type: none"> <li>• TM reduced carotid atherosclerosis among African American hypertensive adults</li> <li>• High rate of attrition questions the generalizability of these findings. 170 participants were randomized but only 60 had completed post-test interpretable cIMT scans, although attrition was equal in both groups.</li> <li>• By nature, intervention not blinded.</li> <li>• Low number of men (~30%)</li> <li>• Only African Americans</li> </ul>
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<p>Ornish et al.          Lancet 1990 (1 yr f/u) (54) and JAMA 1998 (5 yr f/u) (55)</p>	<ul style="list-style-type: none"> <li>• Design: RCT</li> <li>• Population: 28 patients with CAD</li> <li>• Intervention: randomized to a lifestyle intervention vs control. Lifestyle intervention included a very low fat vegetarian diet, moderate aerobic exercise, stopping smoking, stress management program (that included stretching, breathing techniques, meditation, progressive relaxation, and imagery) which they were asked to practice at least 1 hour per day, and group therapy</li> <li>• Outcome: Coronary atherosclerosis by quantitative coronary angiography</li> <li>• Follow-up: 1 yr and 5 years</li> </ul>	<ul style="list-style-type: none"> <li>• At 1 yr, 82% overall experienced some regression of their CAD. Average % diameter stenosis regressed from 40% to 38% in intervention group, yet progressed from 43% to 46% in controls.</li> <li>• More regression of atherosclerosis occurred at patients in the intervention group at 5 years follow-up than was seen at the 1 yr follow-up. There was a 4.5% and 7.9% relative improvement in coronary stenosis in the intervention arm at 1 and 5 years, respectively vs. 5.4% and 28% relative worsening at 1 and 5 years in control.</li> </ul>	<ul style="list-style-type: none"> <li>• A multi-modality lifestyle intervention (that includes meditation stress management as one component) confers coronary atherosclerosis regression</li> <li>• Small sample size. And only 20 out of 28 (71%) had 5 yr follow-up data</li> <li>• Intervention not blinded</li> <li>• Multi-modality of the lifestyle intervention limits the ability to discern the effects of mediation vs. the other components such as the extremely low fat vegetarian diet.</li> </ul>
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**Supplementary Study Summary Table 6. Studies of meditation on endothelial function.**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Vaccarino V et al. Psychosomatic Medicine 2013 (46)	<ul style="list-style-type: none"> <li>• Design: RCT</li> <li>• Population: 68 year old black Americans with metabolic risk factors</li> <li>• Intervention: Randomized to consciously resting meditation (CRM) vs. high education</li> <li>• Outcome: Brachial reactivity (FMD)</li> <li>• Follow-up: 6 and 12 months</li> </ul>	<ul style="list-style-type: none"> <li>• CRM did improve FMD at 12 months but not statistically significantly more than the health education group despite more favorable trends in metabolic risk factors. Mean change was 2.1% (95% CI 0.5%-3.7%, p=0.009) in CRM group and 1.4% (95% CI = -0.2% to 2.9%, p=0.094) for health education, p-interaction 0.51.</li> <li>• Non-endothelium dependent dilation and arterial elasticity also did not change in either group.</li> </ul>	<ul style="list-style-type: none"> <li>• Meditation did not improve endothelial function more than controls</li> <li>• Outcome was endothelial function, not atherosclerosis</li> <li>• As nature of study, intervention not blinded.</li> <li>• Small sample size</li> <li>• Only African Americans</li> </ul>
Paul-Labrador M et al. Arch Intern Med 2006 (44)	<ul style="list-style-type: none"> <li>• Design: RCT</li> <li>• Population: 103 subjects with stable CAD</li> <li>• Intervention: Transcendental Meditation (TM) vs health education</li> <li>• Outcome: Brachial Reactivity assessed by flow mediated dilation (FMD)</li> <li>• Follow-up: 16 weeks</li> </ul>	<ul style="list-style-type: none"> <li>• No significant effect on brachial reactivity with TM, despite beneficial changes in SBP, insulin resistance, and heart rate variability.</li> <li>• There was a non-significant improvement in FMD (-0.11%) in the TM group and a non-significant decline in the health education group (+0.81); (p=0.24 for difference between groups).</li> </ul>	<ul style="list-style-type: none"> <li>• This study failed to show a benefit of TM on endothelial function.</li> <li>• Outcome was endothelial function, not atherosclerosis</li> <li>• As nature of study, intervention not blinded.</li> <li>• High level of statin use and near optimal LDL-C levels in population may have limited TM to confer any additional benefit</li> <li>• Relatively small size and short duration</li> <li>• All had CAD</li> </ul>

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<p>Sivasankaran S et al. Clin Cardiol 2006 (48)</p>	<ul style="list-style-type: none"> <li>• Design: Within group change, no comparator intervention</li> <li>• 33 subjects (mean age 55±11 years). 30% had CAD.</li> <li>• Intervention: Yoga plus meditation combined classes given 90 mins a day three times a day for 6 weeks (each 90 min session was 15 min meditation, 15 min yogic breathing, 20 min of deep relaxation (shavasana), 40 min postural exercises (asanas).</li> <li>• Outcome: Brachial reactivity (endothelial-dependent vasodilation) and also endothelial-independent vasoreactivity with nitroglycerin</li> <li>• Follow-up: 6 weeks</li> </ul>	<ul style="list-style-type: none"> <li>• Overall no significant improvement brachial reactivity with yoga and meditation compared with baseline (16.7% relative improvement from a baseline reactivity of 7.2-8.4%; p=0.3).</li> <li>• In the group with CAD, there was a trend for relative improvement in brachial reactivity with intervention, (69% relative improvement from a baseline of 6.38-10.78%; p = 0.09). No significant change in subgroup without CAD.</li> <li>• No significant change in endothelial-independent vasodilation overall or in either subgroup.</li> </ul>	<ul style="list-style-type: none"> <li>• Yoga plus meditation may improve endothelial function in individuals with CAD.</li> <li>• Outcome was endothelial function, not atherosclerosis</li> <li>• As nature of study, intervention not blinded.</li> <li>• No comparison group</li> <li>• Intervention was yoga and meditation combined. Thus unable to discern the effect of meditation alone.</li> <li>• Small study, short duration</li> <li>• 20% failed to complete some portion of study protocol</li> </ul>
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**Supplementary Study Summary Table 7. Effects of meditation on inducible myocardial ischemia**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Cunningham et al. AUC 2000 (56)	<ul style="list-style-type: none"> <li>Longitudinal pre/post TM intervention study in 9 postmenopausal women with cardiac syndrome X</li> <li>Subjects underwent exercise treadmill testing (Bruce Protocol) pre and post 3 months of TM</li> </ul>	<ul style="list-style-type: none"> <li>Compared to baseline, TM improved time to 1 mm ST segment depression (<math>p = 0.03</math>), maximum ST segment depression (<math>p=0.03</math>), frequency of angina episodes (<math>p=0.04</math>), and quality of life (<math>p=0.003</math>).</li> <li>No significant differences in heart rate, blood pressure, or duration of exercise before and after TM.</li> </ul>	<ul style="list-style-type: none"> <li>Non-randomized</li> <li>Patients served as their own control group</li> <li>TM compliance was high</li> </ul>
Zamorra et al. AUC 1996 (57)	<ul style="list-style-type: none"> <li>Single blinded study in 21 subjects that compared 7.6 months of TM in 12 CAD patients vs. 9 CAD patients who were waitlisted for TM and served as controls</li> <li>Subjects underwent symptom-limited exercise tolerance testing (upright cycle protocol) before and after intervention</li> </ul>	<ul style="list-style-type: none"> <li>TM led to greater exercise tolerance - 14.7% increase in exercise duration (<math>p=0.013</math>), 11.7% increase in maximal work load (<math>p=0.004</math>), and 18.1% delay of onset of ST depression (<math>p=0.029</math>).</li> </ul>	<ul style="list-style-type: none"> <li>Only 16 completed the study due to various reasons (10 in TM and 6 waiting controls)</li> <li>TM compliance was high</li> </ul>

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<p>Orrish et al.          JAMA 1983 (58)</p>	<ul style="list-style-type: none"> <li>• Randomized study comparing the effects of short-term (24 days) stress management training plus dietary changes in 23 subjects with IHD vs 23 controls.</li> <li>• Subjects underwent exercise nuclear ventriculography imaging with wall motion and ejection fraction (EF)</li> </ul>	<ul style="list-style-type: none"> <li>• Stress management training and dietary changes resulted in a 44% increase in exercise duration (p&lt;0.001) and 55% increase in total work performed (p&lt;0.001).</li> <li>• Improved left ventricular wall motion during peak exercise and a net change in EF from rest to maximum exercise of +6.4%.</li> <li>• Lifestyle intervention lowered total cholesterol (p&lt;0.001) and triglyceride levels (p&lt;0.01); decreased HDL levels (p&lt;0.0001), but the ratio of total cholesterol/HDL showed no difference between the two groups.</li> </ul>	<ul style="list-style-type: none"> <li>• Since both dietary changes (mainly vegan-based diet and 1400 kcal/day) and stress management training were included, the relative contribution of stress reduction cannot be assessed.</li> <li>• Changes in EF and wall motion assessed but inducible myocardial ischemia or changes in coronary blood flow not measured.</li> </ul>
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**Supplementary Study Summary Table 8. Meditation and primary prevention of cardiovascular disease.**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
Barnes VA, Journal of Social Behavior and Personality, 2005 (59)	<ul style="list-style-type: none"> <li>• RCT of African Americans <math>\geq 55</math> years old with mild hypertension (n=109) assigned to (a) transcendental meditation (TM); (b) progressive muscle relaxation (PMR) or (c) a health education control (EC) program</li> <li>• Treatment conducted twice daily for 20 minutes, over a 3-month period, after which patients were encouraged to continue with their treatment program on their own long-term.</li> <li>• Follow-up of mortality events conducted an average of eight years after randomization in the original phase of this trial</li> </ul>	<ul style="list-style-type: none"> <li>• Relative risk for all-cause mortality in the TM group compared with PMR was 0.43 (95% CI 0–1.16, <math>p &lt; .08</math>), and for the TM group compared with EC was 0.51 (95% CI 0–1.33, <math>p &lt; .12</math>).</li> <li>• Relative risk of cardiovascular deaths for TM compared to PMR was 0.33 (95% CI 0–2.27, <math>p &lt; .16</math>), and for TM compared to EC was 0.25 (95% CI 0–1.60, <math>p &lt; .08</math>).</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited by small sample size</li> <li>• Mortality not the original primary endpoint</li> <li>• Follow-up of mortality events conducted an average of eight years after randomization in the original phase of this trial</li> <li>• Compliance to the intervention was not monitored after the three-month follow-up was completed.</li> </ul>
Schneider RH, Am J Cardiol, 2005 (60)	<ul style="list-style-type: none"> <li>• Data pooled from 2 RCT (n=202) (see Alexander and Barnes, above) that compared TM, other behavioral interventions, and usual therapy for hypertension</li> <li>• Programs practiced for 20 minutes twice daily for 3 months</li> <li>• All-cause mortality primary endpoint; cardiovascular and cancer mortality secondary endpoints.</li> </ul>	<ul style="list-style-type: none"> <li>• Mean follow-up was <math>7.6 \pm 3.5</math> years.</li> <li>• Compared with controls, TM showed a 23% decrease in all-cause mortality (relative risk 0.77, <math>p = 0.039</math>).</li> <li>• Secondary analyses showed a 30% decrease in cardiovascular mortality (relative risk 0.70, <math>p = 0.045</math>) and a 49% decrease in the rate of cancer mortality (relative risk 0.49, <math>p = 0.16</math>) in the TM group compared with controls</li> </ul>	<ul style="list-style-type: none"> <li>• Retrospective study limited by modest sample size</li> <li>• Only mortality data from national databases were collected</li> <li>• Follow-up of mortality events conducted three to eight years after randomization</li> <li>• Compliance to the intervention was not monitored after the three-month follow-up was completed.</li> </ul>

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<p>Alexander CN, J Pers Soc Psychol 1989 (61)</p>	<ul style="list-style-type: none"> <li>• RCT of institutionalized elderly (n=73) assigned to (a) no treatment (n=11); (b) transcendental meditation (TM) (n=20); (c) mindfulness training (MF) in active distinction making (n=21), or (d) mental relaxation (MR) with low mindfulness (n=21).</li> <li>• Programs practiced for 20 minutes twice daily for 3 months</li> <li>• Assessed cognitive function and health (i.e., blood pressure, mental health, general health and longevity) endpoints</li> </ul>	<ul style="list-style-type: none"> <li>• Mindfulness techniques associated with improvements in blood pressure, cognitive functioning and mental health.</li> <li>• Mindfulness techniques improved 36 month survival rates; mortality 100% for TM; 87.5% for MF; 77.3% for no treatment; and 65% for relaxation (p&lt;0.00025).</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited by small sample size</li> <li>• Highly biased study (i.e., data were unavailable for 3 “no treatment subjects,” so 14 nonrandomized subjects were included in the mortality analysis of these subjects).</li> <li>• Follow-up of mortality events conducted three years after randomization</li> <li>• Compliance to the intervention was not monitored after the three-month follow-up</li> <li>• Longevity assessed from nursing home records</li> </ul>
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**Supplementary Study Summary Table 9. Studies of meditation in patients with established cardiovascular disease.**

Reference	Study type, design, type of meditation, and population	Primary Findings	Comments
DuBroff R, Alternative Therapies, 2015 (62)	<ul style="list-style-type: none"> <li>Longitudinal pilot study of 22 patients with documented CAD treated with ayurvedic therapy (dietary recommendations and restrictions, meditation, breathing exercises, yoga and herbs)</li> <li>So'Ham meditation practiced initially 10 minutes twice daily, with instructions for patients to increase durations weekly</li> </ul>	<ul style="list-style-type: none"> <li>At 90 days, there was significant improvement in arterial pulse wave velocity and significant reductions in BMI, total cholesterol, LDL cholesterol and triglycerides</li> </ul>	<ul style="list-style-type: none"> <li>Study limited by small sample size (19 patients completed the study) and no control group</li> <li>Exact contribution of meditation to study findings cannot be discerned</li> </ul>
Younger JO, Eur J Preventive Cardiology, 2015 (63)	<ul style="list-style-type: none"> <li>Systematic review and meta-analysis of randomized controlled trials of mind-body practices for patients with cardiac disease</li> <li>11 studies included various types of meditation, mindfulness based stress reduction, stress management, and relaxation</li> <li>Studies variably included patients with coronary artery disease or heart failure</li> </ul>	<ul style="list-style-type: none"> <li>Pooled analyses revealed effect sizes of 0.45 (95%CI 0.20–0.72) for physical quality of life, 0.68 (95%CI 0.10–1.26) for mental quality of life, 0.61 (95%CI 0.23–0.99) for depression, 0.52 (95%CI 0.26–0.78) for anxiety, 0.48 (95%CI 0.27–0.69) for systolic blood pressure and 0.36 (95%CI 0.15–0.57) for diastolic blood pressure.</li> </ul>	<ul style="list-style-type: none"> <li>Study authors concluded “promising but heterogeneous results were seen on overall effect sizes of mental and physical quality of life, anxiety, depression, and blood pressure”</li> <li>Study authors rated overall quality of the studies as low and that no firm conclusions could be drawn</li> </ul>

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<p>Parswani MJ, International Journal of Yoga, 2013 (64)</p>	<ul style="list-style-type: none"> <li>• Randomized study of 30 male patients with a diagnosis of coronary artery disease treated with either mindfulness based stress reduction (mindfulness meditation) consisting of 8 weekly instructional session and 30 minutes meditation daily at home or “treatment as usual”</li> <li>• Mindfulness based stress reduction including training in different variants of mindfulness meditation including body scan meditation, sitting meditation, mindful walking and mindful eating</li> <li>• All patients in both groups instructed on health behaviors including regular exercise for at least 30 minutes and suggested diet</li> </ul>	<ul style="list-style-type: none"> <li>• At the end of the intervention, for the mindfulness based stress reduction group, there were significant within group and between group decreases in anxiety, depression, perceived stress, and systolic blood pressure</li> <li>• At 3 month follow-up, there was a further significant reduction in blood pressure</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited by small sample size (15 patients per group) and relatively short-term follow-up</li> <li>• Intervention consisted not only of meditation but also exercise and diet, though only significant changes seen in the group additionally treated with meditation</li> </ul>
<p>Nehra, Dysphrenia (now called Open Journal of Psychiatry &amp; Allied Sciences), 2013 (65)</p>	<ul style="list-style-type: none"> <li>• Randomized study of 50 patients with coronary artery disease (MI or anginal) randomized to 8 week program of mindfulness based stress reduction (mindful meditation) or usual care control group</li> <li>• Mindfulness based stress reduction program included 2.5 hour weekly meetings, six-hour daylong retreat, and home practice at least 45 minutes daily, and included sitting meditation, hatha yoga, and the body scan</li> </ul>	<ul style="list-style-type: none"> <li>• At 10-17 week post-assessment follow-up, there were, compared to changes in the control group, significant decreases in perceived stress, cognitive health complaints, and somatic health complaints in the mindfulness based stress reduction program group</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited by modest sample size (25 patients per group)</li> </ul>
<p>Delui MH, The Open Cardiovascular Medicine Journal, 2013 (66)</p>	<ul style="list-style-type: none"> <li>• Randomized trial of 45 patients with cardiovascular disease and depression referred for cardiac rehabilitation randomized to relaxation, mindful meditation, or control</li> <li>• Mindful meditation instruction included ten 20-25 minute sessions and home practice</li> </ul>	<ul style="list-style-type: none"> <li>• At the end of the study (duration unclear) repeat testing showed significant reductions in depression, systolic blood pressure and heart rate in the meditation group compared to the control group</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited by small sample size (15 patients per group)</li> <li>• Diastolic blood pressure and anxiety score not significantly reduced by any intervention</li> </ul>



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<p>Schneider RH, Circ Cardiovasc Qual Outcomes, 2012 (67)</p>	<ul style="list-style-type: none"> <li>Randomized study of 201 black men and women with angiographic evidence of at least 1 coronary artery with &gt;50% stenosis treated with either transcendental meditation (20 minutes twice daily) or health education</li> </ul>	<ul style="list-style-type: none"> <li>After a mean of 5.4 years, primary composite endpoint (all-cause mortality, nonfatal MI, nonfatal stroke) significantly lower in the transcendental meditation group (adjusted HR=0.52; 95% CI=0.29-0.92; p=0.025)</li> <li>Secondary composite endpoint (CV mortality, nonfatal MI, nonfatal stroke, coronary revascularization, hospitalization for IHD or heart failure) non-significantly reduced (adjusted HR-0.76; 95% CI=0.51-1.13; p=0.17)</li> </ul>	<ul style="list-style-type: none"> <li>Study conducted in two phases after a hiatus in funding with 58 of the 201 subjects not participating in phase 2</li> <li>Study completed in 2007 and published in 2012</li> <li>Significant net difference of -4.9 mmHg in SBP in TM group (95% CI=-8.3 to -1.5 mm Hg; p=0.01)</li> </ul>
<p>Gupta SK, Indian Heart J, 2011 (51)</p>	<ul style="list-style-type: none"> <li>Longitudinal study of 123 patients with angiographically documented stable CAD (67% with history of MI) treated with comprehensive lifestyle modification, including Rajyoga meditation</li> <li>Intervention included stress management through Rajyoga meditation, vegetarian diet, and moderate aerobic exercise</li> </ul>	<ul style="list-style-type: none"> <li>2 year angiographic follow-up performed on 76% of participants. Average percent diameter stenosis decreased by 6.10 absolute percentage points (p&lt;0.003)</li> </ul>	<ul style="list-style-type: none"> <li>Specific independent contribution of meditation to study findings cannot be determined</li> </ul>
<p>Paul-Labrador, Arch Intern Med, 2006 (44)</p>	<ul style="list-style-type: none"> <li>Randomized trial of 103 patients with documented and stable coronary artery disease randomized to 16 weeks of transcendental meditation or active control (health education)</li> <li>Transcendental meditation intervention included personalized and group instruction and maintenance meetings</li> </ul>	<ul style="list-style-type: none"> <li>At study end, compared to changes in the control group, in the transcendental meditation group there were significant reductions in systolic blood pressure and insulin resistance, and a trend towards improved heart rate variability</li> <li>There were no significant changes in diastolic blood pressure, lipoprotein levels, C-reactive protein, BMI, or brachial artery reactivity</li> </ul>	<ul style="list-style-type: none"> <li>Study findings somewhat limited by numerous study endpoints</li> </ul>

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<p>Tacon AM, Fam Community Health, 2003 (68) and Robert-McComb JJ, Journal of Alternative and Complementary Medicine, 2004 (34)</p>	<ul style="list-style-type: none"> <li>• Randomized study of 18 patients with cardiovascular disease randomized to either mindfulness based stress reduction instruction (2 hours each week for 8 weeks) and home practice or a waiting list for such training</li> <li>• Intervention included training in body scan, sitting meditation, and hatha yoga</li> </ul>	<ul style="list-style-type: none"> <li>• At study end, in the intervention group there were significant improvements in measured anxiety, emotional control, and coping styles</li> </ul>	<ul style="list-style-type: none"> <li>• There was no significant change in “health locus of control”</li> <li>• Study limited by small sample size (9 patients per group) and relatively short term follow-up</li> <li>• Participants included a mixed population of those with angina, hypertension, “cardiovascular disease”, and cardiac valve disorders</li> <li>• A second publication of seemingly the same study population reported no significant changes in stress hormones or submaximal exercise responses</li> </ul>
<p>Sullivan, Am Heart J, 2009 (69)</p>	<ul style="list-style-type: none"> <li>• Prospective cohort study of 208 patients with heart failure (46% due to ischemic etiology) geographically assigned to a mindfulness-based intervention (8 weekly meetings plus practice of skills at least 30 minutes each day) or standard care</li> <li>• Mindfulness-based intervention included mindfulness based stress reduction plus education on improving coping skills and an expressive support group discussion</li> </ul>	<ul style="list-style-type: none"> <li>• At 12 month follow-up, intervention resulted in significantly lower anxiety, depression, and heart failure symptoms and clinical scores</li> <li>• No treatment effect on rehospitalization or death at 1 year</li> </ul>	<ul style="list-style-type: none"> <li>• Study limitation is use of a geographic control</li> <li>• Specific contribution of mindful meditation itself to study findings cannot be determined</li> </ul>

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<p>Zamarrá JW, Am J Cardiol, 1996 (57)</p>	<ul style="list-style-type: none"> <li>• 21 male patients with documented CAD (<math>\geq 70</math> lesion on angiography and/or prior MI) with inducible myocardial ischemia on upright cycle ETT were assigned to either transcendental meditation or wait-list control group.</li> <li>• Transcendental meditation intervention included 10 hours of basic instruction, follow up meetings, and home practice 20 minutes twice daily</li> </ul>	<ul style="list-style-type: none"> <li>• At a mean 7.6 month follow-up, repeat ETT demonstrated that compared to the control group, the meditation group had significant increases in exercise duration, maximum workload, and time to ST depression onset</li> </ul>	<ul style="list-style-type: none"> <li>• Study limited by small sample size (only 10 in intervention group and 6 in control group completed study)</li> </ul>
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