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An Exploration of the Mediators and Moderators of Mindfulness-Based Stress Reduction Among Clergy: Secondary Analysis of Data From the Selah Trial, a Preference-Based Randomized Wait-List-Controlled Trial

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We conducted a secondary analysis of the Selah trial, a preference-based, partially randomized, wait-list-controlled trial, to evaluate mediators and effect modifiers of a mindfulness-based stress reduction (MBSR) intervention. Participants were United Methodist clergy enrolled in the Selah trial and allocated to MBSR or wait-list control. Interventions spanned 12 weeks. Self-reported symptoms of stress and cardiac vagal control (CVC) were coprimary outcomes. Participants completed surveys collected 48-hr heart rate data pre- and postintervention and responded to daily text messages to record MBSR practice. Ninety-six participants ($M_{\text{age}} = 52.4$ years; 92% White; 49% female) were allocated to MBSR ($n = 54$) or wait-list control ($n = 42$), with 11 participants completing MBSR following the waiting period. Participants allocated to MBSR evidenced significantly greater change in symptoms of stress, $M_{\text{Diff}} = 0.248$, 95% CI [0.13, 0.37]; CVC, $M_{\text{Diff}} = 2.30$, 95% CI [0.13, 4.47]; mindfulness, $M_{\text{Diff}} = 1.26$, 95% CI [0.27, 3.79]; self-reported reactivity to stressors, $M_{\text{Diff}} = 6.09$, 95% CI [3.00, 9.19]; and positive mental health, $M_{\text{Diff}} = 3.54$, 95% CI [0.69, 6.39], relative to wait-list control. Improvement in symptoms of stress was partially mediated by a change in mindfulness and perceived stress reactivity. Effects were not modified by a preference for MBSR intervention, minutes of daily practice, or sex. Finally, changes in symptoms of stress and CVC were bidirectionally related, acting as a partial mediator and suppressor variable, respectively. Results support a central, biological stress resilience pathway underlying the effects of MBSR on health-related outcomes, which is consistent with the mechanistic stress buffering framework.

Keywords: mindfulness-based stress reduction, stress, cardiac vagal control, mediation and moderation, mechanistic stress buffering framework

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Ideas and data depicted in this article were presented as an abstract at the 17th International Congress of Behavioural Medicine (Rash et al., 2023). The protocol for the Selah trial was registered under https://clinicaltrials.gov identifier NCT04625777. The data sets generated during the present study are not publicly available, but de-identified data will be made available upon reasonable request to Joshua A. Rash wherein such requests are compliant with receipt of ethical approval from the sending and receiving hosts' institutional ethics review boards. All authors have completed the Unified Competing Interests form at https://www.icmje.org/coi_disclosure.pdf and have no competing interests to declare. Procedures for this trial were approved by the Duke University Campus Institutional Review Board (No. 2019-0238).

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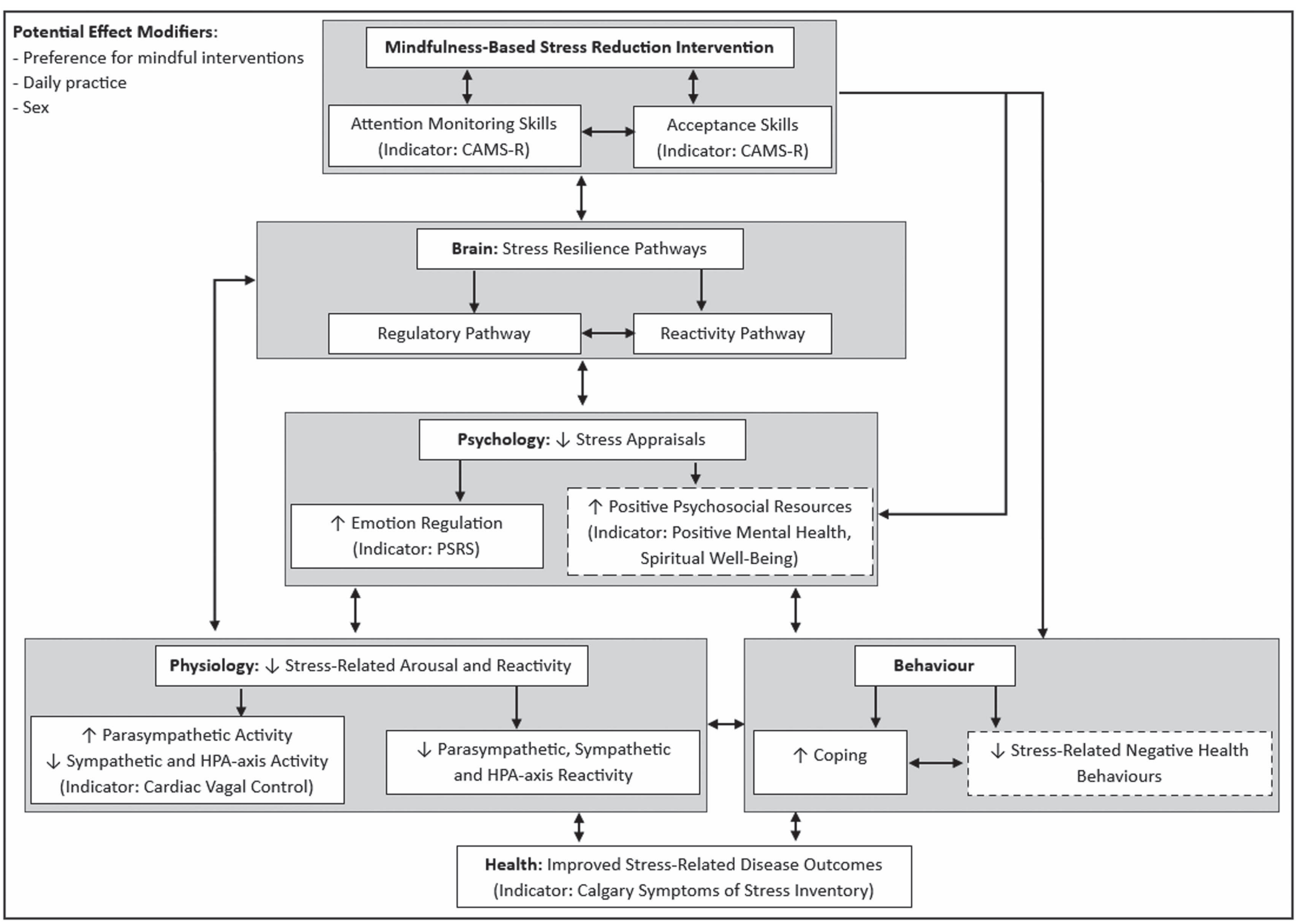
A burgeoning body of evidence from randomized controlled trials (RCTs) attests to the efficacy of mindfulness-based stress reduction (MBSR) on diverse outcomes across clinical and nonclinical samples. One meta-analysis of 49 studies in nonclinical samples ($N = 4{,}733$) reported that MBSR reduced symptoms of rumination/worry, stress, depressed mood, and anxious mood relative to inactive comparison groups with medium effect sizes (Querstret et al., 2020). Another meta-analysis of eight RCTs that evaluated preventive online mindfulness-based interventions reported significant improvement in perceived stress with a medium effect size (Jayewardene et al., 2017). Similarly, MBSR has demonstrated effectiveness for physical health concerns, such as pain (Anheyer et al., 2017), physiological function among cancer survivors (Zhang et al., 2019), and systolic blood pressure among individuals with hypertension (Conversano et al., 2021; Geiger et al., 2023). Considerably less research has evaluated mechanisms and effect modifiers of MBSR, despite clinically relevant reasons why it is important to establish mechanisms and effect modifiers, including (a) optimizing therapeutic effects through enhancing active components of interventions, (b) distinguishing between specific and nonspecific treatment effects, (c) effectively matching interventions to individuals based on identified moderators, and (d) informing theory and interpretation of results (Kazdin, 2007).

Mechanistic Stress Buffering Framework

Creswell et al. developed a mechanistic stress buffering framework that theorized that mindfulness-based interventions train central stress resilience pathways in the brain, which mitigates the cumulative wear and tear of stress on the progression or exacerbation of disease (Creswell et al., 2019). Figure 1 presents a graphical depiction of this framework adapted for the context of the present investigation. In brief, mindfulness interventions are believed to operate through multiple mechanistic pathways, including (a) a brain mechanism that consists of training two stress resilience pathways that involve increased functional connectivity in stress regulatory regions of the prefrontal cortex and decreasing connectivity in regions involved in the stress alarm system, (b)

Figure 1

Plausible Pathways Linking Mindfulness-Based Stress Reduction Intervention With Physical Health-Related Outcomes



Note. Adapted from "Mindfulness Training and Physical Health: Mechanisms and Outcomes," by J. D. Creswell, E. K. Lindsay, D. K. Villalba, and B. Chin, 2019, *Psychosomatic Medicine*, *81*(3), p. 228 (https://doi.org/10.1097/PSY.0000000000000675). CC-BY-NC-ND. CAMS-R = Cognitive and Affective Mindfulness Scale–Revised; PSRS = Perceived Stress Reactivity Scale; HPA = hypothalamic–pituitary–adrenal.

physiological pathways that involve modulating basal activity of the stress response systems (i.e., autonomic nervous system and the hypothalamic–pituitary–adrenal axis) and their reactivity in response to stressors, (c) psychological pathways that operate through enhanced emotion regulation (e.g., dampening stress appraisals) and positive psychosocial resources (e.g., positive emotions), and (d) behavioral mechanisms that involve a shift toward productive coping strategies (e.g., problem-focused coping) and a reduction in problematic stress-related coping strategies (e.g., substance use, eating, sleep). Readers who are interested in a detailed depiction of evidence supporting linkages within this framework are directed to Creswell et al.'s (2019) study. Similarly, readers who are interested in the theorized psychological mechanistic underpinnings of mindfulness-based interventions are referred to recent perspective articles (Creswell, 2017; Goldberg, 2022; Lindsay & Creswell, 2017).

Present Investigation

The present investigation focused on components of the mechanistic stress buffering framework that can be assessed through an evaluation of mediators and moderators of the effect of MBSR on stress-related outcomes through secondary analyses of data collected during the Selah trial, a partially randomized, wait-list-controlled preference trial conducted among clergy Proeschold-Bell et al., 2025; Tice et al., 2021).

Stress can be conceptualized as a latent construct that varies across time and requires multimethod assessment to capture (Crosswell & Lockwood, 2020). Stress can be measured as an exposure or a response and can be approximated through behavioral, cognitive (e.g., appraisals), affective (e.g., mood), or physiological (e.g., operation of the autonomic nervous system) symptoms. We quantified the effects of stress on health through a comprehensive survey that measured physical and psychological symptoms associated with chronic stress (Carlson & Thomas, 2007). Mediators and effect modifiers of change observed in symptoms associated with chronic stress as a result of an MBSR intervention were evaluated using indicators available through the Selah trial that mapped onto components of the mechanistic stress buffering framework.

Mindfulness-based interventions are believed to train skills in monitoring present-moment experiences with an orientation of acceptance that, when used in tandem, are believed to improve cognitive functioning and reduce negative affectivity and stress-related outcomes (Lindsay & Creswell, 2017). In the present investigation, mindfulness was quantified through survey questions measuring attention, present focus, awareness, and acceptance. The items have been shown to capture a higher order construct of mindfulness (Feldman et al., 2007). Change in mindfulness that occurred from pre- to post-MBSR intervention was evaluated as a way of ensuring that the MBSR intervention produced anticipated improvement in mindfulness (i.e., manipulation check) and as one putative mechanism of the effect of MBSR on long-term symptoms of stress (i.e., mediator).

Mindfulness-based interventions have been hypothesized to increase activity and functional connectivity in regions of the prefrontal cortex that regulate stress, leading to modulation of the autonomic nervous system and improved health-related outcomes (Creswell & Lindsay, 2014). The present investigation measured change in cardiac vagal control (CVC) as a physiological marker of the stress resilience regulatory pathway. Resting CVC reflects variations in heart rate that index the capacity of the parasympathetic nervous system to alter heart rate to effectively respond to the environment. While not an indicator within the first iteration (Creswell et al., 2019), we propose extending the mechanistic stress buffering framework to include a parasympathetic physiological pathway, as indicated in Figure 1, for three reasons. First, according to the model of neurovisceral integration (Thayer & Lane, 2000, 2009), the vagus nerve serves as a structural and functional link between the heart and a highly integrated constellation of neural structures known as the central autonomic network (CAN; Benarroch, 1993). Many neural structures in the CAN play a fundamental role in the perception and management of stress (McEwen, 2007) and are believed to be key circuits underlying mindfulness practice (Gu & Zhu, 2022). Importantly, CVC and CAN form a bidirectional feedback loop, the existence of which is supported by a meta-analysis of eight rigorous neuroimaging studies that indicated CVC and cognition are represented by the same regions of the medial prefrontal cortex and the amygdala (Thayer et al., 2012). Second, resting CVC has been associated with affective stability in daily life (Koval et al., 2013), emotion regulation ability (Beauchaine, 2015; Williams et al., 2015), and attentional control (Bögge et al., 2022). Finally, CVC reliably covaries with stress during stress-inducing procedures (Kim et al., 2018) and is a strong indicator of morbidity and risk of mortality in longitudinal studies (Jarczok et al., 2022; Tsuji et al., 1996).

Cultivation of mindfulness is theorized to augment stress appraisals that lead to improved health outcomes through the enhancement of psychosocial resources, especially emotion regulation (Creswell et al., 2019). In the present investigation, a survey that measured perceived reactivity to stressors (Schlotz et al., 2011) was used as an indicator of emotion regulation that was influenced by stress-related appraisals. A broad-band measure of positive mental health (Keyes, 2002) and a focused measure of spiritual well-being (Proeschold-Bell et al., 2014) were selected as indicators of positive psychosocial resources, with the latter selected due to its potential importance as a psychological resource among the clergy (Proeschold-Bell et al., 2014). Of note, indicators reflective of coping behaviors were not available, and the dynamic interplay of this pathway was not explicitly interrogated.

We propose an extension of the mechanistic stress-buffering framework to include potential effect modifiers as depicted by the rectangle encompassing the framework in Figure 1. Three potential effect modifiers were interrogated in the present investigation. Minutes of daily practice and the proportion of days when practice occurred were selected as markers of engagement that were intended to evaluate whether a given "dose" was necessary to observe benefits associated with MBSR. A preference for MBSR as an intervention was an indicator of the expectancy of treatment outcomes. Finally, sex was included as a potential effect modifier given the (a) documented gender differences in stress and health (Mayor, 2015) and (b) the recognition that accounting for sex in health research has the potential to make health research more rigorous, more reproducible, and more applicable to everyone (Johnson et al., 2009).

The mechanistic stress-buffering framework is generally applied to high-stress populations (Creswell et al., 2019). The population recruited in the present investigation were clergy whose occupation has been conceptualized as a helping profession with high demands (DeShon, 2012). Clergy often work long hours, manage complex interpersonal relationships, face the expectation of being on call around the clock, and are often exposed to secondary trauma (Carroll, 2006). Moreover, clergy direct a workforce mainly comprised of volunteers and rarely receive the support needed to match the tasks or emotional challenges faced (Proeschold-Bell & Byassee, 2018). Members of the clergy profession often report emotional exhaustion and a lack of personal accomplishment (Adams & Bloom, 2017). It is important to note that data were collected during a particularly stressful time globally during the COVID-19 pandemic. Religious congregations faced extreme pressures as they adapted to a virtual environment.

Hypotheses

Consistent with the mechanistic stress buffering framework, we hypothesized that (a) MBSR would result in improvement in symptoms of stress that would be mediated by change in mindfulness, CVC, perceived stress reactivity, and positive mental health and spiritual well-being and moderated by daily practice patterns and (b) MBSR would result in improvement in CVC that would be mediated by change in mindfulness, symptoms of stress, perceived stress reactivity, and positive mental health.

Method

Design

The Selah trial was a partially randomized, wait-list-controlled preference trial evaluating the effects of stress-reducing interventions on symptoms of stress and CVC. The protocol was registered under ClinicalTrials.gov identifier NCT04625777 and published online (Tice et al., 2021). Participants who expressed a preference for a specific intervention were randomized to their chosen intervention or wait-list control. Those without preferences were fully randomized. Enrollment was reopened after the start of the COVID-19 pandemic to an "observational" cohort who chose an intervention without a randomization structure (refer to Proeschold-Bell et al., 2025, for additional information). All interventions tested were delivered remotely between April 2020 and October 2021, during the COVID-19 pandemic. The analysis presented here focuses on comparisons between MBSR and wait-list control using data pooled across participants enrolled in the trial and observational cohorts who provided heart rate data.

Participants

United Methodist Church clergy with a current appointment in one of the two North Carolina Annual Conferences were eligible if they were 18 years of age or older. While there were no stress- or health-related inclusion criteria, a subset of participants was invited to provide 48-hr continuous ambulatory heart rate recording pre- and postintervention, which form the basis for this analysis. The subset was limited by the number of available recording devices, and participants were excluded from providing heart rate data if they had underlying medical conditions, including a diagnosis of tachycardia, being pregnant or becoming pregnant during the course of data collection, being diagnosed with COVID-19, having a pacemaker, or documentation of other cardiovascular-related chronic or acute morbidities that could impact the integrity of heart rate variability signals. The present article focused on this subset of participants. Procedures were approved by the Duke University Campus's Institutional Review Board (No. 2019-0238). Participants provided written consent to participate.

Procedure

Recruitment and Enrollment

Eligible clergy were sent an email between November 2019 and January 2020 that explained the trial and directed them to consent to enrollment. The trial cohort consists of participants who enrolled prior to March 1, 2020. Randomization was performed in February 2020 after all trial cohort participants were enrolled.

Enrollment was reopened in March 2020 with the anticipation that interest in stress management may have increased because of the COVID-19 pandemic. Participants who enrolled after February 28, 2020, were not randomized, received their chosen intervention, and represented an observational cohort.

Randomization and Blinding

Participants in the trial cohort specified their preferred intervention, and those with a preference were randomized to their preferred intervention or wait-list control with a 3:1 allocation ratio for the MBSR intervention. Those without a preference were randomized to one of the three active stress management interventions or wait-list control using a 1:1:1:1 allocation ratio. The analysis statistician wrote code to generate the random allocation sequence in Stata Version 16. Two staff members were responsible for accessing randomization results and informing participants of intervention allocation.

One staff member who was not the analysis statistician executed the randomization codes so that the analysis statistician could remain masked to intervention allocation. Staff cleaning heart rate data were also masked to intervention assignment. Participants and intervention workshop instructors were aware of group assignments. Elsewhere, we have reported on coprimary outcomes and provided extensive details on randomization and blinding (Proeschold-Bell et al., 2025).

Interventions

MBSR

Certified instructors from the Duke University Integrative Medicine Centre delivered a criterion standard MBSR intervention (Kabat-Zinn, 2018). An instructor taught eight weekly 90-min, synchronous, web-based sessions, after which participants were offered a 4-hr online "day of mindfulness." Participants were asked to practice MBSR for 45 min daily for 6 months. Sessions were taught by one of four certified instructors.

Wait-List Control

Wait-list participants waited at least 6 months to participate in interventions. They completed surveys at 0 and 12 weeks.

Measures

Symptoms of stress and CVC obtained from 48-hr ambulatory heart rate data were coprimary outcomes and were detailed elsewhere (Proeschold-Bell et al., 2025; Tice et al., 2021). For brevity, only measures pertinent to the present study are described.

Symptoms of Stress

Five of the eight subscales (i.e., anger, muscle tension, cardiopulmonary arousal, neurological/gastroenterological, and cognitive disorganization) that comprised the Calgary Symptoms of Stress Inventory (Carlson & Thomas, 2007; Penwell, 2012) were used to measure symptoms of stress (a total of 41 items). Participants were asked to indicate how often they experienced each symptom when presented with a stressor on a 5-point Likert scale with anchors at 0 (*never*) and 4 (*frequently*). We used continuous mean scores of all the items (range = 0–4), with higher mean scores indicating worse symptoms. Cronbach's α for this scale was .95.

CVC

Ambulatory heart rate was measured across a 48-hr period. Participants were mailed a Bittium eMotion Faros 180 heart rate recording device with electrodes 2 weeks prior to the intervention and taught to connect the device to two pregelled (Ag/AgCl) disposable Ambu BlueSensor wet-gel electrocardiographic electrodes placed beneath the right clavicle and left ribcage. Participants were instructed to wear this ambulatory heart rate monitoring device for a 48-hr period at Weeks 0 and 12, during which time they proceeded with their usual work, exercise, bathing, and sleep routines. Heart rate was measured using continuous Electrocardiogram (ECG) recording sampled at a rate of 1,000 Hz and used to calculate CVC.

Perceived Stress Reactivity

The Perceived Stress Reactivity Scale is a 23-item measure that asked participants to select the response that best described their own reactions to stressful situations, including work overload, social conflicts, failure, social evaluation, and prolonged reactivity (Schlotz et al., 2011). Response options were modified from a 3- to a 4-point Likert scale to promote response variability, and two items were added based on pilot testing and cognitive interviews (refer to Proeschold-Bell et al., 2023). For example, participants were asked to select the response that describes their reaction "When I argue with other people" with anchors at 0 (*I usually calm down quickly*) and 3 (*It usually takes me a long time until I calm down*). Responses were summed on a scale from 0 to 27 with higher scores indicating greater perceived stress reactivity. Cronbach's α within this study was .82.

Mindfulness

The Cognitive and Affective Mindfulness Scale–Revised is a 10-item, single-factor measure of mindfulness skills (Feldman et al., 2007). Items are designed to assess four components: the regulation of attention, orientation to present experience, awareness of experience, and acceptance/nonjudgment toward experience. Participants were asked to respond to how they relate to their thoughts and feelings (e.g., "I accept things I cannot change") using a 4-point Likert scale with anchors at 1 (*rarely/not at all*) and 4 (*almost always*). Scores were summed on a scale from 10 to 40 with higher scores indicating greater mindfulness. Cronbach's α within this study was .86.

Positive Mental Health

The Mental Health Continuum–Short Form is a 14-item measure that asked participants to rate the degree to which they experienced three kinds of well-being during the previous month: emotional (e.g., interested in life; three items), psychological (e.g., that you had warm and trusting relationships with others; six items), and social (e.g., that you belonged to a community; five items; Keyes, 2002). Response options were made on a 6-point Likert scale with anchors at 0 (*never*) and 5 (*daily*). Scores were summed and ranged from 0 to 70 with higher scores reflecting greater positive well-being. Cronbach's α within this study was .92.

Spiritual Well-Being Scale

Spiritual well-being was measured using seven items from the Clergy Spiritual Well-Being Scale that load onto one factor measuring spiritual well-being in daily life (Proeschold-Bell et al., 2014). Participants were asked to rate how often they experienced the presence and power of God over the previous 3-month period (e.g., "Felt that you have a vital relationship with God?") using a 5-point Likert scale with anchors at 0 (*never*) and 4 (*always*). Responses were summed and range from 0 to 28 with higher scores reflecting greater spiritual well-being. Cronbach's α within this study was .93.

Physical Activity

The Godin–Shephard Leisure-Time Physical Activity Questionnaire is a self-report measure of physical activity during the previous 7 days (Godin, 2011). Participants were asked to report the frequency and duration of engagement in activities classified as mild, moderate, and strenuous in nature. Metabolic equivalents per week were calculated by (a) multiplying minutes of mild, moderate, and strenuous activity by 3, 5, and 9, respectively, and (b) adding these numbers and dividing by 15. Higher scores correspond to the expenditure of greater metabolic equivalents through leisure time activity.

Demographics

Responses to a survey questionnaire captured age, sex, marital status, height and weight, caffeine and alcohol intake, and medications prescribed.

Daily Practice Reports

Daily text messages were sent to participants during the intervention and follow-up periods. Participants in the MBSR group were asked to report the number of minutes practiced during the prior day. Two indices of practice were used: (a) mean minutes of practice on days when practice was logged and (b) the percentage of days when text messages were responded to where a participant indicated engaging in practice.

Data Collection and Timing of Assessments

Surveys were administered using REDCap at intervention start (0 weeks) and postintervention (12 weeks). Heart rate monitoring devices were mailed to participants, and 48 hr of ambulatory heart rate data were collected at 0 and 12 weeks. After collecting their 48-hr sample, participants returned their devices by mail. Self-monitoring data were automatically analyzed each week according to embedded algorithms. Participants allocated to the wait-list group started an intervention following the waiting period.

Incentives

Participants received $25 for each occasion of 48-hr ambulatory heart rate data submitted and $20 each for the 0- and 12-week surveys.

Data Processing

CVC

Herein, 48-hr heart rate data were processed using Kubios Premium software 3.4.1. The ECG data were partitioned into 300-s segments and scanned for artifacts according to standards (Berntson et al., 1990). CVC was indexed using root mean square successive difference given that it is less affected by breathing (Minarini, 2020; Penttilä et al., 2001). Raw ECG files from one timepoint among six participants were deemed unusable during data processing (MBSR = 3; WLC = 3), and data were imputed. One timepoint of data from an additional seven participants (WLC = 7) met the threshold of ≥10% corrected ectopic beats and were imputed.

Following recommendations (Refinetti et al., 2007), 5-min segments across 24 hr of recording were subject to a cosinor analysis using the *Cosinor* package for R. Two parameters were estimated by ordinary least squares regression to quantify the circadian variability: (a) midline estimating statistic of rhythm, defined as the rhythm-adjusted 24-hr mean, and (b) amplitude, defined as the distance between midline estimating statistic of rhythm and the maximum of the cosine curve.

Data Screening

Univariate outliers were identified as values that exceeded a z score of 3.29, $p < .001$, from the mean, and winsorized according to recommendations (Tabachnick & Fidell, 2019). Multivariate outliers were cases where the χ^2 observed exceeded the critical $\chi^2(12)$ of 32.91 ($p < .001$) using Mahalanobis distances. Our sample had one multivariate outlier that was retained in the final data set given that inclusion did not appreciably change the pattern of results.

Missing data were handled using a single imputation. Little's test for missing completely at random indicated that data were missing at random, $\chi^2(1, 243) = 1187.34$, $p = .87$ (Little & Rubin, 2019). Missing data were imputed using the expectation–maximization method in SPSS V27.

Statistical Analyses

Evaluating Change Over Time Between MBSR and Control

A series of 2 (time: 0 weeks, 12 weeks) by 2 (group: MBSR, wait-list control) mixed-model analyses of variances were performed to evaluate whether change over time observed among participants allocated to MBSR differed significantly relative to wait-list control for symptoms of stress, CVC, mindfulness, and stress reactivity.

Evaluating Mediators and Moderators of the Effects Observed for MBSR

Mediators and moderators of the effects observed for MBSR were evaluated using ordinary least squares regression performed using the mediation and moderation for repeated measures macro for SPSS (Montoya & Hayes, 2017). Confidence intervals were calculated using Monte Carlo simulation with 5,000 samples. Univariate models were performed testing mediators (i.e., change in mindfulness and stress reactivity) and moderators (i.e., sex, preference for MBSR, and minutes practiced per day), followed by one multivariate model that included variables identified as significant from univariate analyses. Separate models were estimated, which included change in symptoms of stress, and CVC between 0 and 12 weeks were entered as the criterion variable. Change in symptoms of stress and CVC were entered as mediators within each respective model.

Results

Study Flow

In total, 121 participants allocated to MBSR or wait-list control were invited to provide 48-hr heart rate data, of which 14 were excluded due to underlying medical conditions that could affect heart rate assessment. Figure 2 depicts the flow of the 107 participants who provided heart rate data in the study. The analyzable sample was obtained from 107 (MBSR = 65; WLC = 42) participants, 81 (MBSR = 41; WLC = 40) who participated in the trial cohort, 15 (MBSR = 13; WLC = 2) who participated in the observational cohort, and 11 who provided data following the completion of the wait-list period. Data from 13 (20%) participants who commenced the MBSR intervention and 9 (21%) participants who commenced the wait-list control period were lost to follow-up. Missing data were imputed.

Sample Characteristics and Descriptive Statistics

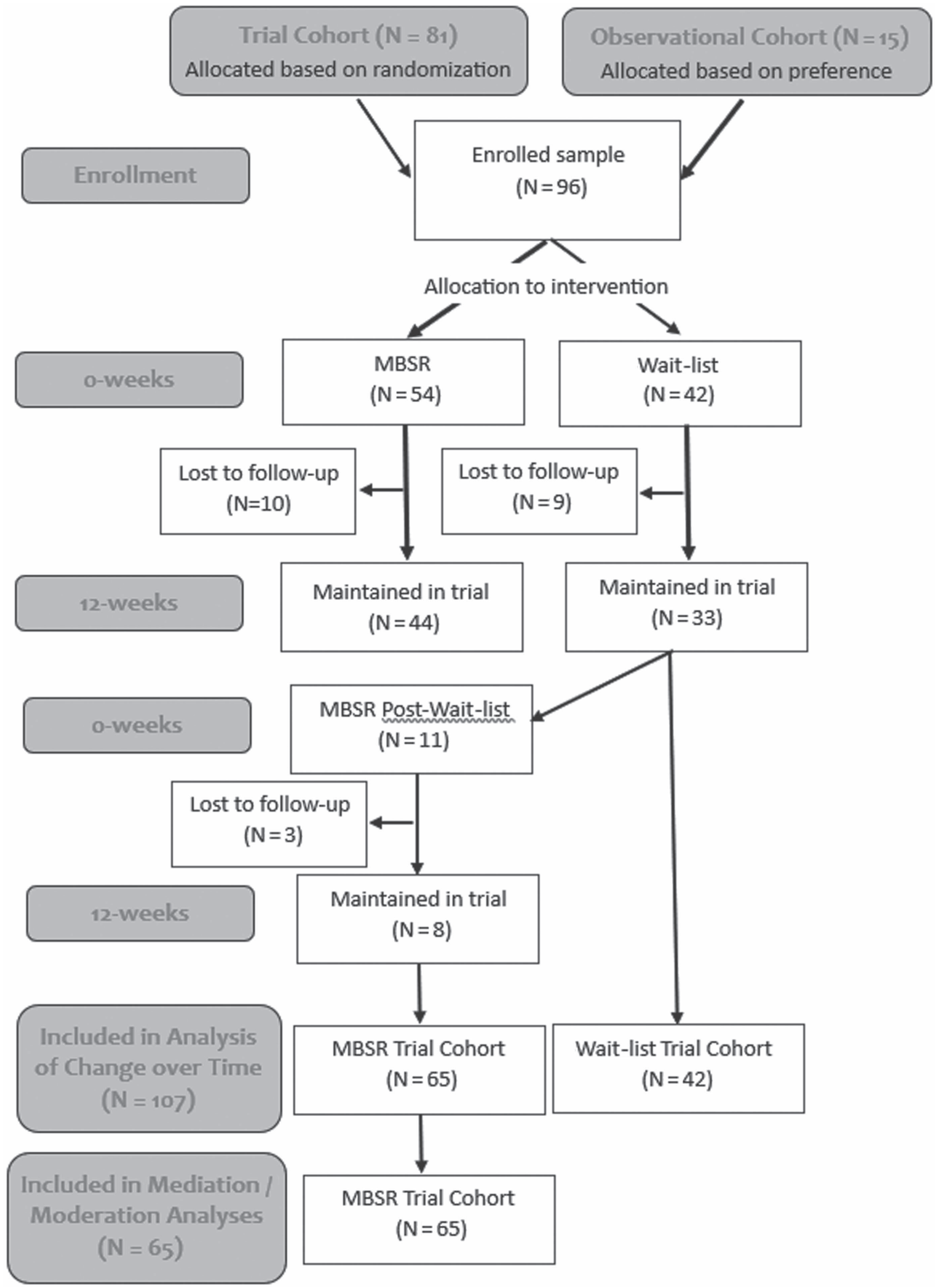
Table 1 depicts demographics and descriptive statistics. Participants were predominantly White (92%), 52.41 years of age on average, and worked in ministry for 17.55 years. Approximately half of the sample was female. The average body mass index was 30.65 kg/m^2. Participants allocated to the MBSR intervention engaged in a mean 27.65 min/day of practice and practiced on 82% of days in which they responded to a text message.

Evaluating Change Over Time Between MBSR and Control

There was a significant[1] Group × Time interaction on symptoms of stress, $F(1, 104) = 19.80$, $SEM = 0.05$, $p < .001$, $\eta_p^2 = .16$. Participants allocated to the MBSR group reported significantly greater reductions in symptoms of stress from 0 to 12 weeks, $M_{\text{Diff}} = -0.27$, relative to control, $M_{\text{Diff}} = -0.024$.

[1] Excluding data from participants who took part in MBSR following completion of a wait-list period did not appreciably change results. Analyses including all available data and modeled postwait-list period as a covariate are presented in text.

Figure 2
Flow of Participants Through the Trial



Note. MBSR = mindfulness-based stress reduction.

Table 1
Demographics and Descriptive Statistics

Variable	MBSR *N* (%)	Wait-list *N* (%)	Full sample *N* (%)	
Gender				
Female	34 (52)	18 (43)	52 (49)	
Male	31 (48)	24 (57)	55 (51)	
Marital status				
Married	54 (83)	35 (83)	89 (83)	
Single	9 (14)	6 (14)	15 (14)	
Divorced/separated	2 (3)	1 (2)	3 (3)	
Race				
White	60 (92)	38 (91)	98 (92)	
African American	2 (3)	3 (7)	5 (5)	
American Indian/Alaskan Native	0 (0)	1 (2)	1 (1)	
Other, including multiracial	3 (5)	0 (0)	3 (3)	
Variable	MBSR *M* (*SE*)	Wait-list *M* (*SE*)	Full sample *M* (*SE*)	Missing data (%)
Age (years)	51.89 (1.43)	53.21 (1.65)	52.41 (1.08)	0
Body mass index (kg/m^2)	30.73 (0.94)	30.52 (1.01)	30.65 (0.69)	0
Years in ministry	16.45 (1.27)	19.34 (1.89)	17.55 (1.08)	0
Symptoms of stress (C-SOSI) 0-weeks	1.00 (0.06)	0.87 (0.09)	0.95 (0.05)	0
Symptoms of stress (C-SOSI) 12-weeks	0.72 (0.06)	0.85 (0.09)	0.77 (0.05)	13.3
CVC (ms) 0 weeks	24.05 (1.60)	23.89 (2.49)	23.99 (1.37)	5.6
CVC (ms) 12 weeks	26.33 (1.59)	23.87 (2.50)	25.36 (1.37)	16.8
Stress Reactivity Scale 0 weeks	27.03 (1.43)	27.24 (1.68)	27.11 (1.09)	4.7
Stress Reactivity Scale 12 weeks	20.90 (1.22)	27.21 (1.74)	23.38 (1.05)	19.6
Mindfulness (CAMS-R) 0 weeks	18.43 (0.75)	21.02 (0.87)	19.45 (0.58)	0
Mindfulness (CAMS-R) 12-weeks	19.67 (0.77)	20.69 (0.95)	20.07 (0.60)	13.3
Positive mental health 0 weeks	41.52 (1.41)	46.35 (1.61)	43.42 (1.08)	0
Positive mental health 12 weeks	45.91 (1.26)	47.20 (1.61)	46.42 (0.99)	13.3
Spiritual well-being 0 weeks	16.18 (0.78)	18.95 (0.92)	17.27 (0.61)	0
Spiritual well-being 12 weeks	16.26 (0.76)	19.01 (0.91)	17.34 (0.60)	13.3
Leisure time activity (METS) 0 weeks	42.27 (8.12)	61.44 (10.71)	49.76 (6.51)	0
Leisure time activity (METS) 12 weeks	56.95 (8.24)	47.30 (9.32)	53.16 (6.19)	13.3
Daily practice (min)	27.56 (1.92)			
% of days practice was logged	82.4 (2.45)			

Note. % of days practice was logged = the percentage of text messages responded to where participants indicated practicing MBSR. MBSR = mindfulness-based stress reduction; *SE* = standard error; C-SOSI = Calgary Symptoms of Stress Inventory; CVC = cardiac vagal control; CAMS-R = Cognitive and Affective Mindfulness Scale–Revised; METS = metabolic equivalents.

There was a significant Group × Time interaction on CVC, $F(1, 104) = 4.44$, $SEM = 15.39$, $p = .039$, $\eta_p^2 = .04$. Participants allocated to the MBSR group experienced significantly greater increases in CVC from 0 to 12 weeks, $M_{\text{Diff}} = 2.27$, relative to control, $M_{\text{Diff}} = -0.024$. This effect persisted after statistically adjusting for physical activity at 0 weeks, though the simplified model is presented for parsimony.

There was a significant Group × Time interaction on self-reported mindfulness, $F(1, 104) = 4.82$, $SEM = 10.12$, $p = .030$, $\eta_p^2 = .05$. Participants allocated to the MBSR group reported significantly greater increases in self-reported mindfulness from 0 to 12 weeks, $M_{\text{Diff}} = 1.23$, relative to control, $M_{\text{Diff}} = -0.034$.

There was a significant Group × Time interaction on self-reported stress reactivity, $F(1, 104) = 17.51$, $SEM = 10.36$, $p < .001$, $\eta_p^2 = .14$. Participants allocated to the MBSR group reported significantly greater reductions in stress reactivity from 0 to 12 weeks, $M_{\text{Diff}} = -6.14$, relative to control, $M_{\text{Diff}} = 0.61$.

There was a significant Group × Time interaction on self-reported positive mental health, $F(1, 104) = 6.91$, $SEM = 26.44$, $p = .010$, $\eta_p^2 = .06$. Participants allocated to the MBSR group reported significantly greater improvement in positive mental health from 0 to 12 weeks, $M_{\text{Diff}} = 4.54$, relative to control, $M_{\text{Diff}} = 0.61$.

There was no significant Group × Time interaction on spiritual well-being, $F(1, 104) = 0.015$, $SEM = 0.21$, $p = .901$, $\eta_p^2 = .00$, nor was there a main effect of time on spiritual well-being, $F(1, 104) = 0.022$, $SEM = 0.01$, $p = .882$, $\eta_p^2 = .00$.

Evaluating Mediators and Moderators of MBSR on Symptoms of Stress

Table 2 presents the results of univariate and multivariate models evaluating mediators and moderators of the effect of MBSR on symptoms of stress. Univariate models indicated that the change in symptoms of stress observed from 0 to 12 weeks was partially mediated by (a) change in CVC, (b) change in mindfulness, (c) change in perceived stress reactivity, and (d) change in positive mental health.

Univariate models indicated that neither preference for MBSR, daily minutes of practice, the percentage of days where a text message was responded to during which participants indicated

Table 2
Mediators and Moderators of the Effects Observed for MBSR on Change in Symptoms of Stress

Variable	Coefficient (*SE*)	95% CI	Total effect coefficient	Total effect 95% CI	Direct effect coefficient	Direct effect 95% CI	Indirect effect coefficient	Indirect effect 95% CI	R^2
Univariate model									
CVC	0.012 (0.006)*	[0.0001, 0.023]	0.273 (0.04)	[0.19, 0.35]	0.299 (0.04)	[0.22, 0.38]	−0.027 (0.017)	[−0.06, −0.001]	.12
Mindfulness	−0.038 (0.007)**	[−0.052, −0.025]	0.273 (0.04)	[0.19, 0.35]	0.226 (0.03)	[0.16, 0.29]	0.047 (0.024)	[0.003, 0.099]	.37
Stress reactivity	0.026 (0.003)**	[0.020, 0.033]	0.273 (0.04)	[0.19, 0.35]	0.112 (0.04)	[0.04, 0.18]	0.161 (0.035)	[0.100, 0.230]	.55
Positive mental health	−0.022 (0.005)**	[−0.032, −0.013]	0.273 (0.04)	[0.19, 0.35]	0.175 (0.04)	[0.10, 0.25]	0.098 (0.030)	[0.046, 0.162]	.31
Preference for MBSR	0.054 (0.075)	[−0.098, 0.205]							.01
Daily minutes practiced	0.003 (0.003)	[−0.002, 0.009]							.02
% of days practice was logged	0.003 (0.002)	[−0.001, 0.008]							.02
Sex	0.004 (0.081)	[−0.159, 0.167]							.00
Multivariate model									.64
CVC	0.005 (0.004)	[−0.002, 0.013]	0.273 (0.04)	[0.19, 0.35]	0.126 (0.04)	[0.05, 0.20]	−0.012 (0.010)	[−0.035, 0.006]	
Mindfulness	−0.019 (0.006)**	[−0.032, −0.007]	0.273 (0.04)	[0.19, 0.35]	0.126 (0.04)	[0.05, 0.20]	0.023 (0.014)	[0.001, 0.054]	
Stress reactivity	0.021 (0.004)**	[0.014, 0.028]	0.273 (0.04)	[0.19, 0.35]	0.126 (0.04)	[0.05, 0.20]	0.114 (0.031)	[0.060, 0.178]	
Positive mental health	−0.005 (0.005)	[−0.014, 0.004]	0.273 (0.04)	[0.19, 0.35]	0.126 (0.04)	[0.05, 0.20]	0.021 (0.021)	[−0.016, 0.064]	

Note. $N = 65$. MBSR = mindfulness-based stress reduction; *SE* = standard error; CI = confidence interval; CVC = cardiac vagal tone.
* $p < .05$. ** $p < .01$.

practicing MBSR, nor sex were significant moderators of change in symptoms of stress observed from 0 to 12 weeks.

The multivariate mediation model evaluating change in symptoms of stress from 0 to 12 weeks was significant, $F(8, 56) = 12.68$, $SE = 0.043$, $R^2 = .64$. Change in mindfulness and stress reactivity, but not CVC nor positive mental health, were partial mediators of change in symptoms of stress from 0 to 12 weeks (refer to Table 2).

Evaluating Mediators and Moderators of MBSR on CVC

Table 3 presents the results of univariate models evaluating mediators and moderators of the effect of MBSR on change in CVC from 0 to 12 weeks. Univariate models indicated that change in CVC observed between 0 and 12 weeks was partially mediated by (a) change in symptoms of stress and (b) change in positive mental health. Neither change in metabolic equivalents, mindfulness, nor perceived stress reactivity mediated the change observed in CVC from 0 to 12 weeks.

Univariate models indicated that neither preference for MBSR, daily minutes of practice, the percentage of days where a text message was responded to during which participants indicated practicing MBSR, nor sex were significant moderators of change in CVC observed from 0 to 12 weeks.

The multivariate mediation model evaluating change in CVC from 0 to 12 weeks was not significant, $F(4, 60) = 2.06$, $SE = 46.92$, $p = .097$, $R^2 = .12$.

Discussion

We sought to identify pathways that accounted for the effects of MBSR on self-reported and physiological indices of stress, along with effect modifiers. Participants allocated to MBSR evidenced significantly greater improvement in symptoms of stress, mindfulness, and self-reported reactivity to stressors relative to wait-list control. These results are consistent with systematic reviews of the effects of MBSR interventions among nonclinical samples. Querstret et al. (2020) reported that MBSR resulted in improvement in stress, $N = 17$, $g = -0.45$, 95% CI [−0.59, −0.30]; nonreactance (i.e., lower stress reactivity), $N = 4$, $g = 0.37$, 95% CI [0.10, 0.64]; and

Table 3
Mediators and Moderators of the Effects Observed for MBSR on Change in Cardiac Vagal Control

Variable	Coefficient (*SE*)	95% CI	Total effect coefficient	Total effect 95% CI	Direct effect coefficient	Direct effect 95% CI	Indirect effect coefficient	Indirect effect 95% CI	R^2
Univariate model									
METS	−0.005 (0.018)	[−0.042, 0.032]	−2.27 (0.88)	[−4.02, −0.52]	−2.33 (0.94)	[−4.21, −0.45]	0.07 (0.07)	[−0.48, 0.71]	.00
Symptoms of stress	6.43 (2.70)*	[1.03, 11.83]	−2.27 (0.88)	[−4.02, −0.52]	−4.03 (1.13)	[−6.28, −1.78]	1.75 (0.79)	[0.30, 3.41]	.09
Mindfulness	−0.27 (0.18)	[−0.64, 0.10]	−2.27 (0.88)	[−4.02, −0.52]	−2.61 (0.90)	[−4.41, −0.80]	0.33 (0.31)	[−0.11, 1.08]	.03
Stress reactivity	0.14 (0.11)	[−0.07, 0.35]	−2.27 (0.88)	[−4.02, −0.52]	−3.13 (1.09)	[−5.31, −0.94]	0.86 (0.67)	[−0.43, 2.25]	.03
Positive mental health	−0.27 (0.12)*	[−0.51, −0.03]	−2.27 (0.88)	[−4.02, −0.52]	−3.46 (1.00)	[−5.47, −1.46]	1.19 (0.60)	[0.13, 2.48]	.08
Preference for MBSR	−2.27 (1.63)	[−5.55, 1.01]							.04
Daily minutes practiced	0.05 (0.06)	[−0.07, 0.16]							.01
% of days practice was logged	0.033 (0.045)	[−0.057, 0.123]							.01
Sex	1.35 (1.76)	[−2.17, 4.87]							.01
Multivariate model									.12
Symptoms of stress	4.99 (3.21)	[−1.43, 11.40]	−2.27 (0.88)	[−4.02, −0.52]	−4.33 (1.14)	[−6.62, −2.03]	1.36 (0.91)	[−0.33, 3.25]	
Positive mental health	−0.16 (0.14)	[−0.44, 0.12]	−2.27 (0.88)	[−4.02, −0.52]	−4.33 (1.14)	[−6.62, −2.03]	0.70 (0.64)	[−0.46, 2.02]	

Note. $N = 65$. MBSR = mindfulness-based stress reduction; *SE* = standard error; CI = confidence interval; METS = metabolic equivalents.
* $p < .05$.

mindfulness, $N = 6$, $g = 0.44$, 95% CI [0.22, 0.65], relative to nonactive control groups (Querstret et al., 2020). Similarly, online-delivered mindfulness-based interventions, including eight RCTs reporting on 1,316 nonclinical participants, demonstrated medium effects on perceived stress, $g = 0.43$, 95% CI [0.21, 0.67] (Jayewardene et al., 2017). Moreover, improvement in long-term CVC was observed among participants allocated to MBSR relative to wait-list control in the present study, which provides the most robust evidence within a community sample to date. Of note, one review identified 19 RCTs evaluating the effect of mindfulness-based interventions on CVC and reported no significant difference pre- to postintervention, $g = 0.38$, 95% CI [−0.014, 0.770] (Brown et al., 2021). Importantly, only two RCTs evaluated the effect of MBSR with long-term CVC (i.e., 24 hr), one within 168 people who lived with fibromyalgia and another within 19 people who experienced heart palpitations.

Improvement in CVC observed in the present investigation acted as a suppressor variable that, when considered, allowed for a more complete understanding of the possible mechanism underlying improvement in symptoms of stress (MacKinnon et al., 2000). This analysis supports a physiological stress resilience pathway of mindfulness training that operates in part through modulation of parasympathetic nervous system activity and suggests that CVC and symptoms associated with chronic stress emerge from a common biopsychological process, which we posit to be an increase in functional connectivity within stress regulatory regions of the CAN (Benarroch, 1993). It is important to note that we assessed the effect of MBSR on basal parasympathetic activity, which is indicative of a physiological regulatory pathway, as opposed to a reactivity pathway, which would be best approximated through a change in parasympathetic activity occurring in response to a discrete stressor. Further, the present investigation focused on the first layer (i.e., parasympathetic activity) of the multilayered human stress response system (i.e., sympathetic and hypothalamic–pituitary–adrenal axis activity), and the physiological pathways that mediate the effects of MBSR on health may be best understood through an evaluation of the dynamic interplay between the stress response systems.

The results observed in this investigation supported the presence of a psychological mechanistic pathway. Participation in MBSR resulted in significant improvement in symptoms associated with stress, which were partially mediated by a concomitant increase in mindfulness. This observation is consistent with evidence from meta-analytic investigations (Visted et al., 2015) and suggests that the cultivation of nonjudgmentally present-focused awareness is one important stress-buffering impact of mindfulness-based interventions. In addition, improvement in self-reported reactivity to stressors partially mediated improvements in symptoms of stress, supporting the notion that mindfulness-based interventions operate through appraisals of stressors (Creswell et al., 2019). Similarly, the mediating role of positive mental health provides support for a psychological mechanism of mindfulness-based interventions (i.e., the cultivation of positive psychosocial resources). Interestingly, participation in MBSR did not result in appreciable change in spiritual well-being, which could indicate that spirituality does not represent a positive psychosocial resource trained by MBSR. This interpretation is at odds with evidence from a meta-analysis of 13 controlled trials that reported increased spirituality as a result of participation in secular mindfulness-based programs (Landau & Jones, 2021). Alternatively, clergy may represent a group practiced in spirituality and have little room for improvement as a result of participation in MBSR.

Participants engaged in MBSR practiced an average of 27.5-min/day, which is below the recommended 45-min of practice (Kabat-Zinn & Hanh, 2009). This estimate is consistent with a recent review of 43 ($N = 1,427$) studies that reported an average daily at-home practice duration of about 30 min (Parsons et al., 2017). Small to moderate associations were observed between home practice duration and intervention outcomes within this review, $r = .26$; 95% CI [0.19, 0.34] (Parsons et al., 2017). In the present study, the effects of MBSR were not moderated by minutes practiced per day, nor the percentage of days during which practice occurred, which could be due to insufficient statistical power, or a sample with relatively homogenous practice patterns. Alternatively, these results suggest that there may not be a single ideal number of practice minutes for MBSR (Creswell, 2017).

Participant ratings of acceptability and preference for MBSR did not moderate treatment effects in the present investigation. This observation is inconsistent with a meta-analysis of 46 independent studies ($N = 8,016$), which indicated that perceptions of treatment plausibility and expectancy of treatment outcomes had a small but significant impact on treatment outcomes, $d = 0.24$ (Constantino et al., 2011). Similarly, allocation to a preferred intervention has been associated with improved outcomes among RCTs (Delevry & Le, 2019). It is important to note that participants in the Selah trial were allocated to their preferred intervention, and outcome expectancies were not measured in a robust manner. As such, the effects of MBSR may operate independently of preferences and expectancy (see also Haddad et al., 2020), or such effect modifiers may be more nuanced. For example, research suggests that such effects may be driven by treatment adherence and improved therapeutic alliance (Constantino et al., 2021; Windle et al., 2020), which may not have impacted outcomes in the Selah trial where MBSR was delivered online and adherence to recommendations was homogeneous.

Limitations

First, this study was characterized by a relatively small sample size through which to examine mediation or moderation of treatment effects and can be considered underpowered. As a frame of reference, an estimated 123 participants would be required to detect mediation with small to medium effect sizes for b_a and b_b pathways using two observations, bootstrapping estimation, and an intraclass correlation coefficient of .40 (Pan et al., 2018). Second, a theoretically informed actuarial approach was used to evaluate mediators and moderators of the effects of MBSR. This involved testing potential mediators and moderators in univariate models before multivariate analysis. No adjustments were made to correct for inflation in family-wise error. Third, rigorous intervention fidelity checks were not performed; although the interventions were delivered by certified MBSR instructors, all instructors followed the same materials throughout the trial, and daily practice patterns were obtained through text messaging. Fourth, all available data were used, including data from the trial cohort and the observational cohort. On an encouraging note, most participants were drawn from the trial cohort, and results did not appreciably change when data were excluded from participants who provided intervention data following participation in the wait-list control group. Fifth, the sample was relatively homogeneous, from a single profession and from a single geographic area, which limits generalizability. Finally, we did not evaluate indicators of a behavioral stress resilience mechanistic pathway of MBSR, which prevented interrogation of all theorized pathways in the mechanistic stress buffering framework.

Conclusions

Change in symptoms of stress and CVC evidenced bidirectional relationships, providing evidence in support of a central, biological stress resilience pathway of MBSR. At the same time, improvement in mindfulness and perceived reactivity to stressors were psychological mechanisms observed to underpin the effect of MBSR on stress. It is unclear which mindfulness practices target these putative mechanisms most efficiently. The effects of MBSR were not moderated by intervention preference or home-based practice.

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