Effect of Meditation on Endothelial Function in Black Americans With Metabolic Syndrome: A Randomized Trial

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Objectives: Psychological stress may play a role in metabolic syndrome. A consequence of metabolic syndrome is endothelial dysfunction, which is also influenced by psychological stress. We sought to compare the effect of consciously resting meditation (CRM), a sound based meditation, with a control intervention of health education (HE) on endothelial function in the setting of metabolic syndrome. **Methods:** Sixty-eight black Americans with metabolic syndrome risk factors (age, 30–65 years) were randomized to either CRM ($n = 33$) or HE ($n = 35$); interventions were matched for frequency and duration of sessions and lasted 12 months. Endothelial function was assessed by brachial artery flow-mediated dilation at baseline and at 6 and 12 months. Arterial elasticity, metabolic risk factors, and psychosocial and behavioral variables were secondary end points. **Results:** Although flow-mediated dilation improved in the CRM group for 12 months, this increase was not significantly higher than that in the HE group ($p = .51$ for the interaction between group and time). Non–endothelium-dependent dilation and arterial elasticity did not change in either group. Most metabolic syndrome risk factors showed beneficial trends in the CRM group only. A risk factor score counting the number of metabolic syndrome components decreased in the CRM group only ($p = .049$ for the interaction between treatment group and time). **Conclusions:** Among black Americans with metabolic syndrome risk factors, CRM, did not improve endothelial function significantly more than a control intervention of HE. CRM resulted in favorable trends in metabolic syndrome risk factors, which were examined as secondary outcomes. **Key words:** Endothelium, stress, metabolic syndrome, obesity.

BP = blood pressure; **CRM** = consciously resting meditation; **CRP** = C-reactive protein; **CVD** = cardiovascular disease; **FMD** = flow-mediated dilation; **HE** = health education; **PWV** = pulse-wave velocity; **NMD** = nitroglycerin-mediated vasodilation; **TM** = transcendental meditation.

INTRODUCTION

Cardiovascular disease (CVD) and its complications carry a significantly higher morbidity and mortality in black Americans compared with white Americans. One factor likely to play a role is obesity, which is more prevalent in black Americans and is associated with insulin resistance and other cardiometabolic risk factors including elevated blood pressure (BP), elevated fasting glucose, and dyslipidemia (1,2). It is anticipated that the explosive epidemic of obesity, which is particularly a problem in the Southeast region of the nation, will trigger an increase in CVD, as already observed for hypertension (2) and Type 2 diabetes (3). These trends herald a further widening of the gap in black-white differences in CVD morbidity and mortality.

Although the etiology of insulin resistance is complex, psychological stress may play a role through increasing inflammation and other metabolic and hormonal abnormalities (4). A major consequence of insulin resistance is endothelial dysfunction (5), an early marker of CVD that is also influenced by psychological stress (6–8). Insulin resistance is thought to affect endothelial function through impaired endothelial nitric oxide synthase activity caused by excess superoxide anion formation in vascular endothelial cells (9,10).

Previous controlled clinical studies have suggested that mind-body interventions for stress reduction that used a variety of meditation techniques may reduce psychological stress and improve CVD risk factors in blacks and whites, although results are heterogeneous (11). Of various meditation techniques, transcendental meditation (TM) (12–15) and breathing awareness meditation (16–18) have been widely used in studies of black Americans and show promise in reducing BP in this population. In addition to elevated BP, it is possible that meditation approaches are beneficial in reducing other adverse consequences of obesity and metabolic syndrome, including endothelial dysfunction, inflammation, and insulin resistance. These effects, however, have never been evaluated in community- dwelling blacks. We therefore conducted a randomized controlled trial among black Americans with metabolic syndrome risk factors to test the hypothesis that consciously resting meditation (CRM), a novel sound (mantra)-based meditation, improves vascular function and metabolic risk profile in participants with metabolic syndrome risk factors compared with a control arm of health education (HE) matched for frequency and duration of sessions. The primary outcome was endothelial function as measured by ultrasound assessment of flow-mediated dilation (FMD) of the brachial artery. Secondary outcomes included measures of arterial elasticity, metabolic syndrome risk factors, psychosocial and behavioral measures (symptoms of anxiety, depression, perceived stress, anger, and hostility, and physical activity), and inflammatory and metabolic biomarkers.

METHODS
Study Design

This trial was part of the "Emory-Morehouse Partnership to Reduce CV Disparities" (U01HL079214), also known as META-Health. The overall goal

of this research program was to characterize potential racial/ethnic differences in obesity-related cardiovascular risk. The present study was a single-site, parallel-group randomized controlled trial. The trial was technically single blinded given that patients were aware of which intervention they were assigned to (CRM or HE). However, participants were masked to the research hypothesis, and both interventions were presented to participants as health promoting; this design should minimize expectation bias (11). Investigators and the staff collecting the data were blinded to the treatment status of the participants. The two treatment providers were not involved with participant recruitment, data collection, analysis, or interpretation. The study was approved by the Emory University and Morehouse University institutional review committees. Informed consent was obtained from all participants.

Selection of Participants

Participants were recruited from the community in metropolitan Atlanta through flyers and at health fairs, churches, university campuses, and other community locations, as well as through direct referrals. They were included in the trial if they were between the ages of 30 and 65 years, self-identified as black, and met specific criteria for metabolic syndrome. According to current Adult Treatment Panel III guidelines (19), metabolic syndrome is defined as having at least three of five of the following criteria: abdominal obesity (waist circumference >102 cm in men and >88 cm in women); triglycerides of 150 mg/dL or greater, high-density lipoprotein (HDL) cholesterol less than 40 mg/dL in men and less than 50 mg/dL in women, BP of at least 130 (systolic) and at least 85 (diastolic) mm Hg, and fasting glucose of 100 mg/dL or greater. However, these criteria have not been extensively validated in the black population. A paradoxical observation is that black Americans meet the metabolic syndrome criteria less often than do whites, despite a higher prevalence of obesity, hypertension, and insulin resistance (20), partly because of a lower triglycerides/HDL ratio (21,22). Thus, there is concern that current metabolic syndrome definitions may underestimate risk in black Americans (23,24). Based on this, in addition to the standard definition above, participants were eligible if they met a modified definition that did not include the lipid criteria, but they met two of the following three criteria: abdominal obesity (waist circumference >102 cm in men and >88 cm in women), BP of at least 130 (systolic) and at least 85 (diastolic) mm Hg, and fasting glucose of 100 mg/dL or greater. Participants were excluded if they had known CVD or renovascular disease; if they had uncontrolled hypertension (systolic BP >160 mm Hg on two or more occasions or diastolic BP >105 mm Hg); if they were current smokers or had been taking over-the-counter vitamins such as vitamin A, C, or E within 3 days of study initiation (because these can affect endothelial function assessments); if they were pregnant; and if they had a documented history of alcohol or drug abuse or other psychiatric or medical diagnoses that would interfere with ability to attend training sessions and clinic visits for 1 year.

Study Protocol

After they were prescreened for eligibility over the telephone, potential participants attended a screening visit (Visit 1). After participants signed the informed consent form, research staff obtained fasting blood, BP measurements, and anthropometric data to verify the inclusion criteria. Qualifying participants were then invited to a baseline visit (Visit 2) within 2 weeks, where a number of measures were obtained, including vascular function testing, BP, anthropometry, and study questionnaires. After completion of baseline assessments, participants were randomized to one of two treatment groups by blocked randomization with stratification on sex. The random allocation sequence was provided in sealed envelopes by the study statistician (who had no contact with participants) to a staff member not involved in data collection. Patients were randomized in subsequent cohorts of participants, with a minimum of 10 and a maximum of 20 in each randomization cohort (yielding no more than 10 participants per group who would start the program at any one time), for a total of five cohorts. All outcome data were collected in a blinded fashion with respect to the participants' treatment status. Follow-up visits for outcome assessments were performed at 6 months (Visit 3) and 12 months (Visit 4) after baseline. Three BP measurements were obtained at each visit (25). Anthropometric measures including height, weight, and waist circumference were measured, and fasting blood was also drawn for laboratory assessments. Visits 1 through 4 took place in the Cardiovascular Research Unit at the Emory University Hospital.

Participant recruitment started on June 7, 2007, and the follow-up of the last randomized cohort ended on January 11, 2010.

Interventions

Both interventions were administered in the National Center for Primary Care at Morehouse School of Medicine, by providers not involved with participant recruitment, data collection, analysis, or interpretation. CRM is a sound- or mantra-based meditation. This meditation approach was chosen because of its standardized protocol and its similarity to the TM program, which has been previously successfully implemented in black American samples. Both TM and CRM use sounds that have no meaning, but their quieting effects have been known for thousands of years. These sounds, when used properly, settle the mind and body down to a state of restful alertness. As with many TM studies, the CRM program included 21 sessions during a 1-year intervention period where participants learned the technique of consciously resting their mind and body. The core instruction involves a four-step course for four consecutive days (Sessions 1–4) and a follow-up program for 12 months (Sessions 5–21). Most sessions last 1 to 1.5 hours, and the general format is group meditation plus a lecture/discussion or videotape. In contrast to TM, CRM does not include a private Sanskrit ceremony, which has been a major objection for inner-city meditation projects. In addition, in contrast to TM, CRM can be taught in groups, is less time consuming for participants, and is potentially more affordable, making it more accessible and easier to disseminate among minority groups. All sessions were taught by the same experienced teacher (K.A.K.). Participants were instructed to practice CRM twice a day for 20 minutes. Participants were also given the same HE reading materials given to the control group.

Participants randomized to HE attended the same number, size, and frequency of group meetings lead by a professional health educator (L.B.). The program included information on prevention of CVD through life-style modification and was modeled on educational material disseminated by the American Heart Association (www.americanheart.org). Topics included the value of a healthy diet, exercise, and weight management. The impact of stress was discussed as it relates to weight management and physical exercise. However, to avoid contamination in the experimental design, the HE sessions did not include instructions on stress reduction or relaxation techniques. To match the 20-minute twice-a-day CRM practice, participants were instructed to undertake a 20-minute twice-a-day home practice session, applying the recommendations given in this course—diet, exercise, or other life-style habits.

Primary Outcome

Endothelium-dependent FMD of the brachial artery was the primary outcome of the trial. It was measured according to established methodology (26) by using an Acuson 10-mHz linear-array transducer and an Acuson Aspen ultrasound system. We imaged the participants after they had rested in a supine position for at least 10 minutes in a quiet setting. Optimal brachial artery images were obtained 2 to 10 cm above the antecubital crease. This location was marked, and all subsequent images were obtained at the same location. After baseline measurements, a BP cuff was inflated to 200 mm Hg over the proximal portion of the right arm for 5 minutes. Endothelium-dependent function was determined during the first 2 minutes of release of the cuff. The flow-dependent response was then allowed to return to baseline over a period of 5 minutes.

Four triggered events (defined as the end of the T wave on the electrocardiogram) were recorded. Each triggered event consisted of three sequential frames, for a total of 12 images. These were subsequently downloaded to an analysis system that allows automatic edge detection of the M-line that defines the intima-media interface for both the near wall and the far wall of the artery through the use of customized software (Medical Imaging Applications Inc, Missouri Valley, IA). Measurements from the 12 frames were averaged. In our laboratory, the mean (standard deviation [SD]) difference and in FMD between assessments performed in 11 participants on consecutive days was 1.26% (0.76%), with a correlation coefficient of 0.75. The mean (SD) difference in the FMD between two readings of the same 11 measurements was 0.82% (0.48%; $r = 0.97$).

Secondary Outcomes

Endothelium-independent nitroglycerin-mediated vasodilation (NMD) and arterial stiffness were secondary vascular outcomes. NMD was evaluated as a
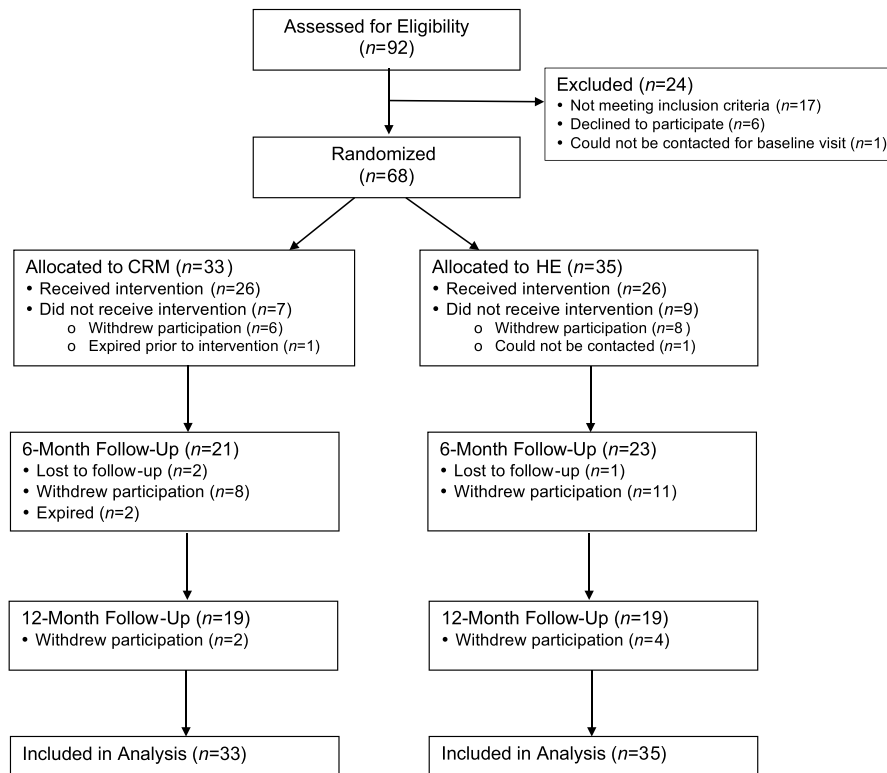
Figure 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram for enrollment and follow-up of study participants. CRM = consciously resting meditation; HE = health education.

control condition for FMD 3 minutes after administration of 0.4 mg of nitroglycerin sublingually. Data acquisition was done in a similar manner. The end point of measurement was the percent change in diameter in response to endothelium-independent NMD (NMD%).

Arterial stiffness was assessed by means of pulse-wave velocity (PWV) and radial pulse-wave analysis by using the SphygmoCor Pulse Wave Velocity system (PWV Medical, West Ryde, NSW, Australia). Peripheral pressure waveforms were recorded from the radial artery at the wrist by using applanation tonometry with a high-fidelity micromanometer. After 20 sequential waveforms were acquired, a validated generalized transfer function was used to generate the corresponding central aortic pressure waveform (27). PWV was calculated as the velocity of the BP waveform between carotid and femoral arteries. Transcutaneous Doppler flow velocity recordings were carried out simultaneously at the base of the neck over the common carotid artery and at the femoral artery in the groin, and the time delay (t) as well as the distance (d) traveled by the pulse wave were measured between the two recording sites with the use of established methods (27). PWV was calculated as $PWV = d/t$. In addition, we obtained the augmentation index (AI) from pulse-wave analysis. The merging point of the incident and the reflected wave (the inflection point) was identified on the aortic pressure waveform. The AI is defined as the augmented pressure (the maximal systolic pressure minus the pressure at the inflection point) divided by pulse pressure and expressed as a percentage. Larger values of AI indicate increased wave reflection from the periphery or earlier return of the reflected wave because of increased PWV, an indication of increased arterial stiffness. Reproducibility studies in our laboratory on consecutive days have demonstrated a coefficient of variation of 20.3% and 3.8% for AI and PWV, respectively.

Psychosocial and behavioral factors were measured as secondary outcomes and included psychosocial stress, measured by means of the Cohen Perceived Stress Scale (28); hostility, by means of the Cook-Medley Hostility Inventory (29); anger, by using the Spielberger Anger Expression Inventory (30); anxiety, by using the Spielberger State-Trait Anxiety Inventory (STAI) (31); and depressive symptoms, by using the Beck II Depression Inventory (32), including two subscales of the Beck II Depression Inventory that meant to capture two distinct dimensions of depression, the cognitive/affective subscale and the

somatic subscale (33). Physical activity was measured using the CAPS Typical Week Physical Activity Survey, a 28-item questionnaire that has been validated in diverse ethnic populations (34). This instrument provides total time spent in light physical activity (<3 metabolic equivalents [METs]), moderate physical activity (3–6 METs), and vigorous physical activity (>6 METs) in a typical week (34). In our analysis, we focused on moderate and vigorous physical activity; because these were highly skewed, log transformation was performed before analysis. Compliance with the interventions was measured by class attendance, as indicated by signed attendance sheets.

Metabolic profile. As additional secondary outcomes, we assessed changes in levels of *metabolic syndrome risk factors* including abdominal obesity, fasting plasma lipids (triglycerides and HDL cholesterol), BP, and fasting plasma glucose. We also computed a score counting the number of metabolic syndrome risk factors meeting the criteria for metabolic syndrome definition at baseline and at each of the follow-up visits. In addition, we assessed changes in *metabolic and inflammatory biomarkers* including leptin, adiponectin, C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor α, and plasminogen activator inhibitor 1 (PAI-1). Blood was drawn after an overnight fast. We measured CRP levels and quantified using the Dade-Behring Nephelometry System–BNII. All the other biomarkers were measured using the Fluorokine MultiAnalyte Profiling Human Obesity Base Kits from R&D Systems (Minneapolis, MN) on a Luminex 200 Bio-Plex platform (Bio-Rad, Hercules, CA). The biomarker assays were done in the Division of Hereditary Blood Disorders at the Centers for Disease Control and Prevention.

Statistical Analysis

Data were analyzed following the intention-to-treat principle; that is, all available data were analyzed on randomized participants ($n = 68$), irrespective of whether they received the intervention or completed the study (35). All outcomes (FMD and secondary outcome measures) were analyzed as continuous variables by using repeated-measures mixed-effects models (36) with treatment group, time point, and other study factors treated as fixed effects. The model-based means are unbiased with unbalanced and missing data, so long as the missing data are noninformative (missing at random) (37). Physical activity

TABLE 1. Baseline Demographics and Risk Factors by Intervention Group

Measure	CRM (n = 33)	HE (n = 35)
Demographic factors		
Age, M (SD), y	51.5 (7.5)	52.1 (7.6)
Male, %	25.0	17.1
Married, %	37.5	34.3
More than high school education, %	76.7	78.1
Metabolic risk factors and medical history		
Body mass index, M (SD), kg/m²	38.2 (11.2)	36.7 (5.6)
Systolic blood pressure, M (SD), mm Hg	138.5 (22.2)	137.5 (21.4)
Diastolic blood pressure, M (SD), mm Hg	83.2 (13.1)	83.5 (12.2)
Heart rate, M (SD), beat/min	73.7 (11.8)	70.9 (13.7)
LDL cholesterol, M (SD), mg/dL	117.3 (32.8)	121.0 (44.0)
HDL cholesterol, M (SD), mg/dL	54.1 (15.3)	55.0 (11.1)
Triglycerides, M (SD), mg/dL	137.9 (80.8)	102.7 (50.2)
Creatinine, M (SD), mg/dL	0.96 (0.31)	0.84 (0.25)
Glucose, M (SD), mg/dL	116.8 (57.4)	100.3 (38.3)
Insulin, M (SD), μIU/mL	18.3 (31.1)	14.1 (12.9)
History of diabetes, %	45.5	41.2
HOMA index	1.04	0.92
Family history of heart disease before age 55 y, %	37.9	39.4
Moderate physical activity, M (SD), min/d	167 (228)	230 (242)
Vigorous physical activity, M (SD), min/d	10.5 (23.8)	38.3 (75.9)
Medications		
On aspirin, %	21.2	14.3
On statins, %	45.5	25.7
On β-blockers, %	18.2	20.0
On ACE inhibitors, %	27.3	28.6
Psychosocial risk factors		
Spielberger Anger-in, M (SD)	14.4 (3.9)	14.0 (4.0)
Spielberger Anger-out, M (SD)	12.9 (3.4)	13.0 (2.5)
Cook-Medley Hostility Inventory, M (SD)	17.2 (8.1)	18.0 (7.4)
Cohen's Perceived Stress Scale, M (SD)	14.8 (8.4)	17.4 (8.6)
Spielberger State Anxiety, M (SD)	36.8 (13.2)	40.0 (14.1)
Spielberger Trait Anxiety, M (SD)	38.2 (11.9)	39.5 (12.4)
Beck Depression Inventory II, M (SD)	10.9 (7.7)	11.0 (9.7)
Beck Depression Somatic Subscore, M (SD)	0.64 (0.44)	0.59 (0.48)
Beck Depression Cognitive Subscore, M (SD)	2.6 (3.1)	3.3 (3.9)

CRM = consciously resting meditation; HE = health education; M= mean; SD = standard deviation; LDL= low-density lipoprotein; HDL = high-density lipoprotein; HOMA = homeostasis model assessment; ACE = angiotensin-converting enzyme.

scores and biomarker data (CRP, IL-6, adiponectin, and PAI-1) were log transformed for analysis when distribution deviated significantly from normality. Because of the lack of preliminary data on the effect of meditation on FMD at the time the study was conceived, we based our sample size on an estimated effect of 3% absolute increase in flow caused by CRM, compared with HE, an SD for FMD in middle-aged individuals of 3.7%, an α of .05 (2-tailed), a β of .80, and an attrition rate of 20%. On the basis of these estimates, 30 participants per group were needed to show a significant difference in FMD between the two groups.

RESULTS

Of 105 potentially eligible participants as determined through telephone prescreening, 92 attended the screening visit to assess eligibility. As shown in Figure 1, of these 92 patients, 68 were randomized to either CRM (n = 33) or HE (n = 35). Of the randomized patients, 21 and 23 participants in the CRM and

HE groups, respectively, attended the 6-month visit and 19 in each group attended the 12-month visit. There was no significant difference in dropout rate between the two randomized groups. There were also no significant differences in any baseline measures comparing participants who dropped out with those who did not drop out. Compliance, assessed by class attendance averaged throughout the 12 months (21 sessions), was also similar: 50% in the CRM group and 51% in the HE group. No adverse events caused by the intervention were reported.

Most participants (82%) were obese (body mass index [BMI] ≥30 kg/m²). Table 1 shows the baseline characteristics of the participants by randomization group. The sample was middle-aged and predominantly female. Participants in the CRM group had higher triglyceride levels (138 [81] mg/dL

TABLE 2. Changes in Flow-Mediated Vasodilation (FMD) and Metabolic Risk Factors by Study Group

Variable	Study Group	Study Visit, M (SD) Baseline	6 mo	12 mo	Change, Baseline to 12 mo (95% CI)[a]	p Value for Trend Within Group	p Value for Group Difference in Trend
FMD%	CRM	3.9 (2.4)	4.8 (2.7)	6.3 (3.3)	2.10 (0.53–3.67)	.009	.51
	HE	5.1 (4.2)	5.6 (4.4)	5.8 (3.4)	1.36 (−0.24 to 2.95)	.094	
SBP, mm Hg	CRM	138.2 (22.3)	135.9 (20.5)	129.6 (11.1)	−3.84 (−13.07 to 5.38)	.41	.78
	HE	137.5 (21.5)	132.7 (25.2)	133.4 (20.1)	−2.08 (−11.02 to 6.86)	.64	
DBP, mm Hg	CRM	83.1 (13.0)	83.1 (15.8)	74.1 (11.1)	−6.24 (−11.71 to −0.77)	.026	.17
	HE	83.5 (12.2)	79.6 (14.0)	82.3 (15.3)	−0.97 (−6.27 to 4.33)	.72	
Weight, kg	CRM	104.8 (32.7)	101.8 (30.9)	100.6 (23.2)	−2.52 (−0.20 to −4.83)	.033	.26
	HE	101.1 (15.1)	102.0 (15.5)	101.0 (16.8)	−0.69 (−1.51 to 2.89)	.54	
BMI, kg/m^2	CRM	37.7 (11.2)	36.8 (10.6)	37.5 (9.8)	−0.99 (0.13 to 1.86)	.025	.34
	HE	36.7 (5.6)	37.0 (0.0)	36.3 (4.9)	−0.43 (−0.38 to 1.23)	.29	
Glucose, mg/dL	CRM	117.5 (58.2)	138.5 (68.8)	111.2 (34.7)	−6.04 (−28.02 to 15.94)	.59	.095
	HE	100.3 (38.3)	112.4 (52.6)	128.1 (58.9)	20.86 (−1.90 to 43.63)	.072	
Insulin, μIU/mL	CRM	18.2 (31.6)	18.4 (21.3)	14.2 (9.6)	−1.13 (−9.12 to 6.85)	.78	.68
	HE	14.1 (12.9)	16.4 (14.8)	16.9 (24.7)	1.22 (−6.90 to 9.34)	.77	
Triglycerides, mg/dL	CRM	136.9 (81.9)	128.9 (57.8)	109.6 (36.6)	−14.35 (−31.75 to 3.06)	.10	.012
	HE	102.7 (50.2)	109.4 (58.1)	123.8 (90.1)	17.72 (−0.19 to 35.63)	.052	
HDL-C, mg/dL	CRM	54.2 (15.5)	55.7 (17.1)	57.1 (17.5)	1.47 (−2.04 to 4.97)	.41	.71
	HE	55.0 (11.1)	54.8 (9.7)	56.3 (12.2)	0.51 (−3.14 to 4.16)	.70	
Metabolic syndrome score	CRM	2.8 (1.1)	2.8 (1.1)	2.3 (1.2)	−0.41 (−0.89 to 0.06)	.089	.049
	HE	2.5 (0.8)	2.3 (1.0)	2.7 (1.2)	0.25 (−0.21 to 0.72)	.28	

M = mean; SD = standard deviation; CI = confidence interval; CRM = consciously resting meditation; HE = health education; SBP = systolic blood pressure; DBP = diastolic blood pressure; BMI = body mass index; HDL = high-density lipoprotein.
[a] Model estimates, adjusted for individual variance, obtained using repeated-measures mixed-effects models. Mean estimates for triglyceride are adjusted for baseline triglyceride values.

versus 103 [50] mg/dL). There were no significant differences in other baseline factors.

FMD and Other Vascular Outcomes

At baseline, there was no significant difference in mean (SD) FMD% between the CRM and the HE group (3.9% [2.4%] versus 5.1% [4.2%], p = .18). FMD% significantly improved in the CRM group during the 12-month intervention (mean change = 2.1%, 95% confidence interval [CI] = 0.5%–3.7%, p = .009), but less so in the HE group (mean change = 1.4%, 95% CI = −0.2% to 2.9%, p = .094) (Table 2 and Fig. 2). The interaction between group and time, however, was not significant (p = .51), denoting no significant difference in FMD change over time between the two groups. Non–endothelium-dependent dilation (%NMD) did not change in either group, and arterial elasticity measures (PWV and AI) were similarly unaffected (Fig. 3). Compliance assessed as class attendance was not correlated with change in FMD, both in the CRM group (Pearson r = −0.08, p = .79) and in the HE group (Pearson r = −0.21, p = .49).

Metabolic Syndrome Risk Factors

Virtually all the metabolic syndrome risk factors showed beneficial trends in the CRM group, whereas they showed less benefit or worsening in the HE group (Table 2). In the CRM arm, changes between baseline and 12 months were significant for

diastolic BP (−6.2 mm Hg, 95% CI = −11.7 to −0.8 mm Hg, p = .026) and weight (−2.5 kg, 95% CI = −4.8 to −0.2 kg, p = .033); in addition, the interaction between treatment arm and time was significant for triglyceride levels, after adjusting for baseline levels (p = .012), and marginally significant for fasting glucose (p = .095). The summation score counting the number of metabolic syndrome risk factors tended to decrease in the CRM group and to worsen in the HE group (p = .049 for the interaction between treatment group and time; Table 2).

Psychosocial and Behavioral Factors

Both interventions significantly improved depressive symptoms and STAI-State anxiety scores. STAI-Trait anxiety and Perceived Stress Scale scores were reduced slightly more in the HE group. No significant changes were observed in anger and hostility measures for both interventions (Table 3). Neither CRM nor HE was associated with significant changes in moderate physical activity. Vigorous physical activity, however, which was log transformed because of its skewed distribution, increased in the CRM group, from a geometric mean (SD) of 3.8 (4.2) to 9.1 (3.9) min/d (p = .023), whereas it tended to decrease in the HE group (from 10.5 [5.7] to 6.3 [4.3] min/d, p = .43; p = .032 for the interaction between group and time). The increase in physical activity, however, did not substantially explain the effect of CRM on FMD. The mean change in FMD in the CRM group decreased only slightly, from 2.1% (95%
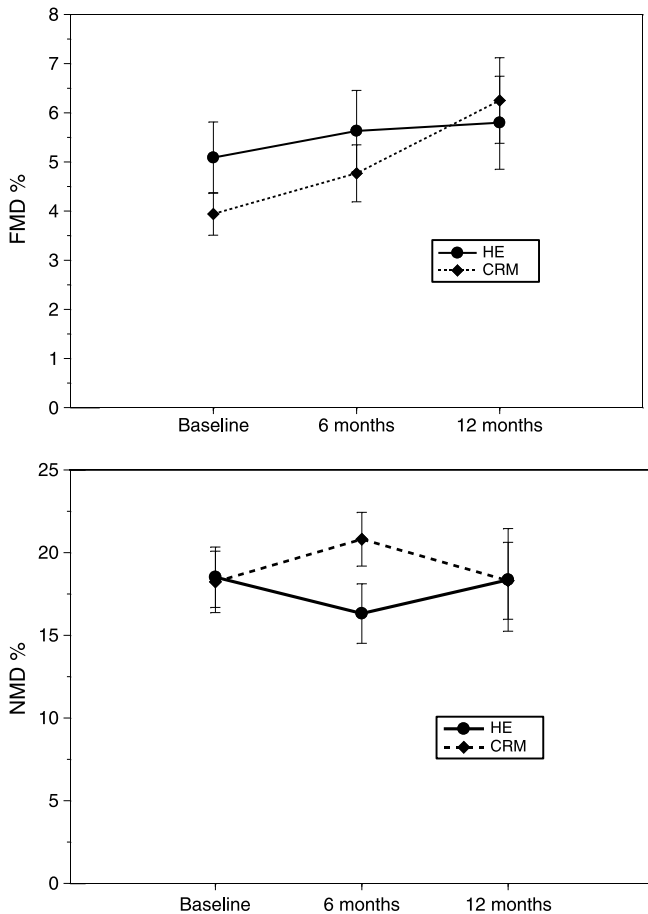
Figure 2. Brachial artery reactivity testing results by intervention group, including flow-mediated vasodilation (FMD%) and endothelium-independent nitroglycerin-mediated vasodilation (NMD%). HE = health education; CRM = consciously resting meditation.

CI = 0.5%–3.7%, p = .009) to 1.9% (95% CI = 0.3%–3.6%, p = .022) once vigorous physical activity was added to the model. Changes in BMI also did not contribute to the findings because there was no significant correlation between changes in BMI and changes in FMD (Pearson r = 0.04, p = .63).

Metabolic/Inflammatory Biomarkers

Biomarker data were available for 27 participants randomized to HE (82%) and 29 participants randomized to CRM (83%). Adiponectin was slightly higher in the HE than in the CRM group at baseline; there were no differences in the baseline levels of leptin or any of the inflammatory biomarkers (CRP, IL-6, tumor necrosis factor α, and PAI-1) between the two groups. Biomarker data did not change significantly in either group during the follow-up (Table 4).

DISCUSSION

Among black Americans with components of the metabolic syndrome, CRM, a sound-based meditation intervention, did not improve endothelial function significantly more than a control intervention of HE, which was matched to the CRM intervention for frequency of meetings and time with the instructor. In the

CRM group, several metabolic risk factors tended to improve at 12 months, whereas they did not improve or tended to worsen in the HE group, as did a cumulative metabolic risk score that included BP, weight, glucose, HDL cholesterol, and triglyceride levels. These effects occurred despite no substantial difference in the impact of the interventions on perceived stress and other psychosocial risk factors.

An innovative aspect of our study is the inclusion of an urban black population, a group that remains understudied. Although studies have linked chronic psychosocial and environmental stressors, such as social and economic disadvantage and discrimination, to CVD and its risk factors (38–41), these associations tend to be more pronounced among blacks (42,43). These differences may, in part, be mediated by race differences in autonomic nervous system responses and behavioral and psychosocial factors such as depression and anger expression (39,44,45). For example, community-dwelling blacks have higher rates of discrimination ratings and depressive symptoms than do whites (42,46–48), and these factors tend to be more predictive of hypertension and CVD in blacks than in whites (42,48–50).

Our results are in agreement with previous clinical trials of stress reduction interventions that used meditation and that showed beneficial effects on CVD risk factors (13,51). Recently,
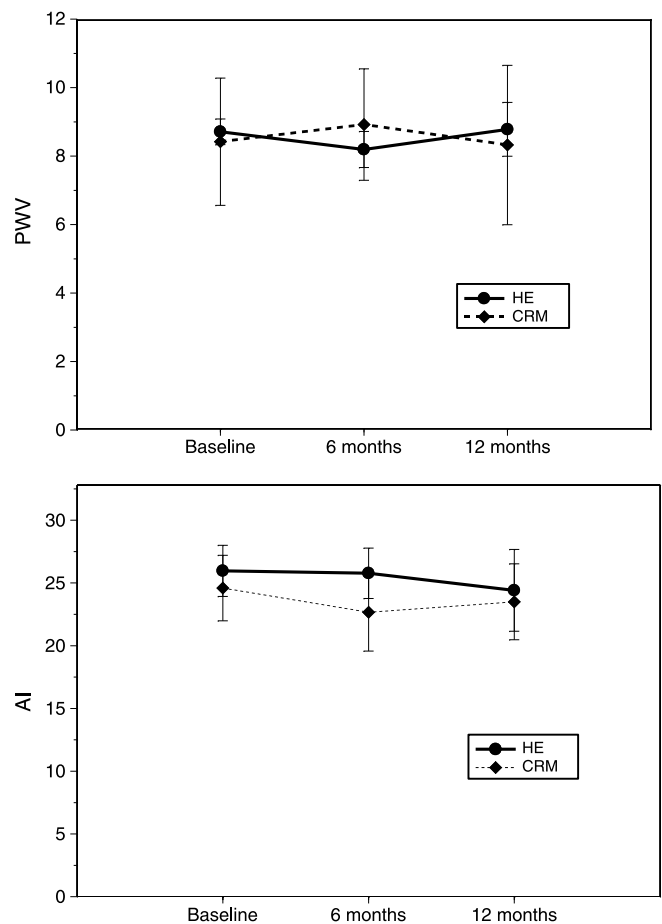

Figure 3. Arterial stiffness results by intervention group, including pulse-wave velocity (PWV) and augmentation index (AI). HE = health education; CRM = consciously resting meditation.

TABLE 3. Changes in Psychosocial Scale Scores by Study Group

Variable	Study Group	Study Visit, M (SD)			Change, Baseline to 12 mo (95% CI)[a]	p Value for Trend Within Group	p Value for Group Difference in Trend
		Baseline	6 mo	12 mo			
Anger-in	CRM	14.4 (3.9)	14.1 (3.8)	13.7 (3.4)	−0.35 (−1.69 to 0.99)	.60	.71
	HE	14.0 (4.0)	13.4 (3.5)	13.3 (3.6)	0.0002 (−1.33 to 1.33)	1.00	
Anger-out	CRM	12.9 (3.4)	12.2 (3.2)	13.4 (3.7)	0.34 (−0.76 to 1.45)	.54	.52
	HE	13.0 (2.5)	13.5 (3.2)	12.4 (2.5)	−0.17 (−1.27 to 0.93)	.76	
Hostility	CRM	17.2 (8.1)	17.6 (8.0)	17.7 (8.0)	1.69 (−0.46 to 3.84)	.12	.10
	HE	18.0 (7.4)	16.7 (8.4)	15.4 (6.7)	−0.84 (−2.98 to 1.30)	.44	
PSS	CRM	14.8 (8.4)	14.0 (6.9)	12.1 (6.2)	−1.66 (−4.42 to 1.11)	.24	.022
	HE	17.4 (8.6)	14.0 (7.7)	9.4 (6.4)	−6.50 (−9.55 to −3.45)	<.001	
STAI-State	CRM	36.8 (13.2)	32.4 (10.1)	28.4 (7.7)	−6.63 (−10.73 to −2.53)	.002	.65
	HE	40.0 (14.1)	35.8 (11.0)	31.7 (7.6)	−8.01 (−12.40 to −3.62)	.001	
STAI-Trait	CRM	38.2 (11.9)	34.4 (11.1)	33.4 (8.7)	−2.43 (−5.22 to 0.37)	.088	.48
	HE	39.5 (12.4)	37.7 (13.5)	33.2 (8.6)	−3.88 (−6.87 to −0.88)	.012	
BDI-Somatic	CRM	0.6 (0.4)	0.5 (0.3)	0.3 (0.2)	−0.19 (−0.34 to −0.05)	.011	.72
	HE	0.6 (0.5)	0.5 (0.4)	0.4 (0.4)	−0.16 (−0.31 to −0.01)	.040	
BDI-Cognitive	CRM	2.6 (3.1)	1.7 (2.1)	0.6 (0.8)	−1.34 (−2.48 to −0.21)	.021	.87
	HE	3.3 (3.9)	2.6 (3.5)	1.2 (1.6)	−1.47 (−2.61 to −0.34)	.011	
BDI-Total	CRM	10.9 (7.7)	7.8 (5.4)	5.1 (3.3)	−3.76 (−6.38 to −1.15)	.005	.86
	HE	11.0 (9.7)	9.0 (7.8)	6.1 (6.0)	−3.44 (−6.04 to −0.84)	.010	

M = mean; SD = standard deviation; CI = confidence interval; CRM = consciously resting meditation; HE = health education; PSS = Perceived Stress Scale; STAI = State-Trait Anxiety Inventory; BDI = Beck Depression Inventory.
[a] Model estimates, adjusted for individual variance, obtained using repeated-measures mixed-effects models.

the effects of TM on insulin resistance were examined in 103 patients with clinically confirmed CVD who were randomized to either a TM or an HE control group for 16 weeks; 84 completed the protocol (52). Consistent with our trial, this study found a significant improvement in BP and other metabolic risk factors in the patients randomized to TM compared with HE. FMD was examined as a secondary outcome. There was a nonsignificant

improvement in FMD (0.11%) in the TM group and a nonsignificant decline in the HE group (−0.81; p = .24 for difference between groups). Our results are in agreement with this previous report in terms of failing to find a significant between-group difference in FMD, although we did find a somewhat larger (2.1%) improvement in FMD within the meditation group. It should be noted that this earlier trial studied a different

TABLE 4. Changes in Biomarker Levels by Study Group

Variable	Study Group	Study Visit, M (SD)			Change, Baseline to 12 mo (95% CI)[a]	p Value for Trend Within Group	p Value for Group Difference in Trend
		Baseline	6 mo	12 mo			
Leptin, ng/mL	CRM	71.1 (40.6)	77.2 (40.4)	72.5 (46.9)	−3.77 (−16.54 to 9.00)	.56	.65
	HE	70.4 (37.4)	71.5 (39.9)	67.5 (37.2)	0.36 (−12.53 to 13.24)	.96	
Lg Adiponectin, ng/mL	CRM	9.0 (0.5)	9.0 (0.5)	9.0 (0.4)	0.05 (−0.13 to 0.23)	.58	.40
	HE	9.2 (0.4)	9.0 (0.4)	9.2 (0.5)	−0.06 (−0.24 to 0.12)	.52	
Lg CRP, mg/L	CRM	1.2 (1.2)	1.2 (0.8)	1.1 (1.1)	−0.04 (−0.41 to 0.32)	.81	.24
	HE	1.4 (1.1)	1.4 (1.0)	1.6 (1.0)	0.27 (−0.11 to 0.64)	.16	
Lg IL-6, pg/mL	CRM	0.1 (1.0)	0.3 (1.0)	0.3 (0.6)	0.16 (−0.29 to 0.62)	.47	.57
	HE	0.1 (1.2)	0.3 (1.5)	0.6 (1.0)	0.35 (−0.10 to 0.79)	.13	
TNF-α, pg/mL	CRM	2.3 (1.3)	2.8 (1.2)	2.4 (1.6)	−0.13 (−0.69 to 0.44)	.66	.24
	HE	2.4 (1.8)	3.4 (1.5)	3.4 (1.4)	0.35 (−0.22 to 0.92)	.23	
Lg PAI-1, pg/mL	CRM	10.3 (1.0)	10.2 (0.5)	10.0 (0.7)	−0.03 (−0.41 to 0.36)	.89	.95
	HE	10.4 (1.1)	9.9 (0.8)	9.9 (0.7)	−0.01 (−0.40 to 0.38)	.96	

M = mean; SD = standard deviation; CI = confidence interval; CRM = consciously resting meditation; HE = health education; CRP = C-reactive protein; IL-6 = interleukin 6; TNF-α = tumor necrosis factor α. PAI-1 = plasminogen activator inhibitor 1.
[a] Model estimates, adjusted for individual variance, obtained using repeated-measures mixed-effects models.

population, that is, patients with established coronary artery disease, many of whom may not have had metabolic syndrome and most of whom had already advanced vascular disease with a limited potential for improvement in endothelial function. In contrast, we excluded persons with previous coronary artery disease and selected participants with metabolic syndrome risk factors.

Several, if not all, of the metabolic syndrome risk factors (53–55), as well as visceral fat and insulin resistance (56,57), have been linked to adrenocortical and autonomic disturbances. Recently, in the Chicago site of the Study of Women's Health Across the Nation, both depressive symptoms and experiences of discrimination were associated with visceral fat, an important substrate for metabolic syndrome, but not with subcutaneous fat, both assessed by computed tomography; these relationships were observed both in black and in white women (47,58). Possible effects of stress reduction on life-style behaviors may also play a role. In fact, we found that participants randomized to CRM increased their level of vigorous physical activity more than participants randomized to HE. One might speculate that this reflects an increase in energy level in the CRM group relative to the control group, or an increased focus on personal physical activity goals. Nonetheless, our physical activity assessment was somewhat imprecise, and the increase in physical activity did not substantially explain the effects of CRM on FMD.

Limitations of our trial include its small size that limited the power to detect a significant difference in the change in outcome measures between the two randomized groups. The study power was also affected by a smaller than anticipated effect on FMD and a higher attrition rate. The relatively high dropout rate, however, is not surprising for a yearlong intervention in an at-risk population, and there was no difference in retention rate between the two randomized groups. Furthermore, we used a statistical approach for unbalanced data that allowed all available data to be included in the analysis. Nonetheless, we recognize that generalizability may be affected. Although participants were masked to the research hypothesis, we were not able to evaluate whether this masking was successful because data on participants' expectations were not collected. It is also possible that baseline differences in metabolic and vascular factors may have influenced the results. However, with exception for triglycerides, the two groups were balanced for baseline factors, and we adjusted for baseline triglyceride levels in the model. Finally, we studied a novel meditation approach, CRM, that has not been evaluated before in a controlled fashion. However, CRM follows closely the TM standardized protocol with few but significant modifications and has the possible advantage of being more acceptable to community-dwelling blacks. TM has failed to disseminate in the black community, possibly because it requires substantial investment in cost and time. CRM could be more successfully disseminated at the community level. Another advantage of our study is the use of a control intervention that rigorously controlled for frequency and duration of the training sessions, as well as practice time at home. Indeed, a limitation of many previous trials is lack of an adequate control intervention (11).

In conclusion, among black Americans with metabolic syndrome risk factors, CRM, a sound-based meditation intervention, did not improve endothelial function significantly more than a control intervention of HE. Favorable trends in metabolic risk factors were observed at the end of the 1-year intervention period, denoting improvement in the CRM group and no change or worsening in the HE group.

REFERENCES

1. Flegal KM, Carroll MD, Ogden CL, Johnson CL. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1723–7.
2. Hajjar I, Kotchen TA. Trends in prevalence, awareness, treatment, and control of hypertension in the United States, 1988–2000 [see comment]. JAMA 2003;290:199–206.
3. Fagot-Campagna A, Pettitt DJ, Engelgau MM, Burrows NR, Geiss LS, Valdez R, Beckles GL, Saaddine J, Gregg EW, Williamson DF, Narayan KM. Type 2 diabetes among North American children and adolescents: an epidemiologic review and a public health perspective. J Pediatr 2000;136: 664–72.
4. Black PH. The inflammatory response is an integral part of the stress response: implications for atherosclerosis, insulin resistance, type II diabetes and metabolic syndrome X. Brain Behav Immun 2003;17:350–64.
5. Caballero AE. Endothelial dysfunction in obesity and insulin resistance: a road to diabetes and heart disease. Obes Res 2003;11:1278–89.
6. Ghiadoni L, Donald AE, Cropley M, Mullen MJ, Oakley G, Taylor M, O'Connor G, Betteridge J, Klein N, Steptoe A, Deanfield JE. Mental stress induces transient endothelial dysfunction in humans. Circulation 2000; 102:2473–8.
7. Sherwood A, Johnson K, Blumenthal JA, Hinderliter AL. Endothelial function and hemodynamic responses during mental stress. Psychosom Med 1999;61:365–70.
8. Spieker LE, Hurlimann D, Ruschitzka F, Corti R, Enseleit F, Shaw S, Hayoz D, Deanfield JE, Luscher TF, Noll G. Mental stress induces prolonged endothelial dysfunction via endothelin-A receptors. Circulation 2002;105:2817–20.
9. Shinozaki K, Kashiwagi A, Nishio Y, Okamura T, Yoshida Y, Masada M, Toda N, Kikkawa R. Abnormal biopterin metabolism is a major cause of impaired endothelium-dependent relaxation through nitric oxide/O_2— imbalance in insulin-resistant rat aorta. Diabetes 1999;48:2437–45.
10. Shinozaki K, Ayajiki K, Nishio Y, Sugaya T, Kashiwagi A, Okamura T. Evidence for a causal role of the renin-angiotensin system in vascular dysfunction associated with insulin resistance. Hypertension 2004;43: 255–62.
11. Ospina MB, Bond TK, Karkhaneh M, Tjosvold L, Vandermeer B, Liang Y, Bialy L, Hooton N, Buscemi N, Dryden DM, Klassen TP. Meditation Practices for Health: State of the Research. Evidence Report/Technology Assessment No. 155. AHRQ Publication No. 07-E010. Rockville, MD: Agency for Healthcare Research and Quality; 2007.
12. Schneider RH, Nidich SI, Salerno JW. The transcendental meditation program: reducing the risk of heart disease and mortality and improving quality of life in African Americans. Ethn Dis 2001;11:159–60.
13. Schneider RH, Alexander CN, Staggers F, Orme-Johnson DW, Rainforth M, Salerno JW, Sheppard W, Castillo-Richmond A, Barnes VA, Nidich SI. A randomized controlled trial of stress reduction in African Americans treated for hypertension for over one year. Am J Hypertens 2005;18:88–98.
14. Barnes VA, Treiber FA, Davis H. Impact of transcendental meditation on cardiovascular function at rest and during acute stress in adolescents with high normal blood pressure. J Psychosom Res 2001;51:597–605.

15. Barnes VA, Treiber FA, Johnson MH. Impact of transcendental meditation on ambulatory blood pressure in African-American adolescents. Am J Hypertens 2004;17:366–9.

16. Barnes VA, Pendergrast RA, Harshfield GA, Treiber FA. Impact of breathing awareness meditation on ambulatory blood pressure and sodium handling in prehypertensive African American adolescents. Ethn Dis 2008;18:1–5.

17. Gregoski MJ, Barnes VA, Tingen MS, Harshfield GA, Treiber FA. Breathing awareness meditation and LifeSkills Training programs influence upon ambulatory blood pressure and sodium excretion among African American adolescents. J Adolesc Health 2010;48:59–64.

18. Barnes VA, Davis HC, Murzynowski JB, Treiber FA. Impact of meditation on resting and ambulatory blood pressure and heart rate in youth. Psychosom Med 2004;66:909–14.

19. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C, for the Conference Participants. Definition of metabolic syndrome: report of the National Heart, Lung, and Blood Institute/American Heart Association Conference on Scientific Issues Related to Definition. Arterioscler Thromb Vac Biol 2004;24:13e–18.

20. Carnethon MR, Palaniappan LP, Burchfiel CM, Brancati FL, Fortmann SP. Serum insulin, obesity, and the incidence of Type 2 diabetes in black and white adults: the atherosclerosis risk in communities study: 1987–1998. Diabetes Care 2002;25:1358–64.

21. Zoratti R. A review on ethnic differences in plasma triglycerides and high-density-lipoprotein cholesterol: is the lipid pattern the key factor for the low coronary heart disease rate in people of African origin? Eur J Epidemiol 1998;14:9–21.

22. Lin SX, Carnethon M, Szklo M, Bertoni A. Racial/Ethnic differences in the association of triglycerides with other metabolic syndrome components: the multi-ethnic study of atherosclerosis. Metab Syndr Relat Disord 2011;9:34–40.

23. Sumner AE. Ethnic differences in triglyceride levels and high-density lipoprotein lead to underdiagnosis of the metabolic syndrome in black children and adults. J Pediatr 2009;155:S7.e7–11.

24. Sumner AE, Harman JL, Buxbaum SG, Miller BV 3rd, Tambay AV, Wyatt SB, Taylor HA, Rotimi CN, Sarpong DF. The triglyceride/high-density lipoprotein cholesterol ratio fails to predict insulin resistance in African-American women: an analysis of Jackson Heart Study. Metab Syndr Relat Disord 2010;8:511–4.

25. Anonymous. The Sixth Report of the Joint National Commitee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Arch Intern Med 1997;157:2413–46.

26. Corretti MC, Anderson TJ, Benjamin EJ, Celermajer D, Charbonneau F, Creager MA, Deanfield J, Drexler H, Gerhard-Herman M, Herrington D. Guidelines for the ultrasound assessment of endothelial-dependent flow-mediated vasodilation of the brachial artery: a report of the International Brachial Artery Reactivity Task Force. J Am Coll Cardiol 2002;39:257–65.

27. Pauca AL, O'Rourke MF, Kon ND. Prospective evaluation of a method for estimating ascending aortic pressure from the radial artery pressure waveform. Hypertension 2001;38:932–7.

28. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav 1983;24:385–96.

29. Barefoot JC, Dodge KA, Peterson BL, Dahlstrom WG, Williams RBJ. The Cook-Medley Hostility Scale: item content and ability to predict survival. Psychosom Med 1989;51:46–57.

30. Spielberger CD. Professional Manual for the State-Trait Anger Expression Inventory. Research Ed. Tampa, FL: University of South Florida, 1988.

31. Spielberger CD, Gorsuch RL, Lushene RE. State-Trait Anxiety (STAI) Manual. Palo Alto, AA: Consulting Psychologists Press; 1970.

32. Beck AT, Steer RA, Brown GK. BDI-II. Beck Depression Inventory. 2nd ed. San Antonio, TX: The Psychological Corporation; 1996.

33. Steer RA, Ball R, Ranieri WF, Beck AT. Dimensions of the Beck Depression Inventory-II in clinically depressed outpatients. J Clin Psychol 1999;55:117–28.

34. Whitt MC, Levin S, Ainsworth BE, Dubose KD. Evaluation of a two-part survey item to assess moderate physical activity: the Cross-Cultural Activity Participation Study. J Womens Health (Larchmt) 2003;12:203–12.

35. Shao J, Zhong B. Last observation carry-forward and last observation analysis. Stat Med 2003;22:2429–41.

36. Littell RC, Milliken GA, Stroup WW, Wolfinger RD. SAS System for Mixed Models. Cary, NC: SAS Institute; 1996.

37. Wood AM, White IR, Thompson SG. Are missing outcome data adequately handled? A review of published randomized controlled trials in major medical journals. Clin Trials 2004;1:368–76.

38. Williams DR, Neighbors H. Racism, discrimination and hypertension: evidence and needed research. Ethn Dis 2001;11:800–16.

39. Guyll M, Matthews KA, Bromberger JT. Discrimination and unfair treatment: relationship to cardiovascular reactivity among African American and European American women. Health Psychol 2001;20:315–25.

40. Lewis TT, Everson-Rose SA, Powell LH, Matthews KA, Brown C, Karavolos K, Sutton-Tyrrell K, Jacobs E, Wesley D. Chronic exposure to everyday discrimination and coronary artery calcification in African-American women: the SWAN Heart Study. Psychosom Med 2006;68:362–8.

41. Brondolo E, Libby DJ, Denton EG, Thompson S, Beatty DL, Schwartz J, Sweeney M, Tobin JN, Cassells A, Pickering TG, Gerin W. Racism and ambulatory blood pressure in a community sample. Psychosom Med 2008;70:49–56.

42. Lewis TT, Barnes LL, Bienias JL, Lackland DT, Evans DA, Mendes de Leon CF. Perceived discrimination and blood pressure in older African American and white adults. J Gerontol A Biol Sci Med Sci 2009;64:1002–8.

43. Troxel WM, Matthews KA, Bromberger JT, Sutton-Tyrrell K. Chronic stress burden, discrimination, and subclinical carotid artery disease in African American and Caucasian women. Health Psychol 2003;22:300–9.

44. Anderson NB, McNeilly M, Myers H. Autonomic reactivity and hypertension in blacks: a review and proposed model. Ethn Dis 1991;1:154–70.

45. Gentry WD, Chesney AP, Gary HE Jr, Hall RP, Harburg E. Habitual anger-coping styles: I. Effect on mean blood pressure and risk for essential hypertension. Psychosom Med 1982;44:195–202.

46. Amyre Morris A, Zhao L, Ahmed Y, Stoyanova N, De Staercke C, Hooper WC, Gibbons G, Din-Dzietham R, Quyyumi A, Vaccarino V. Association between depression and inflammation–differences by race and sex: the META-Health study. Psychosom Med 2011;73:462–8.

47. Lewis TT, Kravitz HM, Janssen I, Powell LH. Self-reported experiences of discrimination and visceral fat in middle-aged African-American and Caucasian women. Am J Epidemiol 2011;173:1223–31.

48. Lewis TT, Guo H, Lunos S, Mendes de Leon CF, Skarupski KA, Evans DA, Everson-Rose SA. Depressive symptoms and cardiovascular mortality in older black and white adults: evidence for a differential association by race. Circ Cardiovasc Qual Outcomes 2011;4:293–9.

49. Davidson K, Jonas BS, Dixon KE, Markovitz JH. Do depression symptoms predict early hypertension incidence in young adults in the CARDIA study? Coronary Artery Risk Development in Young Adults. Arch Intern Med 2000;160:1495–500.

50. Lewis TT, Everson-Rose SA, Colvin A, Matthews K, Bromberger JT, Sutton-Tyrrell K. Interactive effects of race and depressive symptoms on calcification in African American and white women. Psychosom Med 2009;71:163–70.

51. Schneider RH, Staggers F, Alexander C, Sheppard W, Rainforth M, Kondwani K, Smith S, King CG. A randomized controlled trial of stress reduction for hypertension in older African Americans. Hypertension 1995;26:820–7.

52. Paul-Labrador M, Polk D, Dwyer JH, Velasquez I, Nidich S, Rainforth M, Schneider R, Merz CN. Effects of a randomized controlled trial of transcendental meditation on components of the metabolic syndrome in subjects with coronary heart disease. Arch Intern Med 2006;166:1218–24.

53. Bjorntorp P, Holm G, Rosmond R. Hypothalamic arousal, insulin resistance and Type 2 diabetes mellitus. Diabet Med 1999;16:373–83.

54. Liao D, Sloan R, Cascio W, Folsom A, Liese A, Evans G, Cai J, Sharrett A. Multiple metabolic syndrome is associated with lower heart rate variability. The Atherosclerosis Risk in Communities Study. Diabetes Care 1998;21:2116–22.

55. Brunner EJ, Hemingway H, Walker BR, Page M, Clarke P, Juneja M, Shipley MJ, Kumari M, Andrew R, Seckl JR, Papadopoulos A, Checkley S, Rumley A, Lowe GDO, Stansfeld SA, Marmot MG. Adrenocortical, autonomic, and inflammatory causes of the metabolic syndrome: nested case-control study. Circulation 2002;106:2659–65.

56. Epel EE, Moyer AE, Martin CD, Macary S, Cummings N, Rodin J, Rebuffe-Scrive M. Stress-induced cortisol, mood, and fat distribution in men. Obes Res 1999;7:9–15.

57. Raikkonen K, Matthews KA, Kuller LH. Anthropometric and psychosocial determinants of visceral obesity in healthy postmenopausal women. Int J Obes Relat Metab Disord 1999;23:775–82.

58. Everson-Rose SA, Lewis TT, Karavolos K, Dugan SA, Wesley D, Powell LH. Depressive symptoms and increased visceral fat in middle-aged women. Psychosom Med 2009;71:410–6.