ORIGINAL RESEARCH

Perceived Stress Is Associated With Incident Coronary Heart Disease and All-Cause Mortality in Low- but Not High-Income Participants in the Reasons for Geographic And Racial Differences in Stroke Study

Nicole Redmond, MD, MPH, PhD; Joshua Richman, MD, PhD; Christopher M. Gamboa, MPH; Michelle A. Albert, MD, MPH; Mario Sims, MS, PhD; Raegan W. Durant, MD, MPH; Stephen P. Glasser, MD; Monika M. Safford, MD

***Background*—**Perceived stress may increase risk for coronary heart disease (CHD) and death, but few studies have examined these relationships longitudinally. We sought to determine the association of perceived stress with incident CHD and all-cause mortality.

***Methods and Results*—**Data were from a prospective study of 24 443 participants without CHD at baseline from the national Reasons for Geographic And Racial Differences in Stroke (REGARDS) study cohort. Outcomes were expert-adjudicated acute CHD and all-cause mortality. Over a mean follow-up of 4.2 (maximum 6.9) years, there were 659 incident CHD events and 1320 deaths. Analyses were stratified by income level because of significant interactions with stress. For individuals with low income, 3529 (35.4%) reported high stress, and for those with high income, 2524 (22.1%) did so. Compared with reporting no stress, those reporting the highest stress had higher risk for incident CHD if they reported low income (sociodemographic-adjusted HR 1.36, 95% CI: 1.04, 1.78) but not high income (sociodemographic-adjusted HR 0.82, 95% CI: 0.57, 1.16); the finding in low income individuals attenuated with adjustment for clinical and behavioral factors (HR 1.29, 95% CI: 0.99, 1.69, P=0.06). After full adjustment, the highest stress category was associated with higher risk for death among those with low income (HR 1.55, 95% CI: 1.31, 1.82) but not high income (HR 1.13, 95% CI: 0.88, 1.46).

***Conclusions*—**High stress was associated with greater risks of CHD and death for individuals with low but not high income. **(*J Am Heart Assoc*. 2013;2:e000447 doi: 10.1161/JAHA.113.000447)**

Key Words: epidemiology • mortality • myocardial infarction • stress

Coronary heart disease (CHD) is a major contributor to morbidity and mortality in the United States. As of 2010 over 15 million individuals had a history of CHD and 7.6 million had suffered a myocardial infarction (MI).[1] Despite an overall decline in the incidence of MI in the last few decades, the rate of this decline varied by race/ethnicity, sex, age, geographic region, and socioeconomic strata.[2–8] Racial and ethnic differences in the prevalence of traditional CHD risk factors (eg, hypertension, diabetes, obesity, smoking, and dyslipidemia)[9–12] contribute to the observed disparity; however, the role of "non-traditional" risk factors in these disparities is garnering increasing attention. Emerging evidence indicates that chronic exposure to psychological stress/stressors plays a central role in the pathophysiology of CHD through activation of physiologic processes involving the hypothalamic-pituitary-adrenal axis, sympathetic-parasympathetic systems, and inflammatory cascades.[13–16] Moreover, psychosocial risk factors may also be directly related to CHD through their associations with behavioral risk factors (eg, smoking, physical activity, and diet),[17,18] and indirectly via neurohormonal and inflammatory processes.[19]

In fact, stress may be an important contributor to the long-observed associations between lower socioeconomic status (SES) and CHD and mortality outcomes.[20–23] While persons of low SES have higher prevalence of traditional cardiovascular disease (CVD) risk factors such as smoking and diabetes,[24]

From the Division of Preventive Medicine (N.R., C.M.G., R.W.D., S.P.G., M.M.S.), Department of Surgery (J.R.), and Department of Epidemiology (C.M.G.), University of Alabama at Birmingham, Birmingham, AL; Division of Cardiovascular Medicine, Howard University College of Medicine, Washington, DC (M.A.A.); Department of Medicine, University of Mississippi Medical Center, Jackson, MS (M.S.); Birmingham Veterans Affairs Medical Center, Birmingham, AL (R.W.D.).

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Correspondence to: Nicole Redmond, MD, MPH, PhD, Division of Preventive Medicine, University of Alabama at Birmingham, 1717 11th Avenue South, Medical Towers 610, Birmingham, AL 35294-4410. E-mail: nredmond@uabmc.edu

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adjusting for risk factors does not entirely attenuate the association between SES and CHD and mortality outcomes.[25] People living in poverty demonstrate physiologic evidence of chronic stress,[26] but the relationship between stress and CHD outcomes and death have not often been examined longitudinally.

These relationships are particularly relevant for US non-Hispanic blacks, a minority whose members disproportionately live in poverty and who have higher risks for CHD and death than majority non-Hispanic whites.[3,27] Prior studies have explored racial differences in post-MI outcomes[28] and the association of perceived stress in recurrent MI.[29] Although prior prospective studies have assessed the contribution of stress to the incidence of CHD, many of these studies were conducted among non-US populations or did not include sufficient diversity to draw conclusions about racial and socioeconomic disparities.[30–33] Because few longitudinal studies of CVD risk factors and CHD in the United States have a significant number of minorities (eg, Atherosclerosis Risk in Communities [ARIC] study, Jackson Heart Study [JHS], Coronary Artery Risk Development in Young Adults [CARDIA], Multi-Ethnic Study of Atherosclerosis [MESA]), there remain a paucity of longitudinal data about the relationship between stress and incident CHD in US populations and whether this relationship varies by race/ethnicity and/or SES. Consequently, using a short version of the Cohen Perceived Stress Scale (PSS) as a global measure of self-reported stress[34] in the Reasons for Geographic And Racial Differences in Stroke (REGARDS) study, we investigated the association of perceived stress with incident fatal and nonfatal CHD and all-cause mortality, focusing on the role of race/ethnicity and SES on any observed associations.

Methods

Setting and Study Population

The REGARDS study is a prospective study intended to determine the causes for the excess stroke mortality in the southeastern United States (ie, the stroke "belt" and "buckle") and among blacks through targeted recruitment of participants from specific age/race/geographic strata from January 2003 to October 2007. It recruited 30 239 community dwelling participants (42% blacks and 55% women) residing in the continental United States.[35] This study used data from REGARDS-MI, an ancillary study of REGARDS, which adjudicates all heart-related events and merges these data with the existing REGARDS data. Baseline data collection for REGARDS was completed using computer-assisted telephone interviews to collect medical history, functional status, health behaviors, and psychosocial measures. In-home examinations were conducted by trained health care professionals using standardized, quality-controlled protocols to collect physiologic measures (blood pressure [BP], height and weight, waist circumference), blood and urine samples, electrocardiograms (ECGs), and medication use by pill bottle review. Blood and urine samples were centrally analyzed at the University of Vermont. ECGs were centrally analyzed at Wake Forest University.

Living participants or their proxies were followed up every 6 months by telephone with retrieval of medical records for reported hospitalizations. Deaths were detected by report of next-of-kin or through online sources (eg, Social Security Death Index) or the National Death Index. Proxies or next-of-kin were interviewed about the circumstances surrounding death including the presence of chest pain. Death certificates, medical records, and autopsy reports were obtained to adjudicate cause of death, and cardiovascular outcomes were adjudicated using methods previously described.[4] Briefly, definite MIs were those with diagnostic cardiac enzymes or ECG. Probable MIs were those with elevated but not diagnostic (ie, equivocal) enzymes with a positive but not diagnostic ECG or, if enzymes were missing, with a positive ECG in the presence of ischemic signs or symptoms. Only definite or probable MIs were included as events in this study. Cases were assigned to 2 adjudicators, and disagreements were adjudicated by committee. The test for agreement between adjudicators yielded a κ statistic >0.80 for the presence of definite or probable MI or definite or probable acute CHD death. The study protocol was reviewed and approved by the institutional review boards at the participating institutions, and all participants provided informed consent.

For this study, we examined REGARDS participants without CHD at baseline (defined as a self-reported history of MI, coronary artery bypass surgery, percutaneous coronary intervention, or evidence of MI on ECG). Events through December 31, 2009, were included in this analysis; at that time, 9.5% of the original sample was lost to follow-up.

Study Variables

Our dependent variables were incident total CHD (defined as definite or probable MI or definite or probable acute CHD death), incident fatal CHD (definite or probable acute CHD death), and all-cause mortality from study entry through December 31, 2009. Since revascularization procedure utilization differs markedly by race[36] and racial differences were of interest, we did not include coronary revascularization in the primary analysis but included them as part of a sensitivity analysis.

Our primary independent variable was baseline perceived stress, as assessed by a 4-item version of the PSS.[34] The PSS measures over the past month the degree to which respondents feel they were unable to control important things in

their life, their confidence in their ability to handle personal problems, how often they felt they could not cope with all the things they needed to do, and how often difficulties were overwhelming, scored using a 5-point scale (0=never, 1=almost never, 2=sometimes, 3=fairly often, 4=very often), with final scores ranging from 0 to 16. Because of the skewed distribution of the PSS score and lack of defined cut-points, it was categorized into approximate quartiles of no stress (PSS score=0), low stress (score 1 to 2), moderate stress (scores 3 to 4), and high stress (scores 5 to 16).

Additional covariates included baseline sociodemographic, clinical, and health behavior related variables. Demographic variables included age, sex, race (black or white), urban residence as classified by 2000 Rural-Urban Commuting Area Codes (RUCA) 1 through 3,[37] and stroke region (stroke belt, stroke buckle, or other parts of the continental United States). SES variables included education (less than high school, high school graduate, some college, college graduate) and household annual income (<$20 000; $20 000 to $34 000; $35 000 to $74 000; ≥$75 000). Clinical CHD risk factors included systolic blood pressure (<120, 120 to 139, ≥140 mm Hg), total cholesterol (<200, 200 to 239, ≥240 mg/dL), low HDL cholesterol (<40 mg/dL in men and <50 mg/dL in women), diabetes status (defined as a fasting blood sugar >126 mg/dL, a nonfasting blood sugar >200 mg/dL, a self-reported history of diabetes, or treatment with a diabetes medication), and other medication use (use of antihypertensive and/or cholesterol-lowering medications). Health behavior–related variables included smoking (never, past, current), exercise to work up a sweat (none, at least once weekly), alcohol use (none, moderate [1 to 2 drinks/day for men and 1 drink/day for women], and heavy [>2 drinks/day for men and >1 drink/day for women]), and body mass index (<25, 25 to 29.9, 30 to 39.9, ≥40 kg/m^2).

Statistical Analysis

Summary statistics were calculated for baseline characteristics overall and across PSS quartiles. Associations between characteristics were tested in unadjusted analyses using the χ^2 test of association for categorical characteristics and ANOVA for continuous characteristics. We calculated crude incidence of acute CHD, fatal CHD, and all-cause death by income group, since we observed a significant interaction for income. We examined the cumulative incidence of acute CHD and all-cause mortality by high (score 5 to 16) and no (score 0) stress quartiles by income group using Kaplan–Meier survival curves, omitting the low and medium stress categories to facilitate comparison. A Wilcoxon test of equality was performed to test differences in cumulative incidence among the 4 stress–income groups (high stress and low income, no stress and low income, high stress and high income, and no stress and high income), and the *P* value was reported for each outcome. We used Cox proportional hazards models to examine the association of perceived stress with incident CHD, incident fatal CHD, and all-cause mortality. Incident nonfatal CHD and fatal CHD are mutually exclusive events; therefore, in analyses of incident fatal CHD, nonfatal CHD events were censored at their event date. The assumptions of proportionality were met and there were no time-dependent variables. Models were constructed incrementally to examine changes in the hazard ratios (HRs) for each quartile of perceived stress score compared with the quartile of lowest stress as covariates were added. Model 1 adjusted for age, sex, race, education, region, and urban/rural status. Model 2 added to the model 1 covariates systolic blood pressure, antihypertensive medication use, total cholesterol, HDL cholesterol, statin use, and diabetes. Model 3 added to the model 2 covariates smoking, exercise, alcohol use, and body mass index. To explore potential effect modification, interaction terms for stress×age, stress×sex, stress×race, stress×education, and stress×income were placed separately into fully adjusted models. We observed no significant interaction for age, sex, race, or education, but the *P* value for the stress×income interaction was significant (overall CHD *P*=0.09, fatal CHD *P*=0.03, all-cause mortality *P*=0.07). Splines indicated that effect modification occurred above and below an income of $35 000; thus, the analysis was stratified on this level of income. More than 12% of participants (n=3031) declined to provide information on income, and an additional 15.1% (n=3680) had missing laboratory or survey elements, resulting in a total of 6711 with missing data; therefore, we used multiple imputation to estimate missing covariate information using chained equations with 30 data sets.[38,39] Statistical significance for all analyses was *P*<0.05. We conducted a sensitivity analysis with cardiac revascularization included in the CHD outcomes using the same modeling procedures as previously described. We also conducted all analyses excluding the individuals who declined to report their income. All analyses were conducted using SAS version 9.2 (SAS Institute, Inc) and Stata version 12 (StataCorp).

Results

Sample Characteristics

After excluding subjects with CHD at baseline and missing data for the PSS, 24 439 participants were eligible for this analysis. As of December 31, 2009, 444 first definite or probable nonfatal MIs and 215 first definite or probable fatal CHD events were adjudicated for a total of 659 incident CHD events. There were 1620 deaths from any cause. Baseline characteristics of the study sample overall and by PSS category are shown in Table 1. Participants who reported high

Table 1. Baseline Characteristics of REGARDS Participants Without CHD at Baseline

Characteristics	Overall (n=24 439)	Perceived Stress Scale—4 Item (Score)				*P* Value
		No Stress (0) n=6117	Low Stress (1 to 2) n=5779	Moderate Stress (3 to 4) n=5571	High Stress (5 to 16) n=6972	
Age, mean±SD	64.1±9.3	66.0±9	64.8±9.3	64.8±9.5	64.0±9.9	<0.001
Female, n (%)	14 282 (58.4)	2962 (48.4)	3207 (55.5)	3367 (60.4)	4746 (68.1)	<0.001
Black, n (%)	10 345 (42.3)	2582 (42.2)	2025 (35.0)	2281 (40.9)	3457 (49.6)	<0.001
Region of residence, n (%)						<0.001
Nonbelt	10 851 (44.4)	2780 (45.4)	2675 (46.3)	2522 (45.3)	2874 (41.2)	
Belt	8478 (34.7)	2112 (34.5)	1949 (33.7)	1869 (33.5)	2548 (36.5)	
Buckle	5110 (20.9)	1225 (20.0)	1155 (20.0)	1180 (21.2)	1550 (22.2)	
Urban residence, n (%)	17 845 (80.8)	4467 (80.8)	4247 (81.1)	4081 (81.0)	5050 (80.4)	0.77
Education, n (%)						<0.001
Less than high school	2823 (11.6)	2290 (37.5)	2428 (42.0)	2127 (38.2)	1961 (28.2)	
High school graduate	6192 (25.3)	1695 (27.7)	1580 (27.4)	1487 (26.7)	1840 (26.4)	
Some college	6602 (27.0)	1500 (24.5)	1316 (22.8)	1380 (24.8)	1996 (28.7)	
College graduate	8806 (36.1)	628 (10.3)	451 (7.8)	575 (10.3)	1169 (16.8)	
Annual household income						<0.001
≥$35 000	11 442 (46.8)	3113 (50.9)	3105 (53.7)	2700 (48.5)	2524 (36.2)	
<$35 000	9966 (40.8)	2273 (37.2)	1990 (34.4)	2174 (39.0)	3529 (50.6)	
Declined to report	3031 (12.4)	731 (12.0)	684 (11.8)	697 (12.5)	919 (13.2)	
Systolic blood pressure, mm Hg						<0.001
<120	7709 (31.6)	1763 (28.9)	1874 (32.5)	1832 (33.0)	2240 (32.2)	
120 to 139	11 818 (48.5)	3071 (50.3)	2816 (48.9)	2669 (48.1)	3262 (46.9)	
>140	4848 (19.9)	1273 (20.8)	1071 (18.6)	1050 (18.9)	1454 (20.9)	
Total cholesterol (mg/dL), n (%)						0.01
<200	13 686 (58.4)	3503 (60.0)	3220 (57.7)	3143 (58.8)	3820 (57.5)	
200 to 240	6882 (29.4)	1657 (28.4)	1712 (30.7)	1545 (28.9)	1968 (29.6)	
>240	2848 (12.2)	683 (11.7)	646 (11.6)	659 (12.3)	860 (12.9)	
Low HDL cholesterol* (mg/dL), n (%)	8069 (34.7)	1989 (34.2)	1875 (33.8)	1781 (33.5)	2424 (36.7)	<0.001
Had diabetes, n (%)	5450 (22.3)	1312 (21.4)	1141 (19.7)	1162 (20.9)	1835 (26.3)	<0.001
Antihypertensive medication use, n (%)	13 222 (54.1)	3368 (55.1)	2984 (51.6)	2926 (52.5)	3944 (56.6)	<0.001
Statin use, n (%)	6322 (25.9)	1650 (27.0)	1454 (25.2)	1407 (25.3)	1811 (26.0)	0.09
Smoking status, n (%)						<0.001
Never	11 536 (47.4)	2743 (45.0)	2772 (48.1)	2711 (48.8)	3310 (47.7)	
Past	9357 (38.4)	2557 (42.0)	2288 (39.7)	2128 (38.3)	2384 (34.3)	
Current	3453 (14.2)	790 (13.0)	700 (12.2)	716 (12.9)	1247 (18.0)	
Exercised at least once a week, n (%)	16 015 (66.5)	4198 (69.6)	3965 (69.5)	3703 (67.4)	4149 (60.5)	<0.001
Alcohol use†, n (%)						<0.001
None	14 905 (62.2)	3654 (61.0)	3358 (59.0)	3339 (61.0)	4554 (66.9)	
Moderate	8055 (33.6)	2046 (34.1)	2093 (36.8)	1901 (34.7)	2015 (29.6)	
Heavy	1012 (4.2)	292 (4.9)	244 (4.3)	234 (4.3)	242 (3.6)	
BMI (kg/m^2), n (%)						<0.001
<25	6107 (25.2)	1493 (24.5)	1515 (26.4)	1405 (25.4)	1694 (24.5)	
25 to 29.9	8906 (36.7)	2430 (39.9)	2141 (37.3)	2083 (37.6)	2252 (32.6)	
30 to 39.9	7713 (31.8)	1866 (30.7)	1757 (30.6)	1706 (30.8)	2384 (34.5)	
≥40	1543 (6.4)	297 (4.9)	321 (5.6)	342 (6.2)	583 (8.4)	

BMI indicates body mass index; CHD, coronary heart disease; REGARDS, Reasons for Geographic And Racial Differences in Stroke Study.
*Low HDL cholesterol for men is <40 mg/dL and for women is <50 mg/dL.
†Moderate alcohol use for men is 1 to 2 drinks/day and for women is 1 drink/day. Heavy alcohol use for men is >2 drinks/day and for women is ≥2 drinks/day.

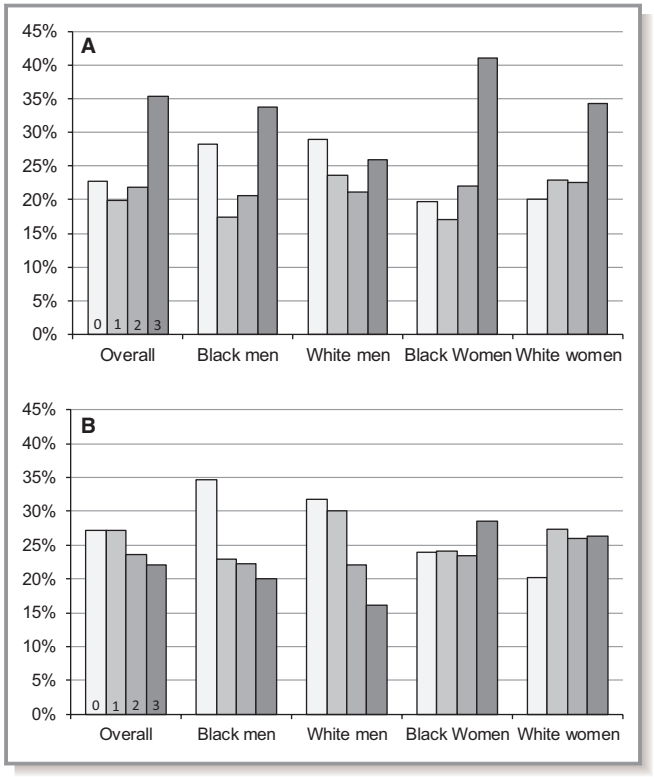

Figure 1. PSS categories overall and by race–sex group among (A) low-income and (B) high-income REGARDS participants. Legend: 0, no stress; 1, low stress; 2, moderate stress; 3, high stress. PSS indicates Perceived Stress Scale; REGARDS, Reasons for Geographic And Racial Differences in Stroke Study.

stress were more likely to be women, black, and residents of the stroke belt or buckle compared with participants in the other stress categories. More participants reporting high stress were college graduates; smoked currently; did not exercise weekly; and had high cholesterol or diabetes or were obese. In addition, >50% of participants reporting high stress reported an annual household income of <$35 000. Of note, 3529 (35.4%) of individuals reporting income of <$35 000 also reported high stress, whereas 2524 (22.1%) of those reporting income of ≥$35 000 did so (Figure 1). Furthermore, there were disproportionate distributions of PSS across race–sex categories when stratified by income. Among the low-income participants, black men (33.5%) and women (40.9%) and white women (34.0%) had higher proportions in the high-stress strata compared with white men (26.5%).

Risks for Incident Total CHD, Incident Fatal CHD, and All-Cause Mortality

Cumulative incidences of total CHD (Figure 2A), fatal CHD (Figure 2B), and all-cause mortality (Figure 2C) were significantly different between the stress–income groups. As seen in Figure 2, individuals with low income reporting high stress

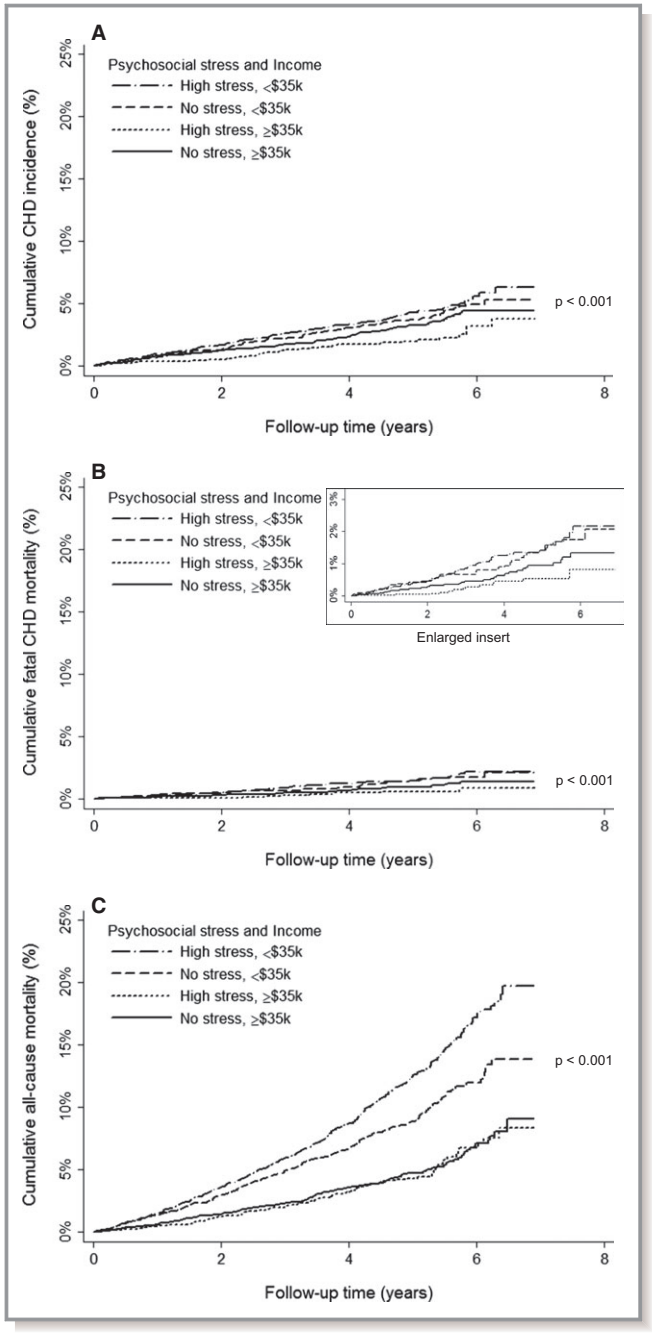

Figure 2. Cumulative incidence Kaplan–Meier graphs for (A) incident total CHD, (B) incident fatal CHD, and (C) all-cause mortality comparing participants that reported high stress (PSS=5 to 16) to participants that reported no stress (PSS=0). A Wilcoxon test of equality was performed and the *P*-value is reported. CHD indicates coronary heart disease; PSS, perceived stress scale.

had the highest cumulative incidence for all 3 outcomes, followed by those with low income reporting low stress. For all 3 outcomes, those with high income had cumulative incidence that was lower than either stress group for individuals reporting low income. Although the Kaplan–Meier curves for those with high income and high stress are below those with

high income and low stress, the multivariable adjusted results presented in Table 2 suggest that this difference is not statistically significant once differences in patient characteristics are accounted for. Although there were fewer individuals reporting low income than high income, the group with lower income accounted for substantially more events. Among those reporting income of <$35 000, there were 131 fatal incident CHD events, 333 total incident CHD events, and 953 deaths, whereas among those reporting income of ≥$35 000, there were 61 fatal incident CHD events, 247 total incident CHD events, and 429 deaths (Table 2).

The results of the multivariable analysis testing the associations of perceived stress and incident total CHD, fatal CHD, and all-cause mortality stratified by income group are also presented in Table 2. Risks for individuals in the low-, moderate-, and high-stress categories were compared with those with no stress. Among participants reporting income of <$35 000, the HR for incident total CHD was 1.36 (95% CI 1.04 to 1.78) for the high-stress compared with the no-stress group in models adjusting for sociodemographic characteristics (model 1) and 1.29 (95% CI 0.99 to 1.69) in the model adjusting for all covariates (model 3). Among participants reporting income of ≥$35 000, the HR for incident total CHD was 0.82 (95% CI 0.57 to 1.16) for the high- compared with the no-stress group in model 1 and 0.80 (95% CI 0.56 to 1.14) in model 3.

Stress was not statistically significantly associated with incident fatal CHD in demographic or fully adjusted models for either income category, but the point estimates were remarkably similar to those for incident total CHD (Table 2). Among participants reporting income of <$35 000, the HR for incident fatal CHD was 1.35 (95% CI 0.86 to 2.11) for the high- compared with the no-stress group in model 1 and 1.27 (95% CI 0.81 to 1.99) in model 3. Among participants reporting income of ≥$35 000, the HR for incident fatal CHD was 0.70 (95% CI 0.34 to 1.40) for the high- compared with the no-stress group in model 1 and 0.67 (95% CI 0.33 to 1.34) in model 3.

Among participants reporting income of <$35 000, the HR for all-cause mortality was 1.65 (95% CI 1.40 to 1.94) for the high- compared with the no-stress group in model 1 and 1.55 (95% CI 1.31 to 1.82) in model 3 (Table 2). Among participants reporting income of ≥$35 000, the HR was 1.20 (95% CI 0.93 to 1.55) for the high- compared with the no-stress group in model 1 and 1.13 (95% CI 0.88 to 1.46) in the model 3.

The sensitivity analysis including coronary revascularization (eg, percutaneous coronary intervention or coronary artery bypass grafting) in the CHD outcome showed similar associations as for incident total CHD (Table 3). There were 461 total CHD or revascularization outcomes for those with income of <$35 000 and 414 for those with income of ≥$35 000. The fully adjusted HR for the high- compared with the no-stress group was 1.20 (95% CI 0.96 to 1.52) for those with income of <$35 000, and it was 0.88 (95% CI 0.67 to 1.16) for those with income of ≥$35 000.

We conducted a sensitivity analysis excluding those who did not report income and had missing covariates (Table 3). The results were generally similar, although CIs were consistently wider and the fully adjusted HR for incident total CHD was higher and statistically significant (HR 1.44 [95% CI 1.05 to 1.98] for the complete case analysis versus HR 1.29 [95% CI 0.99 to 1.69] for the analysis using multiple imputation to replace missing data).

Discussion

In this study of REGARDS participants, high perceived stress was associated with incident total CHD and all-cause mortality among low- but not high-income participants. These results persisted for all-cause mortality even after adjustment for demographic, clinical, and behavioral characteristics, and the findings showed a trend for significance after full adjustment for incident total CHD (P=0.06). There was no evidence that these findings differed by race or sex, thus suggesting that stress may be an important mechanism contributing for the observed higher risks for worse CVD and mortality outcomes among individuals with low income.

The relationship between stress and CHD or mortality outcomes by income has not been widely examined. Our findings are consistent with a recent study of the Health Survey for England that also showed stronger effects of psychological distress on all-cause and CHD mortality among lower occupational classes compared with higher occupational classes.[40] The incidence of CHD was not examined in that study. In our study, among low-income participants, only the highest level of perceived stress was associated with an increased hazard for incident total CHD, and a trend for significance remained after adjustment for all covariates. The association of perceived stress with all-cause mortality showed more of a dose-response pattern of progressively increasing hazard with each level of increased stress among low-income participants. Prior research has shown that low SES is an independent risk factor for incident CHD and that the Framingham risk score underestimates CHD risk in low-income populations.[41–43] Taken together, these findings suggest that stress may be an important contributor to CHD and mortality disparities long observed for individuals with low income relative to those with higher income.

Our findings have implications for efforts to eliminate racial disparities in health outcomes. In our study, we did not observe statistically significant interactions between

Table 2. Incidence and Hazard Ratios (With 95% CI) for Association of Perceived Stress and Incident Total and Fatal CHD and All-Cause Mortality Stratified by Annual Household Income (N=24 439 Individuals Free of CHD at Baseline)

	Incident Total CHD (n=659)				Incident Fatal CHD (n=215)			
	Income <$35 000		Income ≥$35 000		Income <$35 000		Income ≥$35 000	
Number of events*	333		247		131		61	
Crude incidence rate per 1000 person-years*	7.9		5.1		3.1		1.2	
Models†‡	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Model 1 (demographics, education)								
No stress (ref)	1.00	—	1.00	—	1.00	—	1.00	—
Low stress	1.08 (0.79 to 1.47)	0.64	0.79 (0.58 to 1.08)	0.14	1.15 (0.69 to 1.92)	0.59	0.65 (0.35 to 1.23)	0.18
Moderate stress	1.03 (0.75 to 1.40)	0.86	0.77 (0.55 to 1.07)	0.12	1.43 (0.88 to 2.32)	0.15	0.62 (0.31 to 1.26)	0.19
High stress	1.36 (1.04 to 1.78)	0.02	0.82 (0.57 to 1.16)	0.26	1.35 (0.86 to 2.11)	0.19	0.70 (0.34 to 1.40)	0.31
Model 2 (demographics, education, and clinical factors)								
No stress (ref)	1.00	—	1.00	—	1.00	—	1.00	—
Low stress	1.08 (0.80 to 1.48)	0.61	0.79 (0.58 to 1.08)	0.14	1.14 (0.68 to 1.91)	0.61	0.65 (0.34 to 1.22)	0.18
Moderate stress	1.02 (0.75 to 1.40)	0.88	0.79 (0.56 to 1.10)	0.16	1.40 (0.86 to 2.28)	0.17	0.64 (0.31 to 1.29)	0.21
High stress	1.33 (1.02 to 1.73)	0.04	0.82 (0.58 to 1.17)	0.27	1.32 (0.85 to 2.07)	0.22	0.69 (0.34 to 1.40)	0.31
Model 3 (demographics, education, clinical, and behavioral factors)								
No stress (ref)	1.00	—	1.00	—	1.00	—	1.00	—
Low stress	1.07 (0.79 to 1.46)	0.66	0.80 (0.58 to 1.10)	0.16	1.12 (0.67 to 1.88)	0.65	0.65 (0.34 to 1.22)	0.18
Moderate stress	1.00 (0.73 to 1.37)	0.99	0.80 (0.57 to 1.12)	0.20	1.36 (0.84 to 2.21)	0.22	0.64 (0.32 to 1.30)	0.22
High stress	1.29 (0.99 to 1.69)	0.06	0.80 (0.56 to 1.14)	0.22	1.27 (0.81 to 1.99)	0.30	0.67 (0.33 to 1.34)	0.26

	All-Cause Mortality (n=1620)			
	Income <$35 000		Income ≥$35 000	
Number of events*	953		429	
Crude incidence rate per 1000 person-years*	22.5		8.7	
Models†‡	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Model 1 (demographics, education)				
No stress (ref)	1.00	—	1.00	—
Low stress	1.26 (1.05 to 1.52)	0.01	0.86 (0.67 to 1.10)	0.24
Moderate stress	1.38 (1.15 to 1.66)	0.001	1.11 (0.86 to 1.42)	0.42
High stress	1.65 (1.40 to 1.94)	<0.001	1.20 (0.93, 1.55)	0.15
Model 2 (demographics, education, and clinical factors)				
No stress (ref)	1.00	—	1.00	—
Low stress	1.26 (1.05 to 1.52)	0.01	0.85 (0.66 to 1.10)	0.22
Moderate stress	1.37 (1.14 to 1.65)	0.001	1.12 (0.87 to 1.44)	0.38
High stress	1.62 (1.37 to 1.90)	<0.001	1.19 (0.92 to 1.54)	0.18
Model 3 (demographics, education, clinical, and behavioral factors)				
No stress (ref)	1.00	—	1.00	—
Low stress	1.25 (1.03 to 1.50)	0.02	0.85 (0.66 to 1.10)	0.22
Moderate stress	1.31 (1.09 to 1.57)	0.004	1.12 (0.87 to 1.44)	0.36
High stress	1.55 (1.31 to 1.82)	<0.001	1.13 (0.88 to 1.46)	0.34

CHD indicates coronary heart disease; HR, hazard ratio.

*Number of events and crude incidence rates based on data that exclude participants that refused to provide income (n=3031).

†Model 1: adjusts for age, sex, race, urban, stroke region, and education. Model 2: adjusts for model 1 characteristics and systolic blood pressure, antihypertensive medication use, total cholesterol, high density lipoprotein cholesterol, statin use, diabetes. Model 3: adjusts for model 2 characteristics and smoking, exercise, alcohol use, body mass index.

‡Referent group is the lowest category for perceived stress scale, which represents participants with the lowest perceived stress scale score.

Table 3. Incidence and Hazard Ratios (With 95% CI) for Association of Perceived Stress and Incident Total and Fatal CHD and All-Cause Mortality Stratified by Annual Household Income (N=24 439 Individuals Free of CHD at Baseline; Complete Case Analysis Results)

	Incident Total CHD (n=659)				Incident Fatal CHD (n=215)			
	Income <$35 000		Income ≥$35 000		Income <$35 000		Income ≥$35 000	
Number of events*	333		247		131		61	
Crude incidence rate per 1000 person-years*	7.9		5.1		3.1		1.2	
Models†‡	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Model 1 (demographics, education), n=19 334	n_{events}=302		n_{events}=219		n_{events}=120		n_{events}=53	
No stress (ref)	1.00	—	1.00	—	1.00	—	1.00	—
Low stress	0.95 (0.67 to 1.34)	0.76	0.73 (0.52 to 1.02)	0.07	1.20 (0.68 to 2.13)	0.53	0.51 (0.24 to 1.06)	0.07
Moderate stress	0.95 (0.67 to 1.34)	0.76	0.68 (0.47 to 0.98)	0.04	1.53 (0.89 to 2.61)	0.12	0.55 (0.25 to 1.17)	0.12
High stress	1.42 (1.06 to 1.90)	0.02	0.76 (0.52 to 1.12)	0.16	1.55 (0.94 to 2.54)	0.08	0.72 (0.34 to 1.50)	0.38
Model 2 (demographics, education, and clinical factors), n=18 406	n_{events}=279		n_{events}=212		n_{events}=111		n_{events}=52	
No stress (ref)	1.00	—	1.00	—	1.00	—	1.00	—
Low stress	1.10 (0.76 to 1.58)	0.61	0.75 (0.53 to 1.06)	0.10	1.36 (0.75 to 2.47)	0.30	0.50 (0.24 to 1.05)	0.07
Moderate stress	1.09 (0.76 to 1.56)	0.65	0.65 (0.44 to 0.96)	0.03	1.69 (0.97 to 2.97)	0.06	0.50 (0.22 to 1.11)	0.09
High stress	1.45 (1.06 to 1.99)	0.02	0.80 (0.55 to 1.18)	0.26	1.55 (0.92 to 2.64)	0.10	0.72 (0.34 to 1.50)	0.38
Model 3 (demographics, education, clinical, and behavioral factors), n=17 728	n_{events}=268		n_{events}=204		n_{events}=105		n_{events}=49	
No stress (ref)	1.00	—	1.00	—	1.00	—	1.00	—
Low stress	1.07 (0.73 to 1.54)	0.74	0.77 (0.54 to 1.09)	0.15	1.36 (0.74 to 2.49)	0.32	0.52 (0.25 to 1.10)	0.09
Moderate stress	1.02 (0.70 to 1.48)	0.93	0.70 (0.47 to 1.03)	0.07	1.49 (0.83 to 2.68)	0.18	0.52 (0.23 to 1.17)	0.11
High stress	1.44 (1.05 to 1.98)	0.02	0.72 (0.48 to 1.08)	0.11	1.57 (0.92 to 2.69)	0.10	0.57 (0.25 to 1.27)	0.17

Continued

Table 3. Continued

	All-Cause Mortality (n=1620)			
	Income <$35 000		Income ≥$35 000	
Number of events*	953		429	
Crude incidence rate per 1000 person-years*	22.5		8.7	
Models†‡	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
Model 1 (demographics, education), n=19 334)	n_{events}=863		n_{events}=383	
No stress (ref)	1.00	—	1.00	—
Low stress	1.25 (1.01 to 1.54)	0.04	0.88 (0.67 to 1.15)	0.34
Moderate stress	1.36 (1.11 to 1.67)	0.003	1.12 (0.86 to 1.47)	0.40
High stress	1.63 (1.36 to 1.96)	<0.001	1.17 (0.88 to 1.55)	0.28
Model 2 (demographics, education, and clinical factors), n=18 406	n_{events}=791		n_{events}=366	
No stress (ref)	1.00	—	1.00	—
Low stress	1.36 (1.09 to 1.69)	0.006	0.85 (0.65 to 1.13)	0.27
Moderate stress	1.41 (1.14 to 1.75)	0.002	1.12 (0.85 to 1.48)	0.40
High stress	1.63 (1.34 to 1.98)	<0.001	1.12 (0.84 to 1.49)	0.46
Model 3 (demographics, education, clinical, and behavioral factors), n=17 728	n_{events}=747		n_{events}=351	
No stress (ref)	1.00	—	1.00	—
Low stress	1.36 (1.09 to 1.71)	0.007	0.84 (0.63 to 1.12)	0.23
Moderate stress	1.33 (1.06 to 1.66)	0.01	1.12 (0.84 to 1.48)	0.43
High stress	1.57 (1.28 to 1.91)	<0.001	0.97 (0.72 to 1.31)	0.84

CHD indicates coronary heart disease; hazard ratio.

*Number of events and crude incidence rates based on data that exclude participants that refused to provide income (n=3031).

†Model 1: adjusts for age, sex, race, urban, stroke region, and education. Model 2: adjusts for model 1 characteristics and systolic blood pressure, antihypertensive medication use, total cholesterol, HDL cholesterol, statin use, diabetes. Model 3: adjusts for model 2 characteristics and smoking, exercise, alcohol use, body mass index.

‡Referent group is the lowest category for perceived stress scale, which represents participants with the lowest Perceived Stress Scale score.

stress and race and stress and sex for any of the outcomes. However, blacks and women were disproportionately represented in the low-income/high-stress strata compared with whites in our study, reflecting similar distributions nationally.[44,45] Prior research shows that exploring the interplay of race, SES, and stress found that as income increases among blacks and whites, psychological distress decreases, and this is especially true for blacks. However, there was no significant difference between blacks and whites at the lowest income levels.[44] Thus, race may be associated with an increased risk of being low income and therefore experiencing a high level of stress, but the impact of high stress on health is primarily dependent on income. Much attention has been given to the disproportionate burden of modifiable CVD risk factors such as hypertension, smoking, and obesity among blacks.[46–48] Emerging data suggest that stress in low-income blacks may also be a potentially modifiable risk factor through behavioral interventions such as transcendental meditation.[49]

While REGARDS-MI is a prospective study with a large biracial cohort and expert adjudication of outcomes, this study is not without limitations. Although the ability to draw causal inferences is limited, the prospective nature of the study did allow for the measurement of perceived stress and other covariates as antecedents to the defined outcomes. However, because stress and income were ascertained at a single time point, we were not able to explore the potential impact of changes in stress and/or income over time. Furthermore, the limitations of self-reported variables are well known leading to possible misclassification and reporting biases, a problem that is common among all epidemiologic studies. Medical records are retrieved to identify and adjudicate incident events detected during follow-up; not all events may be detected this way, and some records are inevitably not able to be retrieved. Also, REGARDS used an abbreviated version of the PSS, which, though validated, has modestly lower internal reliability (Cronbach's α=0.60) when compared with the 10- and 14-item versions (Cronbach's α=0.78 and 0.75, respectively).[50] However, recent studies have shown that higher stress as measured by the 4-item PSS is associated with poorer health outcomes including higher 2-year mortality post-MI[29] in a US cohort, higher postnatal depression and lower quality of life among Canadian women,[51] and increased asthma morbidity across a 1-year

follow-up among US inner-city asthmatics.[52] Furthermore, a very recent publication exploring the association of the 4-item PSS with high blood pressure among a French cohort showed perceived stress was negatively associated with high blood pressure among individuals of high occupational status but positively associated among those of low status or unemployed.[53] In addition, similar to our study, the study by Arnold et al showed that groups with higher stress as measured by the 4-item PSS had a higher proportion of women and a lower proportion of whites.[29] Their study did not have information on income; however, the high-stress group had a higher proportion of individuals who "avoided care due to cost." Last, baseline data were assessed at a single time point, and stress may vary over time. Of note, a recent study using the 10-item version of the PSS showed that across 3 national surveys administered in 1983, 2006, and 2009, women reported greater stress than did men; stress decreased with increasing age, education, and income; and minorities tended to report more stress than did whites.[54]

In conclusion, we found that perceived stress was associated with incident CHD and all-cause mortality for low-income individuals but not for those reporting high income, adding to prior literature reporting a significant association of stress with CVD and mortality.[14,16,55,56] Our findings suggest that screening for stressors within the health care setting may be warranted among low-income individuals. Furthermore, these findings support the expansion of tailored clinical and community-based interventions aimed toward reducing stress in low-income communities, which may contribute to the reduction of disparities in CHD outcomes and all-cause mortality.

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Author Contributions

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Disclosures

None.

References

1. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Magid D, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, Moy CS, Mussolino ME, Nichol G, Paynter NP, Schreiner PJ, Sorlie PD, Stein J, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Heart disease and stroke statistics—2013 update: a report from the American Heart Association. *Circulation*. 2013;127:e6–e245.
2. Ford ES, Capewell S. Proportion of the decline in cardiovascular mortality disease due to prevention versus treatment: public health versus clinical care. *Annu Rev Public Health*. 2011;32:5–22.
3. Mensah GA, Mokdad AH, Ford ES, Greenlund KJ, Croft JB. State of disparities in cardiovascular health in the United States. *Circulation*. 2005;111:1233–1241.
4. Safford MM, Brown TM, Muntner PM, Durant RW, Glasser S, Halanych JH, Shikany JM, Prineas RJ, Samdarshi T, Bittner VA, Lewis CE, Gamboa C, Cushman M, Howard V, Howard G. Association of race and sex with risk of incident acute coronary heart disease events. *JAMA*. 2012;308:1768–1774.
5. Pickle LW, Gillum RF. Geographic variation in cardiovascular disease mortality in US blacks and whites. *J Natl Med Assoc*. 1999;91:545–556.
6. Rosamond WD, Folsom AR, Chambless LE, Wang CH. Coronary heart disease trends in four United States communities. The Atherosclerosis Risk in Communities (ARIC) study 1987–1996. *Int J Epidemiol*. 2001;30(suppl 1):S17–S22.
7. Rosamond WD, Chambless LE, Folsom AR, Cooper LS, Conwill DE, Clegg L, Wang CH, Heiss G. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994. *N Engl J Med*. 1998;339:861–867.
8. Kaplan GA. Going back to understand the future: socioeconomic position and survival after myocardial infarction. *Ann Intern Med*. 2006;144:137–139.
9. Prevalence of regular physical activity among adults–United States, 2001 and 2005. *MMWR Morb Mortal Wkly Rep*. 2007;56:1209–1212.
10. Prevalence of fruit and vegetable consumption and physical activity by race/ethnicity—United States, 2005. *MMWR Morb Mortal Wkly Rep*. 2007;56:301–304.
11. Prevalence of self-reported physically active adults—United States, 2007. *MMWR Morb Mortal Wkly Rep*. 2008;57:1297–1300.
12. Differences in prevalence of obesity among black, white, and hispanic adults—United States, 2006–2008. *MMWR Morb Mortal Wkly Rep*. 2009;58:740–744.
13. Stewart JC, Rand KL, Muldoon MF, Kamarck TW. A prospective evaluation of the directionality of the depression-inflammation relationship. *Brain Behav Immun*. 2009;23:936–944.
14. Cohen S, Janicki-Deverts D, Miller GE. Psychological stress and disease. *JAMA*. 2007;298:1685–1687.
15. Matthews KA, Schott LL, Bromberger JT, Cyranowski JM, Everson-Rose SA, Sowers M. Are there bi-directional associations between depressive symptoms and C-reactive protein in mid-life women? *Brain Behav Immun*. 2010;24:96–101.
16. Everson-Rose SA, Lewis TT. Psychosocial factors and cardiovascular diseases. *Annu Rev Public Health*. 2005;26:469–500.
17. Hamer M, Chida Y. Associations of very high C-reactive protein concentration with psychosocial and cardiovascular risk factors in an ageing population. *Atherosclerosis*. 2009;206:599–603.
18. Rod NH, Gronbaek M, Schnohr P, Prescott E, Kristensen TS. Perceived stress as a risk factor for changes in health behaviour and cardiac risk profile: a longitudinal study. *J Intern Med*. 2009;266:467–475.

19. Albert MA, Glynn RJ, Ridker PM. Effect of physical activity on serum C-reactive protein. *Am J Cardiol*. 2004;93:221–225.
20. Pickering T. Cardiovascular pathways: socioeconomic status and stress effects on hypertension and cardiovascular function. *Ann N Y Acad Sci*. 1999;896: 262–277.
21. Albert MA, Glynn RJ, Buring J, Ridker PM. Impact of traditional and novel risk factors on the relationship between socioeconomic status and incident cardiovascular events. *Circulation*. 2006;114:2619–2626.
22. Clark AM, DesMeules M, Luo W, Duncan AS, Wielgosz A. Socioeconomic status and cardiovascular disease: risks and implications for care. *Nat Rev Cardiol*. 2009;6:712–722.
23. Kaplan GA, Keil JE. Socioeconomic factors and cardiovascular disease: a review of the literature. *Circulation*. 1993;88:1973–1998.
24. Kanjilal S, Gregg EW, Cheng YJ, Zhang P, Nelson DE, Mensah G, Beckles GL. Socioeconomic status and trends in disparities in 4 major risk factors for cardiovascular disease among US adults, 1971–2002. *Arch Intern Med*. 2006;166:2348–2355.
25. Sharma S, Malarcher AM, Giles WH, Myers G. Racial, ethnic and socioeconomic disparities in the clustering of cardiovascular disease risk factors. *Ethn Dis*. 2004;14:43–48.
26. Brunner E. Socioeconomic determinants of health: stress and the biology of inequality. *BMJ*. 1997;314:1472.
27. Thomas AJ, Eberly LE, Davey Smith G, Neaton JD, Stamler J. Race/ethnicity, income, major risk factors, and cardiovascular disease mortality. *Am J Public Health*. 2005;95:1417–1423.
28. Spertus JA, Jones PG, Masoudi FA, Rumsfeld JS, Krumholz HM. Factors associated with racial differences in myocardial infarction outcomes. *Ann Intern Med*. 2009;150:314–324.
29. Arnold SV, Smolderen KG, Buchanan DM, Li Y, Spertus JA. Perceived stress in myocardial infarction: long-term mortality and health status outcomes. *J Am Coll Cardiol*. 2012;60:1756–1763.
30. Strodl E, Kenardy J, Aroney C. Perceived stress as a predictor of the self-reported new diagnosis of symptomatic CHD in older women. *Int J Behav Med*. 2003;10:205–220.
31. Eaker ED, Pinsky J, Castelli WP. Myocardial infarction and coronary death among women: psychosocial predictors from a 20-year follow-up of women in the Framingham study. *Am J Epidemiol*. 1992;135:854–864.
32. Matthews KA, Gump BB. Chronic work stress and marital dissolution increase risk of posttrial mortality in men from the multiple risk factor intervention trial. *Arch Intern Med*. 2002;162:309–315.
33. Richardson S, Shaffer JA, Falzon L, Krupka D, Davidson KW, Edmondson D. Meta-analysis of perceived stress and its association with incident coronary heart disease. *Am J Cardiol*. 2012;110:1711–1716.
34. Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. *J Health Soc Behav*. 1983;24:385–396.
35. Howard VJ, Cushman M, Pulley L, Gomez CR, Go RC, Prineas RJ, Graham A, Moy CS, Howard G. The reasons for geographic and racial differences in stroke study: objectives and design. *Neuroepidemiology*. 2005;25:135–143.
36. Kressin NR, Petersen LA. Racial differences in the use of invasive cardiovascular procedures: review of the literature and prescription for future research. *Ann Intern Med*. 2001;135:352–366.
37. Rural Health Resource Center. RUCA Data. http://depts.washington.edu/uwruca/ruca-codes.php. (Archived by WebCite at http://www.webcitation.org/6FaXINqQE). Accessed February 4, 2013.
38. Rubin DB. Multiple imputation after 18+ years. *J Am Stat Assoc*. 1996;91:473–489.
39. Rubin DB, Schenker N. Multiple imputation in health-care databases: an overview and some applications. *Stat Med*. 1991;10:585–598.
40. Lazzarino AI, Hamer M, Stamatakis E, Steptoe A. The combined association of psychological distress and socioeconomic status with all-cause mortality: a national cohort study. *JAMA Intern Med*. 2013;173:22–27.
41. Fiscella K, Tancredi D, Franks P. Adding socioeconomic status to Framingham scoring to reduce disparities in coronary risk assessment. *Am Heart J*. 2009;157:988–994.
42. Fiscella KTD. Socioeconomic status and coronary heart disease risk prediction. *JAMA*. 2008;300:2666–2668.
43. Franks P, Winters PC, Tancredi DJ, Fiscella KA. Do changes in traditional coronary heart disease risk factors over time explain the association between socio-economic status and coronary heart disease? *BMC Cardiovasc Disord*. 2011;11:28.
44. Cockerham WC. A test of the relationship between race, socioeconomic status, and psychological distress. *Soc Sci Med*. 1990;31:1321–1326.
45. Baum A, Garofalo JP, Yali AM. Socioeconomic status and chronic stress: does stress account for SES effects on health? *Ann N Y Acad Sci*. 1999;896:131–144.
46. Cooper R, Cutler J, Desvigne-Nickens P, Fortmann SP, Friedman L, Havlik R, Hogelin G, Marler J, McGovern P, Morosco G, Mosca L, Pearson T, Stamler J, Stryer D, Thom T. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the national conference on cardiovascular disease prevention. *Circulation*. 2000; 102:3137–3147.
47. Flack JM, Ferdinand KC, Nasser SA. Epidemiology of hypertension and cardiovascular disease in African Americans. *J Clin Hypertens (Greenwich)*. 2003;5:5–11.
48. Hozawa A, Folsom AR, Sharrett AR, Chambless LE. Absolute and attributable risks of cardiovascular disease incidence in relation to optimal and borderline risk factors: comparison of African American with white subjects—Atherosclerosis Risk in Communities Study. *Arch Intern Med*. 2007;167:573–579.
49. Schneider RH, Grim CE, Rainforth MV, Kotchen T, Nidich SI, Gaylord-King C, Salerno JW, Kotchen JM, Alexander CN. Stress reduction in the secondary prevention of cardiovascular disease: randomized, controlled trial of transcendental meditation and health education in blacks. *Circ Cardiovasc Qual Outcomes*. 2012;5:750–758.
50. Cohen S, Williamson GM. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S, eds. *The Social Psychology of Health*. Thousand Oaks, CA: University of Michigan/Sage Publications; 1988:31–67.
51. Karam F, Berard A, Sheehy O, Huneau MC, Briggs G, Chambers C, Einarson A, Johnson D, Kao K, Koren G, Martin B, Polifka JE, Riordan SH, Roth M, Lavigne SV, Wolfe L, Committee OR. Reliability and validity of the 4-item perceived stress scale among pregnant women: results from the OTIS antidepressants study. *Res Nurs Health*. 2012;35:363–375.
52. Wisnivesky JP, Lorenzo J, Feldman JM, Leventhal H, Halm EA. The relationship between perceived stress and morbidity among adult inner-city asthmatics. *J Asthma*. 2010;47:100–104.
53. Wiernik E, Pannier B, Czernichow S, Nabi H, Hanon O, Simon T, Simon JM, Thomas F, Bean K, Consoli SM, Danchin N, Lemogne C. Occupational status moderates the association between current perceived stress and high blood pressure: evidence from the IPC cohort study. *Hypertension*. 2013;61:571–577.
54. Cohen S, Janicki-Deverts D. Who's stressed? Distributions of psychological stress in the United States in probability samples from 1983, 2006, and 20091. *J Appl Soc Psychol*. 2012;42:1320–1334.
55. Backe EM, Seidler A, Latza U, Rossnagel K, Schumann B. The role of psychosocial stress at work for the development of cardiovascular diseases: a systematic review. *Int Arch Occup Environ Health*. 2012;85:67–79.
56. Din-Dzietham R, Nembhard WN, Collins R, Davis SK. Perceived stress following race-based discrimination at work is associated with hypertension in African-Americans. The metro Atlanta Heart Disease Study, 1999–2001. *Soc Sci Med*. 2004;58:449–461.