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The Contribution of Stress to the Social Patterning of Clinical and Subclinical CVD Risk Factors in African Americans: The Jackson Heart Study

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Abstract

It is often hypothesized that psychosocial stress may contribute to associations of socioeconomic position (SEP) with risk factors for cardiovascular disease (CVD). However, few studies have investigated this hypothesis among African Americans, who may be more frequently exposed to stressors due to social and economic circumstances. Cross-sectional data from the Jackson Heart Study (JHS), a large population-based cohort of African Americans, were used to examine the contributions of stressors to the association of SEP with selected cardiovascular (CVD) risk factors and subclinical atherosclerotic disease. Among women, higher income was associated with lower prevalence of hypertension, obesity, diabetes and carotid plaque and lower levels of stress. Higher stress levels were also weakly, albeit positively, associated with hypertension, diabetes, and obesity, but not with plaque. Adjustment for the stress measures reduced the associations of income with hypertension, diabetes and obesity by a small amount that was comparable to, or larger, than the reduction observed after adjustment for behavioral risk factors. In men, high income was associated with lower prevalence of diabetes and stressors were not consistently associated with any of the outcomes examined. Overall, modest mediation effects of stressors were observed for diabetes (15.9%), hypertension (9.7%), and obesity (5.1%) among women but only results for diabetes were statistically significant. No mediation effects of stressors were observed in men. Our results suggest that stressors may partially contribute to associations of SEP with diabetes and possibly hypertension and obesity in African American women. Further research with appropriate study designs and data is needed to understand the dynamic and interacting effects of stressors and behaviors on CVD outcomes as well as sex differences in these effects.

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Keywords

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Introduction

Multiple studies have shown that socioeconomic position (SEP) is inversely associated with clinical and subclinical cardiovascular disease (CVD) and its risk factors, including hypertension, diabetes, and obesity (e.g., Diez Roux, 1995; Galobardes et al., 2006; Kaplan & Keil, 1993; Ranjit et al., 2006). The reasons for the graded inverse association between SEP and cardiovascular risk remain a topic of research.

Psychosocial factors, including chronic and short-term stressors, are often hypothesized to partially account for SEP differences in the prevalence and incidence of chronic diseases such as CVD (Adler & Snibbe, 2003; Baum et al., 1999; Lantz et al., 2005; Matthews et al., 2010). Chronic stressors include minor irritants and hassles as well as more severe, but regularly occurring circumstances. Short-term stressors are usually infrequent but more intense and may include negative life events or major life changes.

It is well established that chronic and short-term stressors are inversely associated with SEP (Baum et al., 1999; Grzywacz et al., 2004; Hatch & Dohrenwend, 2007; Skodova et al., 2008; Stronks et al., 1998; Turner et al., 1995). In addition, there are a number of plausible mechanisms through which stressors may be linked to CVD and its risk factors (Everson-Rose & Lewis, 2005; Krantz & McCeney, 2002). Persons may cope with stress through behavioral changes such as initiating or increasing tobacco use or increasing energy intake (Dallman et al., 2003; Lindquist et al., 1997; McEwen & Gianaros, 2010) both of which have been linked to CVD. Stress may also be linked to cardiovascular disease through stress-elicited responses of the hypothalamic-pituitary-adrenocortical axis (HPA) and the sympathetic-adrenal-medullary (SAM) system, which may result in increased blood pressure, greater adiposity, and insulin resistance (McEwen, 1998).

Although several studies have linked psychosocial factors to CVD risk (Everson-Rose & Lewis, 2005; Krantz & McCeney, 2002; Rozanski et al., 1999; Steptoe & Marmot 2002; Yan et al., 2003), the extent to which stressors contribute to SEP differences in CVD remains an elusive question (Matthews et al., 2010; Schulz et al., 2008). In the United States, African Americans may be more frequently exposed to certain stressors because of their social and economic circumstances. For example, African Americans report experiencing greater cumulative exposures to stressors than whites (Hatch & Dohrenwend, 2007; Williams et al., 1997; Williams & Mohammed, 2009). Such exposures include greater numbers of both chronic and short-term stressors linked to adverse life circumstances and discrimination (Williams et al., 1997; Williams & Mohammed, 2009). It is therefore plausible that psychosocial stress may be an especially strong contributor to SEP differences in cardiovascular risk factors in African Americans. However, few if any studies have included SEP, psychosocial stress and cardiovascular risk data necessary to investigate this research question in large population samples of African Americans.

Using data from the baseline examination (2000-2004) of the Jackson Heart Study (JHS), we investigated the contribution of psychosocial stressors to the relationship between SEP and CVD risk. We hypothesized that SEP would be inversely associated with psychosocial stressors and CVD risk factors, and that psychosocial stressors would be positively associated with the CVD risk factors. We also hypothesized that psychosocial stressors

would be important contributors to the inverse association between SEP and cardiovascular risk. In addition we contrasted the role of stressors and behaviors separately in the social patterning and also examined the extent to which stressors remained associated with outcomes after adjustment for behaviors.

Methods

The JHS is a population-based prospective cohort study of CVD in non-institutionalized African American adults aged 21-95 residing in the Jackson, Mississippi metropolitan statistical area (MSA) (Taylor et al., 2005). The state of Mississippi has the largest percentage of African American residents (36.9%) of any state in the U.S. and the lowest per capita income (United States Department of Commerce, 2008). Study participants were recruited between September 2000 and March 2004 from the Jackson MSA (Hinds, Madison and Rankin County) using four approaches. First, all Jackson, MS participants in the Atherosclerosis Risk in Communities (ARIC) study who were alive, still enrolled in ARIC (48.2% of the surviving Jackson, MS ARIC participants), and aged 35-84 years at the time of the initiation of the JHS were invited to participate in the JHS. Jackson ARIC participants were originally sampled (1987-1989) from City of Jackson residents listed in the Mississippi Driver's License and Identification List. In total, 31% of the JHS participants were recruited from the ARIC study. The second approach recruited participants through random sampling (17% of the total JHS sample) from a commercially available list (AccuData Integrated Marketing, Fort Myers, FL) of all of community residents 35-84 years in the tri-county area. The third approach recruited volunteers (30% of the total JHS sample) aged 35-84 years through targeted advertisements: radio, newspaper, local churches, and civic/social organizations. Volunteers were approximately representative of the Jackson MSA African American population in terms of age, sex and socioeconomic characteristics. Finally, family members of other JHS participants (22% of the total JHS sample) were recruited from enumerated households to permit future genetic studies. Family members were included even if they were <35 or over 84 years of age. The final study sample for JHS consisted of 5,301 men and women between the ages of 21 and 94 and has been shown to be geographically representative of the age-eligible African American population in the Jackson MSA (Hickson et al., 2011). ARIC participants were slightly older than other study participants. Details of the study design and data collection methods are described elsewhere (Carpenter et al., 2004; Taylor et al., 2005). As part of the baseline examination, participants underwent clinical examinations, provided blood specimens, and completed questionnaires. The JHS was approved by the institutional review boards of Jackson State University, Tougaloo College and the University of Mississippi Medical Center. All participants provided informed consent.

Socioeconomic Measures

SEP was defined based on annual family income reported during the home induction interview., Income was self-reported into 11 categories ranging from under $5,000 to $100,000 or more and classified into five categories: low, lower-middle, upper-middle, and high, which were based upon family size, number of children < 18 years of age, and the United States Census designated poverty level for the year in which the income information was obtained. Low income was defined as income below the poverty level. Lower-middle income was defined as income at or above the poverty level but below 2.5 times the poverty level. Upper-middle income was defined as income at or above 2.5 times the poverty level, but below four times the poverty level. High income was defined as income of four times the poverty level or more. Participants who did not know their income or refused to respond were classified as “Unknown.” In addition, a measure of continuous income was estimated by taking the interval midpoint of family income for each of the 11 income categories. In

order to report associations for a meaningful difference in income compatible with the income distribution observed in the sample, associations with income are reported for a difference in income equivalent to moving from the 10^{th} to the 90^{th} percentile of continuous income in the sample (equivalent to a difference of $77,500 dollars). Income was selected for investigation because prior research has suggested that differential returns to education by race (Williams et al., 2010) may make education a less strong predictor of health in African Americans and because of the known difficulty in measuring a categorizing occupation in large studies (MacDonald et al., 2009).

Measures of Stress and Life Events

We investigated three measures of stress. The Global Perceived Stress Scale (GPSS) was administered as part of the baseline examination. The Weekly Stress Inventory (WSI) was given to study participants at the conclusion of the baseline examination with instructions to complete at home and mail back to the JHS Coordinating Center. Negative Life Events (NLE) were assessed by telephone interview during the annual surveillance follow-up. Stress measures were investigated in four categories (based on quartiles) and as continuous variables in standard deviation units.

GPSS is an 8-item questionnaire that measures the severity of chronic stress experienced over a prior period of twelve months in the following areas: employment, relationships, the neighborhood, caring for others, legal problems, medical problems, experiences of racism and discrimination, and meeting basic needs. This questionnaire was created for the JHS (Payne et al., 2005) and was adapted from Kohn & MacDonald's (1992) Survey of Recent Life Experiences, Cohen et al.'s (1983) Perceived Stress Scale, and Sarason et al.'s (1978) Life Events Scale. Participants were asked to rate the severity in each domain; response choices ranged from “not stressful” to “very stressful” and scored 0 to 3. Of the JHS participants who completed the baseline examination, 5,256 had complete GPSS data. The Cronbach's alpha for the GPSS in this sample was .72.

Developed by Jones & Brantley (1989), the WSI is an 87-item questionnaire that assesses experiences of minor irritants or hassles over the past week across a broad range of life domains including, work tasks, relationships, finances, transportation, household tasks and responsibilities, leisure time activities, and others. Participants were asked to assess the severity of the stressors during the past week on a 7-point scale with levels ranging from “did not happen” to “extremely stressful” coded 0-7. A smaller number of JHS participants returned the WSI (67.9% completion rate). A total of 2,920 JHS participants had complete WSI data. The Cronbach's alpha for the WSI in the sample was .98.

The NLE survey used in the JHS was adapted from the Holmes & Rahe (1967) Life Changes Scale and included 11 items for which respondents were asked if they had major events (or stressors) to occur in the last 12 months by answering “yes” or “no.” The items pertained to victimization, death of close relatives/friends, serious illness, violence, relocation, job loss, and divorce. JHS participants with complete NLE data totaled 4,811. Because this is strictly speaking an index rather than a true scale the Cronbach's alpha was not calculated.

Outcomes

The clinical and subclinical CVD risk factors examined as outcomes included hypertension, diabetes, obesity, and carotid plaque. Two resting blood pressure readings were taken one minute apart in the seated position using a Hawksley random-zero sphygmomanometer (Hawksley & Sons Ltd.) and averaged. Hypertension was defined according to JNC VII criteria as a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg at

exam, or use of antihypertensive medications (self-report and actual) within 2 weeks prior to the examination, or self-reported history of hypertension (Chobanian et al., 2003).

Type II diabetes was defined according to American Diabetes Association 2004 criteria as fasting glucose ≥ 126 mg/dl, or confirmed medication inventory or self-reported use of anti-diabetic medications, or self-reported diabetes diagnosis (American Diabetes Association, 2004).

Body mass index (BMI) was calculated in kg/m^2 using measurements of weight and height at the exam while participants wore light clothing and no shoes. Persons were classified as obese if they had a BMI ≥ 30 kg/m^2.

Carotid plaque, an indicator of subclinical atherosclerosis of the carotid arteries, is a well established risk factor for cardiovascular events (Prabhakaran et al., 2007; Simon et al., 2010). The presence of carotid plaque was determined from ultrasound examination of the left and right carotid arteries at the common, bifurcation, and internal sites using a Hewlett Packard Sonos 4500 ultrasound imaging device (Carpenter et al., 2004). Three circumferential views were assessed at the common and bifurcation segments (anterior, lateral, and posterior). A single view was obtained at the internal segment. Carotid plaque at any of sites was assessed by staff radiologists and recorded as “present” or “absent.”

Covariates

Behavioral covariates included cigarette smoking, physical activity, and diet. Cigarette smoking was self-reported by participants and classified as current smoker, former smoker, or never smoked. Pack-years of cigarette smoking was also included as a continuous covariate for finer adjustment for former and current smokers. Physical activity was assessed using the JHS Physical Activity instrument derived from modification of the Baecke physical activity survey (Baecke et al., 1982, Dubbert et al., 2005). Total physical activity was computed as a summary score of the intensity, frequency, and duration of activities associated various aspects of life (active living, home life, sport and work). The summary score was validated against results from 24-hour accelerometer and pedometer monitoring (Smitherman et al., 2009) and investigated as a continuous variable. Dietary intake, defined as total energy, total dietary fiber (grams/day), and percent calories from fat and carbohydrates, were calculated from the contributions of each of the 158 food items contained in a validated food frequency questionnaire (Carithers et al., 2009) and included as continuous covariates.

Statistical Analysis

Only participants with complete data on psychosocial stress measures, clinical and subclinical CVD risk factors (hypertension, diabetes, obesity and carotid plaque), SES (income), and covariate information (cigarette smoking status and pack-years of smoking for former and current smokers, physical activity, and dietary intake) were included in these analyses. Because of the smaller sample size for WSI, we performed two sets of analyses: the first set focused on participants with complete data on the GPSS and NLE measures, CVD risk factors, and covariates (n = 3980); the second set of analyses included the subset of participants who also had complete data on the WSI measure (n = 2478).

Descriptive statistics were used to compare key variables across the two analytic samples (GPSS/NLE and WSI) and the entire JHS Cohort. We stratified all analyses by sex because of prior work showing differential associations of SES with CVD outcomes by sex (Thurston et al., 2005).

In order to investigate the contribution of stress to the associations of income with cardiovascular risk factors we followed the classic approach proposed by Baron & Kenny (1986). First we examined whether income was related to the outcomes (cardiovascular risk factors) and to stress. Second we examined whether stress was related to cardiovascular risk factors. Third we examined the change in the association of income with cardiovascular risk factors when stress was added to the models.

To assess the association of income and stress with CVD risk factors, we estimated age-adjusted proportions of CVD risk factors by income categories and by quartiles of stress levels using logistic regression. Linear trends across income categories and quartiles of stress measures was tested by including income and stress measures as ordinal covariates (i.e., coded as 1-4). To assess whether income was associated with stress measures, we estimated age-adjusted mean values of GPSS and NLE by levels of income using linear regression and tested for linear trends. We investigated income and stress measures in categories in initial analyses in order to investigate whether there was evidence of any thresholds. Since no clear thresholds were identified, income and stress measures were investigated as continuous predictors in subsequent analyses.

In order to investigate the contribution of stress to the associations of income with CVD risk factors, we fit a series of multivariable Poisson regression models (Spiegelman & Hertzmar, 2005) to estimate prevalence ratios (PR) of CVD risk factors associated with income before and after adjusting for stress measures and health behaviors. Prevalence ratios were estimated instead of odds ratios because the prevalence of CVD risk factors was high and to avoid the potential influence of the non-collapsibility of the odds ratio in comparing estimates across models (Greenland, 1987). We then examined the extent to which the associations of income with cardiovascular risk factors changed when the stress measures and behaviors were added to the models. The first model (model 1) included income (as continuous variable) and age only. In order to examine the potential mediating role of stress, we added the stress measures (as continuous variables) and inspected the change in the regression coefficient and associated prevalence ratio. GPSS and NLE were examined separately in models 2 and 3, respectively, and then simultaneously in the model 4. We also fit a model adjusting for behaviors only (model 5), to evaluate whether the stress measures or behaviors explained a greater amount of the associations of income with the CVD risk factors. Finally, we fit a full model that included both stress measures and behaviors (model 6). This allowed us to determine whether any stress effects or remaining SEP effects observed in model 4 could be mediated in part by behavioral factors. The contributions of WSI were examined in a separate set of analogous models in the subsample with WSI measures. All statistical analyses were performed with the SAS statistical software (SAS Institute, Inc., Cary, NC).

Inferring mediation based on a change in the prevalence ratio associated with the exposure after adjustment for the hypothesized mediator (the common approach used in many prior epidemiologic investigations of the mediating role of psychosocial factors (Matthews et al., 2010) requires several assumptions: (1) no unmeasured confounders of the exposure-outcome and mediator-outcome relations and (2) no interaction between the exposure and the mediator (Baron & Kenny, 1986). In order to explore the robustness of the conclusions derived from the simple (“naïve”) approach described above, we also conducted a formal mediation analysis based on the causal inference approach to mediation analysis (Pearl, 2001; Robins and Greenland, 1992; VanderWheele & Vansteelandt, 2009). This approach permits the decomposition of a total effect into natural direct and natural indirect effects in cases with interactions and non-linearities (Valeri & VanderWeele, 2011; VanderWheele & Vansteelandt, 2009; VanderWheele & Vansteelandt, 2010-). This approach was useful in

our case because of the presence of statistically significant interactions (P<0.05) between income and GPSS for diabetes and between income and NLE for obesity in women.

Using the approach and SAS macro developed by Valeri & VanderWeele (2011), we estimated the natural direct effect and the natural indirect effect by fitting two models. First, we fit a log-linear model (Poisson model) for CVD risk factors conditional on income, stress, and a set of confounders (age in one set of analyses, age and behaviors in another set of analyses). Second, we fit a linear regression model for stress measures conditional on income and the same set of confounders. From these combined models, we estimated the prevalence ratios for natural direct effects (PR_{NDE}), natural indirect effects (PR_{NIE}), and total effect (PR_{TE}), as well as, the proportion of the total effects that is mediated by stress. The natural direct effect expresses how much the outcome would change if the exposure were set at level a=1 vs. a*=0 (or analogously at a higher vs. lower level of a continuous exposure) but the mediator were kept at the level it would have taken in the absence of exposure (this is distinct from the controlled direct effect which sets the level of the mediator at a uniform level across all individual in the population) (Valeri & VanderWeele, 2011). The natural indirect effect expresses how much the outcome would change if the exposure were set at level a=1 vs. a*=0 and the level of the mediator were allowed to change from the level it would have had when a*=0 to the level it would have had when a=1. The total effect can be decomposed into the natural direct and indirect effect even in the presence of non-linearities and interactions (Pearl, 2001; VanderWheele & Vansteelandt, 2009). It has been argued that natural direct and indirect effects are especially useful when interest centers in enhancing mechanistic understanding as in our case (Pearl, 2001; Robins, 2003).

We performed these mediation analyses for GPSS and NLE separately in women. This approach has the advantage of allowing for interactions between the exposure and the mediator, but it still requires the no confounding assumptions noted above for the “naïve” approach (Valeri & VanderWeele, 2011; VanderWeele & Vansteelandt, 2009-). In addition, the estimation of natural direct and indirect effects also requires two additional assumptions (1) no unmeasured confounder of the exposure –mediator relation; and (2) no confounder of the mediator –outcome relation affected by prior exposure (Imai et al., 2010; VanderWheele & Vansteelandt, 2009).

Results

Comparisons of the GPSS and NLE sample and the full JHS cohort on showed that differences between the samples were not statistically significant. However, the WSI sample was slightly younger (p<0.001), reported higher income (p<0.001) and had a lower prevalence of hypertension (p<0.001), diabetes (p=0.003), and carotid plaque (p<0.001) than the full JHS cohort. Overall, GPSS was moderately correlated with WSI (Pearson's correlation coefficient: 0.37) and NLE (0.24); WSI and NLE were weakly (0.17) correlated.

Sex-specific sample characteristics by analytic sample are reported in Table 1. The mean age ranged from 52.2 to 55.1 years. The percent of participants who were low income ranged from 12.3 to 14.7% in women and from 7.3 to 8.3% in men. Unadjusted prevalence rates were between 55.1 and 63.9% for hypertension, 14.5 and 19.3% for diabetes, 41.2 and 60.3% for obesity, and 33.4 and 38.6% for carotid plaque.

Table 2 shows age-adjusted CVD risk factor proportions and stress score means across income categories in women and men. In women, income was inversely associated with all CVD risk factors. Although dose response trends were not clearly present for obesity or plaque, tests for linear trends were statistically significant for all risk factors. Higher income was also approximately linearly related to decreasing stress scores for GPSS, NLE and WSI

(P for trend <0.001). Among men, diabetes was the only cardiovascular risk factor associated with income. There was no linear gradient but men in the highest category of income had lower prevalence of diabetes than the three other income categories. However, the prevalence of diabetes was higher in the middle income categories than in the low income categories. Higher income was also associated with lower stress scores in men with statistically significant trends for all three stress measures, although a consistent dose response trend was not present for NLE.

Table 3 shows associations of stress measures with the age-adjusted prevalence of CVD risk factors. Higher GPSS and NLE were generally associated with a higher prevalence of hypertension, diabetes, and (less consistently) obesity in women although dose response trends were not always observed: tests for trend were statistically significant for hypertension and diabetes in the case of GPSS and for hypertension, diabetes and obesity in the case of NLE. No statistically significant trends were observed for WSI. In men, a statistically significant trend was observed for carotid plaque by levels of WSI but no clear dose-response was evident. No other statistically significant associations were observed in men.

Table 4 shows the adjusted prevalence ratios (aPR) of CVD risk factors associated with a difference in income equivalent to the difference between the 90^{th} and the 10^{th} percentile of the sample distribution before and after adjustment for stress and behavioral measures in women. Higher income was associated with decreased prevalence ratio of hypertension and diabetes after adjustment for age (model 1). These associations were very slightly attenuated after simultaneously (model 4) adjusting for GPSS and NLE. The aPR (95% confidence interval) before and after adjustment for GPSS and NLE were 0.86 (0.78, 0.94) and 0.87 (0.79, 0.96) for hypertension and 0.61 (0.46, 0.81) and 0.63 (0.47, 0.84) for diabetes. In contrast, adjustment for health behaviors alone (model 5) did not alter the association of income with hypertension (aPR 0.86 (0.78, 0.95), and actually increased the association of income with diabetes (aPR 0.57 (0.43, 0.76)).

Income was also inversely associated with obesity after adjustment for age. Adjustment for stress resulted in very slight reductions of the associations of income with obesity (age-adjusted PR (model 1) 0.85 (0.77,0.94) and stress adjusted PR (model 4) 0.86 (0.78,0.95)) whereas adjustment for behavioral measures had no effect (model 5, 0.85 (0.77,0.94)). Analyses of continuous BMI yielded approximately similar patterns. Adjusted mean differences in BMI (kg/m2) (± SE) associated with income before and after adjustment for GPSS and NLE were -2.45± 0.43 and -2.29± 0.43, respectively. In contrast, adjustment for health behaviors alone resulted in a smaller reduction of the association of income with continuous BMI (-2.41± 0.44). Higher income was also associated with decreased prevalence ratio of plaque. Adjustment for stress measures (model 4) had no impact on these associations; in contrast, adjustment for behaviors reduced the associations of income with plaque (aPR before and after behavioral adjustment 0.84 (0.71, 0.99) and 0.89 (0.75, 1.05).

In general higher stress levels, as assessed by GPSS or NLE, were associated with greater prevalence of hypertension, diabetes and obesity although associations were not always statistically significant. A 1 SD increase in GPSS or NLE was associated with a 2-6% increase in the prevalence of hypertension, diabetes, and obesity. GPSS and NLE were not associated with carotid plaque. Statistically significant associations of income with hypertension, diabetes, and obesity remained in the fully adjusted model (model 6 aPR 0.88 (0.80, 0.97) for hypertension, 0.60 (0.45, 0.80) for diabetes, and 0.87 (0.78, 0.96) for obesity.

Table 5 shows the aPR of diabetes associated with income among men before and after adjustment for stress measures and behavioral factors. Only diabetes is shown because it was the only risk factor significantly associated with income in men. High income was associated with lower prevalence ratio of diabetes after age adjustment (models 1). Adjustment for stress measures and/or behavioral risk factors did not substantially modify the associations of income with diabetes in men. In fact, adjustment for behavioral risk factors (models 5 and 6) appeared to strengthen the inverse associations between income and diabetes. Associations of GPSS and NLE with diabetes were very weak and not statistically significant.

WSI was not significantly associated with any CVD risk factors in women or men and the addition of WSI did not materially alter the income differences in CVD risk (results not shown).

Table 6 presents the estimated natural direct, indirect, and total effects as well as the percentage of total effects of income mediated through GPSS or NLE as estimated using the approach of Valeri & VanderWeele (2011) in women. Diabetes and obesity analyses account for interactions between income and stress measures. In general results were consistent with the simpler analyses. As expected, the natural direct effects estimates show that high income was associated with lower risk ratio of hypertension, diabetes, obesity, and plaque. The prevalence ratios for the natural direct effects showed stronger associations than prevalence ratios for the indirect effects. For instance, the prevalence ratio of the natural direct and indirect effects of income on diabetes were 0.68 (0.49, 0.95) and 0.91 (0.84, 0.99), respectively. The portion of the total effect of income on diabetes that was mediated through GPSS was found to be 15.9 % and statistically significant. The portions of the total effect of income on hypertension, obesity, and plaque that were mediated through GPSS were estimated to be 7.9%, 5.1%, and 0.7%, respectively and none were statistically significant. The percentage of the total effects of income that was mediated through NLE for hypertension, diabetes, obesity, and plaque were estimated to be 4.1%, 2.3 %, -3.3%, and -1.7 %, respectively with none being statistically significant. Results were qualitatively similar regardless of whether behavioral risk factors were or were not accounted for (Table 6). There was no evidence that stress mediated any of the effect of income on diabetes in men (results not shown).

Discussion

We investigated how various dimensions of stress contribute to the association of income with several CVD risk factors in a large African American population. Among women, income was inversely associated with hypertension, diabetes, obesity, and carotid plaque prevalence. Higher income was associated with lower levels of reported stressors, and higher stress levels were weakly albeit positively associated with hypertension, diabetes, and obesity. Adjustment for the stress measures resulted in small reductions in the association of income with hypertension, diabetes, and obesity. These reductions were comparable to or larger than the reduction observed after adjustment for behavioral risk factors. In men, high income was associated with lower prevalence of diabetes. Although stressors were also inversely associated with income in men, they were not consistently related to the cardiovascular outcomes, and adjustment for stressors did not alter the associations of income with diabetes. Mediation analyses that accounted for interactions between income and stress showed that 15.9% of the excess risk of diabetes associated with income in women was mediated through stress (as measured by the GPSS). Stress (the GPSS) also explained smaller percentages of the associations of income with hypertension (7.9%) and obesity (5.1%) although these indirect effects were not statistically significant. This

relatively small contribution of stress to income differences in consistent with the weak association between stressors and the CVD risk factors in our data.

Despite frequent references to the role of stressors in health inequalities, relatively few empirical studies have directly investigated the contributions of stressors to associations of SEP with health, including CVD. Matthews et al. (2010) identified only nine studies that explicitly investigated this question, with 5 of the nine finding little or no evidence for a mediating role of stress (Matthews et al., 2010). Of these, five (Avendano et al., 2006; Gallo et al., 2001; MacLeod et al., 2005; Matthews et al., 2008; Prescott et al., 2007) did not observe an inverse associations of SES with stress, so the failure to observe a mediating role of stress in these studies was not surprising. The four remaining studies found that stressors contributed to varying amounts of the inverse associations of SES with mortality (Khang & Kim 2005; Lantz et al., 2005; van Oort et al., 2005) or metabolic factors (Lehman et al., 2005). Several additional studies have focused on job- related stressors such as job strain or job control in relation to inequalities in cardiovascular disease (Kaikkonen et al., 2009; Kuper et al., 2007; Marmot et al., 1997; Wamala et al., 1999; Wamala et al., 2000; Warren et al., 2004) with some although not all finding support for a mediating role (Kaikkonen et al., 2009; Marmot et al., 1997; Wamala et al., 1999; Wamala et al., 2000;).

Of the studies reviewed by Matthews et al. (2010), only three studies (all of which used data from the Coronary Artery Risk Development in Young Adults (CARDIA) study) have specifically examined the mediation hypothesis in African Americans. One study by Lehman et al. (2005) found that associations of childhood SES with the metabolic syndrome in adulthood were partly mediated through psychological functioning (defined as depression, hostility, and poor quality of social contacts) in African American women, but not African American men. Using the same cohort, two additional studies found that associations of low SES in childhood with inflammatory processes (Taylor et al., 2006) and blood pressure (Lehman et al., 2009) in adulthood were partly mediated through psychosocial functioning in both African American men and women. Our results are also compatible with a mediating role of stress in the association of income with diabetes in women and possibly a smaller role of stress in mediating associations with hypertension and obesity in women.

We expand prior work in mediation by using both the “naïve” approach as well as analyses that take into account the possibility of interactions between income and the mediator. We only found statistically significant mediation effects of stress (15.9%) on diabetes. Although there were small mediation effects of stress for hypertension (7.9%) and obesity (5.1%), they were not statistically significant. Stress as assessed by the GPSS was a more consistent mediator than stress assessed by the NLE. It is plausible that general measures of perceived stress (like the GPSS) are better able to capture the kinds of stressors most related to conditions like diabetes, hypertension and obesity, which may develop over long periods. Reports of negative life events (like the NLE) may not capture the stressful components of these events and the weekly stress inventory (WSI) may not have been substantially related to the outcomes because it only captures experiences only over the prior week. Unfortunately the methods we used to characterize mediation in the presence of interactions do not yet allow simultaneous examination of multiple mediators so we were not able to examine multiple measures of stress together in the mediation analyses.

Our results also indicate that a substantial amount of the association of income with hypertension, diabetes, obesity and plaque is not mediated through the stress or behavioral domains as measured in this study. Measurement error in stress and behavioral factors is likely major and could be an important contributor to our inability to detect stronger mediation effects. Both sets of factors are notoriously difficult to measure and measurement differences may lead to differences in the impact of adjusting for factors. The inclusion of a

more complete set of behavioral factors or better measured behavioral factors could also have substantially affected our results. In fact measurement problems could overwhelm the impact of omitted confounders on estimating mediation (Blakely, 2002).

Although broader than in many other studies, our measures of stress were limited and may not reflect the measures most relevant to the experiences of this population (Williams et al., 2010) or most relevant to the biological consequences of stress, which may vary depending upon the type of stress experienced, and its duration, frequency, and intensity (Cohen et al., 2007; Pickering, 1999; Steptoe & Marmot, 2002). We focused on stressors because the frequency and intensity of exposure to stress is one of the key psychosocial domains hypothesized to contribute to SES differences in health (Matthews et al., 2010). However, other work has shown that not only stress exposures but also the interpretation of ambiguous events as stressful or not, emotional responses to stressors, and the interpersonal and interpersonal resources necessary to respond to stress may also vary by SES (Matthews et al., 2010). Our analyses are simplistic in that they do not account for responses to stress, interactions between stressors, or the availability of resources to cope with stress. We also did not investigate other important psychosocial domains such as emotional factors, psychosocial resources (such as social support or social integration) or early childhood psychosocial factors (Matthews et al., 2010). This could cause us to underestimate the impact of psychosocial stress on inequalities. We did not specifically investigate experiences of discrimination as a stressor (although the GPSS captures some dimensions of discrimination), but other work in this cohort and other samples has shown that reports of discrimination are positively rather than inversely associated with SES (Borrell et al., 2006; Sims et al., 2009), making reports of discrimination an unlikely contributor to SES differences in cardiovascular risk.

Importantly, our conclusions are based on the assumption that there are no strong omitted confounders of the SEP-outcome or mediator-outcome association (Cole & Hernan, 2002; Kaufman et al., 2004; Vanderweele & Vansteelandt, 2009). The estimation of natural direct and indirect effects further assumes no confounding of the exposure –mediator relation and no confounder of the mediator –outcome relation affected by prior exposure (Imai et al., 2010; Vanderweele & Vansteelandt, 2009). Sensitivity analyses to violations of these assumptions directly linked to the approach that we used for binary outcomes are not yet available. Our estimates of the effects mediated through stress were small and often not statistically significant. The extent to which the mediation effects we observed could plausibly be explained by omitted confounders depends on the presence and prevalence of plausible confounders as well as on the directionality and strength of the omitted confounder associations. Other work has suggested that in the case of confounding of the mediator – outcomes relationship, the relationships of the omitted confounder with the mediator and the outcomes have to be large and the confounder neither rare nor ubiquitous for it to substantially affect estimates of direct and indirect effects (Blakely, 2002; Greenland, 2003). The development of practical methods to conduct sensitivity analyses is an important need in the field.

Behaviors are likely to play a complex role in the relations between income, stress and CVD risk. Behaviors may contribute to pathways linking income to CVD that are not mediated through stress, i.e., they may explain part of the large direct effect that was evident in our stress mediation analyses. In addition, they may themselves be part of the pathway through which stress exerts its mediating effect (i.e., they may themselves be part of the “indirect” effect) (Cohen et al., 2007). Finally, if behaviors also affect stress levels they may confound the associations between stress and CVD risk factors. Our general conclusions regarding the mediating role of stress were generally robust to the inclusion of behaviors in the models, perhaps because behaviors themselves (at least as measured) were not strongly associated

with the outcomes. However, we cannot fully disentangle the relations between income, stress, and behaviors using cross-sectional data. In addition, our estimates of natural direct and indirect effects will be biased if behaviors are affected by income, and in turn are causally related to stress and CVD outcomes.

A major limitation of our data in the investigation of mediation is its cross-sectional nature. Ideally one would include measures of mediators subsequent to the measures of exposure. This requires longitudinal data with time varying data on income, stress, behaviors and outcomes that few studies have. The cross-sectional nature of our analyses allows only very indirect explorations of mediating factors. Future longitudinal studies using appropriate analytical methods are needed to better understand the mediating role of stress. An additional complexity is that health behaviors and stress may affect each other; health behaviors may be one of the pathways through which individuals cope with stress and in turn certain health behaviors impact physiologic responses to stress. Both kinds of factors could also interact. These kinds of dynamic relations involving feedbacks and interactions may be difficult to investigate using standard statistical approaches, even modern methods. Other approaches that account for dynamic relations over time may be needed (Diez Roux, 2011).

Similar to findings from previous work (Boykin et al., 2011; Robbins et al., 2001-), the inverse associations of SEP with CVD risk factors in this African American sample were stronger and more consistent in women than in men. African American women in this cohort may have been especially impacted by civil rights laws (e.g., integrated racially segregated schools) and affirmative action legislation (which prohibits discrimination based on factors such as age, race, and gender) that enabled them to take advantage of expanded educational and occupational opportunities at a higher rate than African American men (Kaplan et al., 2008). These socioeconomic advancements may have allowed higher income African American women to translate their higher social standing and access to resources into improved health, thus, resulting in stronger SEP associations with CVD risk factors.

The absence of clear socioeconomic patterning in men (with the possible exception of diabetes) may reflect differential material and psychosocial consequences of greater income in African American men and African American women. The absence of clear SES gradients in cardiovascular risk factors in African American men is consistent with other work (Boykin et al., 2011; Diez Roux et al., 1997; Williams et al., 2010).

Although stressors were inversely and similarly associated with income in women and in men, they were only related to selected cardiovascular risk factors (most consistently hypertension, diabetes, and obesity) in women. Men may be more resilient to the negative effects of stress, may consider discriminatory or stress events as ‘normal’ aspects of being an African American male in the United States or may have more resources to cope with stress than women. The behavioral coping mechanisms implemented in response to stressors (e.g., stress related changes in diet, physical activity and smoking) could be different in men and in women. Stressors may also interact with other gender-patterned exposures in generating adverse cardiovascular risk profiles. Differential measurement validity in men and in women resulting in greater measurement error in men could also explain the sex differences in the associations with outcomes, although it is not consistent with the fact that stress was similarly patterned by SES in women and men.

Strengths of this study include the large African American population sample, the multiple multi-item stress measures, and the state-of-the-art measures of cardiovascular risk factors.. . The sample was not intended to be representative of all African Americans. However it is among the largest population based studies of cardiovascular disease among African

Americans in the US. Within the limitations of our study design and data, our results suggest that stressors appear to contribute to at least some of the income patterning of diabetes and to a lesser extent hypertension and obesity in African American women. This mediation effects is consistent with the fact that in our data stressors were patterned by income and were also related to very small albeit consistent increases in the prevalence of diabetes, hypertension, and obesity. Further work is needed to better understand the interacting and dynamic effects of stress and health behaviors on the cardiovascular related outcomes among populations such as African Americans exposed to high levels of stressors. Important challenges for future work include the collection of rich, time varying longitudinal data with valid and reliable measures of SEP, stressors, behaviors, and outcomes as well as the development of stress measures that validly capture the most relevant stressors in these populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research Highlights

- In African American women, higher income was associated with lower prevalence of hypertension, diabetes, obesity, and carotid plaque and with lower levels of stress.
- Higher stress levels were weakly associated with hypertension, diabetes, and obesity.
- Stressors appeared to contribute to a small proportion of the income patterning of diabetes and to a lesser extent hypertension and obesity in African American women.
- Only diabetes was associated with socioeconomic factors in men and stress did not contribute to this patterning.

Table 1

Selected characteristics of study samples, JHS 2000-2004.

	Women			Men		
Characteristics	**GPSS & NLE***	**WSI***	**JHS***	**GPSS & NLE**	**WSI**	**JHS**
*N	2541	1590	2795	1439	888	1609
Age (yrs), mean (sd)	55.06 (12.54)	53.21 (12.34)	55.13 (12.64)	53.60 (12.87)	52.22(12.62)	53.79 (12.84)
Income, %						
Low	13.93	12.33	14.74	7.64	7.32	8.27
Lower Middle	22.31	20.69	22.40	16.89	14.64	17.65
Upper Middle	25.34	27.17	25.33	26.55	28.15	26.23
Affluent	22.35	25.66	21.68	33.29	37.27	32.69
Unknown	16.06	14.15	15.85	15.64	12.61	15.16
Stress Measures						
GPSS, mean (range)	5.53 (0 - 23)	-	-	4.35 (0 - 21)	-	-
NLE, mean (range)	1.41 (0 - 7)	-	-	1.22 (0 - 6)	-	-
WSI, mean (range)		77.23 (0 - 435)	-		69.19 (0 - 476)	-
CVD Risk Factors						
Hypertension, %	63.60	59.43	63.86	58.51	55.07	59.54
Diabetes, %	18.89	16.86	19.32	16.19	14.53	16.59
Obesity, %	60.33	59.56	60.07	41.21	41.33	41.21
Carotid Plaque, %	36.21	33.40	36.60	37.18	34.35	38.60
Behaviors						
Current Smoker, %	8.70	8.99	9.19	16.40	14.08	17.03
Former Smoker, %	14.52	13.21	14.42	24.95	24.77	24.74
Never Smoker, %	76.78	77.80	76.39	58.65	61.15	58.23
Pack Years	4.54 (11.83)	4.42 (11.96)	4.75 (12.31)	10.37 (18.84)	9.47 (18.31)	11.02 (20.55)
Physical Activity Score, mean (sd)	8.21 (2.54)	8.43 (2.48)	8.19 (2.55)	8.74 (2.57)	8.94 (2.50)	8.68 (2.59)
Energy (Kcal)	1939.41 (1049.32)	1962.53 (1080.79)	1950.08 (1071.36)	2494.93 (1319.75)	2478.63 (1365.75)	2506.10 (1365.01)
Total Dietary Fiber (g)	14.67 (6.64)	14.75 (6.85)	14.73 (6.81)	18.09 (8.90)	18.11 (8.89)	18.09(9.05)
% Calories from fat (%)	35.02 (7.06)	35.20 (7.11)	35.04 (7.12)	35.04 (6.52)	35.07 (6.59)	34.99 (6.52)

	Women			Men		
Characteristics	**GPSS & NLE***	**WSI***	**JHS***	**GPSS & NLE**	**WSI**	**JHS**
% Calories from carbohydrate (%)	51.59 (9.58)	51.41 (9.63)	51.53 (9.68)	49.41 (8.96)	49.34(8.87)	49.38 (8.93)

Abbreviations: GPSS = Global perceived stress scale; NLE = Negative life events; WSI = Weekly stress inventory, JHS=Jackson Heart Study

*N (Total) = 3980 for GPSS & NL, 2478 for WSI, & 4404 for JHS. The N values for JHS refer to the whole sample of cohort excluding observations with missing covariates and the values for GPSS & NLE and WSI are given separately because of the variations in the sample size.

Table 2

Age-adjusted cardiovascular disease risk factor proportions and mean stress scores by level of income among women and men in the Jackson Heart Study, 2000-2004.

WOMEN*	Hypertension	Diabetes	Obesity	Carotid Plaque	GPSS	NLE	WSI
Low	0.72	0.22	0.61	0.41	6.54	1.64	105.46
Lower Middle	0.67	0.19	0.65	0.31	5.74	1.45	85.15
Upper Middle	0.66	0.17	0.61	0.34	5.58	1.39	69.28
High	0.58	0.13	0.55	0.30	4.68	1.23	61.59
p for the trend	0.0002	0.0003	0.0132	0.0148	<.0001	<.0001	<.0001

MEN*							
Low	0.59	0.14	0.36	0.33	5.92	1.57	111.06
Lower Middle	0.64	0.16	0.42	0.38	4.46	1.20	73.22
Upper Middle	0.62	0.18	0.38	0.36	4.36	1.25	66.68
High	0.60	0.10	0.42	0.36	3.89	1.07	59.52
p for the trend	0.5629	0.0465	0.4509	0.9909	<.0001	0.0002	<.0001

Abbreviations: GPSS = Global perceived stress scale; NLE = Negative events; WSI = Weekly stress inventory.

*N = women: 2541, men: 1439 for GPSS & NLE and women: 1590, men: 888 for WSI. The N values for GPSS & NLE and for WSI are given separately because of the variations in the sample size

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Table 3

Age-adjusted cardiovascular disease risk factor proportions by stress quartile.

	WOMEN*				MEN*			
GPSS	**Hypertension**	**Diabetes**	**Obesity**	**Carotid Plaque**	**Hypertension**	**Diabetes**	**Obesity**	**Carotid Plaque**
Q1	0.59	0.13	0.61	0.33	0.58	0.15	0.39	0.38
Q2	0.67	0.17	0.57	0.35	0.62	0.16	0.42	0.36
Q3	0.65	0.19	0.61	0.34	0.64	0.15	0.41	0.36
Q4	0.70	0.19	0.63	0.34	0.64	0.16	0.44	0.33
p for the trend	0.0049	0.0152	0.1609	0.9589	0.1608	0.7484	0.2816	0.2943

NLE								
Q1	0.61	0.15	0.60	0.33	0.60	0.15	0.36	0.36
Q2	0.68	0.17	0.58	0.36	0.61	0.14	0.43	0.35
Q3	0.64	0.18	0.59	0.33	0.64	0.18	0.48	0.39
Q4	0.70	0.20	0.68	0.31	0.61	0.16	0.37	0.37
p for the trend	0.0280	0.0471	0.0201	0.3112	0.5311	0.3246	0.0914	0.5260

WSI								
Q1	0.61	0.16	0.60	0.34	0.56	0.13	0.41	0.27
Q2	0.59	0.17	0.60	0.30	0.53	0.11	0.42	0.35
Q3	0.58	0.14	0.59	0.32	0.61	0.16	0.47	0.28
Q4	0.64	0.16	0.60	0.28	0.58	0.17	0.34	0.41
p for the trend	0.4561	0.8462	0.9380	0.1032	0.3797	0.1023	0.2707	0.0253

Abbreviations: GPSS = Global perceived stress scale; NLE = Negative life events; WSI = Weekly stress inventory.

*N = women: 2541, men: 1439 for GPSS & NLE and women: 1590, men: 888 for WSI. The N values for GPSS & NLE and for WSI are given separately because of the variations in the sample size

Table 4

Prevalence Ratio (95% CI) of cardiovascular risk factors associated with higher income*, before and after controlling for stress measures and behavioral factors in women.

	Hypertension						Diabetes					
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**	**Model 1**	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Income	0.86 (0.78,0.94)	0.87 (0.79,0.95)	0.86 (0.78,0.95)	0.87 (0.79,0.96)	0.86 (0.78,0.95)	0.88 (0.80,0.97)	0.61 (0.46,0.81)	0.63 (0.47,0.84)	0.62 (0.47,0.83)	0.63 (0.47,0.84)	0.57 (0.43,0.76)	0.60 (0.45, 0.80)
GPSS	---	1.04 (1.01,1.08)	---	1.04 (1.01,1.07)	---	1.05 (1.01,1.08)	---	1.09 (1.00,1.19)	---	1.08 (0.99,1.18)	---	1.12 (1.03, 1.23)
NLE	---	---	1.03 (1.00,1.06)	1.02 (0.99,1.05)	---	1.02 (0.99,1.05)	---	---	1.06 (0.98,1.15)	1.04 (0.96,1.14)	---	1.05 (0.96, 1.14)

	Obesity						Plaque					
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**	**Model 1**	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Income	0.85 (0.77,0.94)	0.86 (0.77,0.95)	0.86 (0.78,0.95)	0.86 (0.78,0.95)	0.85 (0.77,0.94)	0.87 (0.78,0.96)	0.84 (0.71,0.99)	0.84 (0.71,0.99)	84 (0.71,0.99)	0.84 (0.71,0.99)	0.89 (0.75, 1.05)	0.88 (0.75, 1.04)
GPSS	---	1.03 (1.00,1.07)	---	1.02 (0.99,1.06)	---	1.03 (1.00,1.07)	---	1.00 (0.94,1.07)	---	1.01 (0.95,1.07)	---	1.00 (0.93, 1.06)
NLE	---	---	1.04 (1.01,1.08)	1.04 (1.01,1.07)	---	1.04 (1.00,1.07)	---	---	0.99 (0.93,1.05)	0.99 (0.93,1.04)	---	0.98 (0.93, 1.04)

Abbreviations: GPSS = Global perceived stress scale; NLE = Negative life events; CVD=Cardiovascular disease.

CVD risk factors (binary outcome), Income and GPSS & (continuous, GPSS in 4.38 values of SD and NLE in 1.21 values of SD).

Model 1: Age + Income; Model 2: Age + Income + GPSS; Model 3: Age + Income + NLE; Model 4: Age + Income + GPSS + NLE; Model 5: Age + Income + Behaviors; Model 6: Age + Income + GPSS + NLE + Behaviors.

*Associations shown correspond to an income difference equivalent to moving from the 10^{th} to the 90^{th} percentile of the observed income distribution in the sample.

Table 5

Prevalence ratio (95% CI) of diabetes associated with higher income*, before and after controlling for stress measures and behavioral factors in men.

	Diabetes					
	Model 1	**Model 2**	**Model 3**	**Model 4**	**Model 5**	**Model 6**
Income	0.59 (0.42,0.84)	0.59 (0.42,0.84)	0.59 (0.42,0.84)	0.59 (0.42,0.84)	0.56 (0.39,0.80)	0.56 (0.39,0.80)
GPSS	---	0.99 (0.86,1.15)	---	0.99 (0.86,1.15)	---	0.99 (0.85,1.16)
NLE	---	---	1.01 (0.88,1.16)	1.01 (0.88,1.12)	---	1.01 (0.88,1.17)

Abbreviations: GPSS = Global perceived stress scale; NLE = Negative life events; CVD=Cardiovascular disease.

CVD risk factors (binary outcome), and GPSS & NLE (continuous, GPSS in 4.38 values of SD and NLE in 1.21 values of SD).

Model 1: Age + Income; Model 2: Age + Income + GPSS; Model 3: Age + Income + NLE; Model 4: Age + Income + GPSS + NLE; Model 5: Age + Income + Behaviors; Model 6: Age + Income + GPSS + NLE + Behaviors.

*Associations shown correspond to an income difference equivalent to moving from the 10^{th} to the 90^{th} percentile of the observed income distribution in the sample

Table 6

Estimates of direct and indirect effects of income and the proportion of the effects of income on cardiovascular risk factors that is mediated through stress measures with and without adjustment for health behaviors in women.

	GPSS stress mediator							NLE stress mediator						
	Natural Direct Effect		Natural Indirect Effect		Total Effect		Proportion Mediated Through GPSS Stress	Natural Direct Effect		Natural Indirect Effect		Total Effect		Proportion Mediated Through NLE Stress
CVD risk factors	PR_{NDE}	95%CI	PR_{NIE}	95% CI	PR_{TE}	95%CI	%	PR_{NDE}	95%CI	PR_{NIE}	95% CI	PR_{TE}	95%CI	%
Hypertension														
Model 1	0.87	0.74, 1.01	0.99	0.97, 1.00	0.86	0.73, 1.00	7.9	0.86	0.74, 1.01	0.99	0.98,1.01	0.86	0.73, 1.00	4.1
Model 2	0.87	0.75, 1.02	0.98	0.97, 1.00	0.86	0.74, 1.01	9.8	0.87	0.74, 1.01	0.99	0.98,1.01	0.86	0.74, 1.01	3.7
†Diabetes														
Model 1	0.68	0.49, 0.95	0.91	0.84, 0.99	0.62	0.45, 0.85	15.9	0.62	0.46, 0.84	0.99	0.96, 1.01	0.61	0.45, 0.83	2.3
Model 2	0.64	0.46, 0.91	0.91	0.83, 0.99	0.58	0.42, 0.81	14.5	0.58	0.42, 0.80	0.99	0.96, 1.01	0.57	0.42, 0.79	2.0
†Obesity														
Model 1	0.86	0.73, 1.00	0.99	0.97, 1.01	0.85	0.73, 0.99	5.1	0.85	0.73, 0.99	1.01	0.98, 1.04	0.85	0.73, 0.99	-3.3
Model 2	0.86	0.74, 1.01	0.99	0.97, 1.01	0.85	0.73, 1.00	7.1	0.85	0.72, 0.99	1.00	0.98, 1.03	0.85	0.73, 0.99	-2.8
Plaque														
Model 1	0.84	0.68, 1.04	1.00	0.98, 1.02	0.84	0.68, 1.03	0.7	0.84	0.68, 1.03	1.00	0.99, 1.02	0.84	0.68, 1.03	-1.7
Model 2	0.89	0.71, 1.10	1.00	0.98, 1.03	0.89	0.72, 1.10	-1.8	0.88	0.71, 1.09	1.00	0.99, 1.02	0.89	0.72, 1.10	-2.9

Abbreviations: GPSS = Global perceived stress scale; NLE = Negative life events; CVD=Cardiovascular disease; PR=Prevalence Ratios; NDE=Natural direct effect; NIE= Natural indirect effect; TE=Total effect.

CVD risk factors (binary outcome), Income (difference between the 10th and the 90th percentile), and GPSS & NLE (continuous, GPSS in 4.38 values of SD and NLE in 1.21 values of SD).

Model 1: Age + Income + Stress (GPSS or NLE); Model 2: Age + Income + Stress (GPSS or NLE) + Behaviors.

†Interaction between income and GPSS and between income and NLE were included for diabetes and obesity outcomes, respectively.